UC DAVIS
BIOLOGICAL SCIENCES
NEWS FROM THE DIVISION OF BIOLOGICAL SCIENCES VOL.7 NO.4

UC DAVIS TO HOST UC LIFE SCIENCES INFORMATICS PROGRAM

The University of California is establishing a new matching-grant program in life sciences informatics in which UC and California businesses will jointly invest in research and training in this computer-based field.

The UC Office of the President has selected UC Davis to host the universitywide Life Sciences Informatics Program. The president's office is currently finalizing a memorandum of understanding with UC Davis that outlines the campus's role in administering the program. UC has earmarked $6 million for the program in the first two years.

Jim von Rummelhoff

The demand for training in informatics has grown considerably in recent years. A summer course in bioinformatics, taught at UC Davis by Tom Slezak (left) of the Lawrence Livermore National Laboratory, was filled to capacity.

The Life Sciences Informatics Program will support research in UC laboratories on methods to organize, analyze, and integrate the enormous data sets and databases that are being generated in the biological, environmental, and health sciences.

The new program is one of several Industry-University Cooperative Research Programs created by UC that partners university scientists with companies in areas of research that offer opportunities for economic expansion in high-technology industrial sectors in California.

Martina McGloughlin, director of the UC Davis Biotechnology Program, will also direct the Life Sciences Informatics Program. "UC has a long tradition of research excellence in all areas of the

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LAGARIAS APPOINTED TO STUMPF PROFESSORSHIP

Internationally known for his contributions to the study of plant photoreceptors, Professor J. Clark Lagarias of the Section of Molecular and Cellular Biology is the first faculty appointee to the Paul K. and Ruth R. Stumpf Professorship in Plant Biochemistry. The endowed professorship, which began in July and continues through June 2004, will help support his teaching and research program.

Lagarias made his first contribution to the field of photoreceptor biochemistry as a graduate student at UC Berkeley. He determined the structure of phytochromobilin, the light-absorbing portion, or chromophore, of the photoreceptor phytochrome. Phytochrome functions as a photodetector that tells a plant whether light is present and enables it to adapt to changes in light conditions.

In 1980 Lagarias joined the UC Davis faculty as an assistant professor in the Department of Biochemistry and Biophysics. Early in his academic career, he developed a purification method for isolating intact phytochrome molecules that facilitated research in many laboratories. He went on to study the molecular forms of phytochrome and the biosynthesis of its chromophore.

Lagarias' laboratory has been a leader in research on the assembly of phytochrome. Perhaps most significant is his laboratory's recent discovery that phytochrome is a light-regulated enzyme. This work has been a major breakthrough in understanding

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Chinese Connection

A UC Davis contingent that included Martina McGloughlin, director of the campus's Biotechnology Program and UC Life Sciences Informatics Program, traveled to China in July to establish formal ties between the campus and six Chinese universities. McGloughlin and UC Davis Professors Gary Anderson from animal science and Shu Geng from agronomy and range science met with university affiliates at the lead Chinese institution, Northwestern Agricultural University, located in Yang Ling. McGloughlin signed a memorandum of understanding on behalf of Davis' Chancellor Larry Vanderhoef that will bring postdoctoral scientists and graduate students from the Chinese universities to UC Davis for training in agricultural biotechnology.

Jackson Laboratory West

The Jackson Laboratory, a nonprofit institute in Maine that rears and sells the world's greatest variety of genetically altered mice for scientific research, is collaborating with UC Davis to establish a West Coast center on the campus. The center, "JAX Research Systems at UC Davis," will house mice genetically designed for susceptibility to many diseases. In exchange for providing space to the Jackson Laboratory, UC Davis will benefit from the lab's expertise in breeding and rearing the high-maintenance mice. JAX president Warren Cook and Center for Comparative Medicine director Stephen Barthold predict the partnership will lead to collaborative research on how genes help resist infectious diseases. The Jackson Laboratory's UC Davis location will also make genetically customized mice more easily available to researchers across the western U.S.

...Informatics Program

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life sciences and has been very active in forging partnerships with industry," she says. "We enthusiastically welcome the opportunity to support new partnerships that focus on the critical area of informatics."

Researchers increasingly rely on computers to manage and analyze the flood of new data in the life sciences. For example, environmental scientists are creating and using extensive databases to monitor the status of natural resources, such as rivers and lakes. Neuroscientists are linking data sets on brain anatomy and chemistry to study phenomena such as the movement disorder associated with Parkinson's disease.

Massive amounts of data are being generated in efforts to determine the entire DNA sequence, or genome, of an organism. The federally funded Human Genome Project will produce sequence data for the three billion chemical bases that make up human DNA.

In each case, the data must be stored and organized so that it can be easily accessed, and software must be developed to interpret it. Also needed are computer-based tools to integrate databases with disparate information.

The multi-million dollar program will award grants for one- or two-year periods for research projects that focus on the development of these tools. Each project must carry a commitment from a private sponsor in California to provide funding that at least matches the funding awarded by the program.

"An emphasis will be placed on projects that provide opportunities to train graduate students and postdoctorates," says McGloughlin. "This will enable young scientists to get the research experience they need to seek future careers in industry."

The Life Sciences Informatics Program will be located at UC Davis in the Division of Biological Sciences dean's office, adjacent to the campus's Biotechnology Program.

Research News

A Mouse Is Not A Mouse

Laboratory mice vary greatly from strain to strain in their sensitivity to the hormone estrogen, according to a report in the August 20 issue of the journal *Science* by research geneticist Jimmy Spearow and Associate Professor Marylynn Barkley of the Section of Neurobiology, Physiology, and Behavior, and Division of Biological Sciences' undergraduates Paul Doemeny, Robyn Sera, and Rachael Leffler.

The researchers found that when genetically different strains of young male mice are implanted with estrogen, the hormone significantly reduces testis weight and sperm production in some strains but produces little change in the CD-1 strain, which is widely used for animal testing.

Their findings suggest that current laboratory-animal-based tests of estrogen and estrogen-like chemicals greatly underestimate the risk for estrogen-sensitive individuals.

"Considering these genetic variations in the estrogen sensitivity of an individual or species will be important not only when testing for endocrine-disrupting properties in industrial chemicals and pesticides, but also when determining therapeutic doses of estrogen and related steroid compounds in human medicine," Spearow and Barkley emphasize.

Estrogen is a naturally occurring hormone mimicked by other chemicals dubbed "endocrine disruptors" because they appear to hinder reproduction in fish, wildlife, and other mammals by interfering with the normal function of the endocrine system. Such chemicals are found in certain pesticides, plastics, detergents, and estrogens derived from plants.

The U.S. Environmental Protection Agency is preparing to screen thousands of pesticides and industrial chemicals for several endocrine-disrupting effects. Previous studies have indicated that estrogen-like endocrine disruptors found in the environment can cause decreased

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...Lagarias

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light-sensing signal transduction pathways in plants.

Lagarias has also shown that the light-absorbing chromophore of phytochrome, phytochromobilin, can be substituted with other chromophores (phycocyanobilin or phycoerythrobilin). The resulting molecules, or adducts, are intensely fluorescent, photostable, and chemically stable and can be reconstituted in living cells. His laboratory is currently exploring the use of these adducts, named "phytofluors," *in vivo* as fluorescent probes.

Professor Emeritus Paul Stumpf and his wife, Ruth, established the endowed professorship in recognition of Paul Stumpf's deep ties to the University of California and his five-decade academic career in plant biochemistry.

Jim von Rummelhoff

Research by plant biochemist Clark Lagarias has contributed substantially to our understanding of how plants respond to light.

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sperm counts, deformed genitals, aberrant mating behavior, and sterility in wildlife.

Spearow contends that the issue of genetic variation in susceptibility to endocrine disruption should not be ignored by the Environmental Protection Agency in its testing of thousands of chemicals for this activity.

Reference: Spearow JL, P Doemeny, R Sera, R Leffler, and M Barkley. 1999. *Science* 285: 1259-1261.

Where are they now? Undergraduate researcher **Paul Doemeny**, B.S., Biochemistry, 1998, is now a medical student at Georgetown Medical School in Washington, D.C. **Robyn Sera**, B.S., Biological Sciences, 1998, was accepted to medical school but deferred entry to work in a new women's clinic in San Francisco, Calif., through the Americorps program. **Rachael Leffler**, B.S., Biological Sciences, 1997, is employed at Genentech in South San Francisco, Calif.

Jim von Rummelhoff

Researchers Jimmy Spearow (left) and Marylynn Barkley (right) have observed major genetic differences in sensitivity to the disruption of reproductive development and sperm formation in young male mice.

Viral Protein Structure First Of Its Kind

Programmed cell death, or apoptosis, is often likened to cellular suicide and can be a defensive response to viral invasions. By dying, infected cells prevent a virus from spreading. However, some viruses cleverly produce proteins that inhibit apoptosis.

X-ray crystallographer Andy Fisher's laboratory is the first to have determined the three-dimensional structure of one of these anti-apoptic viral proteins, baculovirus P35. "It's a significant structure because, in terms of P35's

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News Briefs

Junior College Partnership

A National Institutes of Health grant has enabled Modesto Junior College, Modesto, Calif., and the Division of Biological Sciences to create a program that will prepare underrepresented students attending the junior college for transfer to UC Davis and, ultimately, biomedical research careers. The new program, named "Bridges," targets chemistry and biology majors at the junior college and has a number of components including intensive tutoring in math and chemistry, seminars, and mentoring by both campus's faculty members. Mark Sanders, Section of Molecular and Cellular Biology lecturer, and Lance Thompson of Modesto Junior College are the UC Davis and Modesto Junior College project coordinators, respectively. Bridges project directors are **Pam Upton,** B.A., Biological Sciences, 1975, for Modesto and Thomas Rost, associate dean in the Division of Biological Sciences at UC Davis.

Send Us A Postcard

We invite you to send us an Internet postcard. On the Web go to http://www.dbs.ucdavis.edu/alumni/postcards/, our new alumni site. Let us and other alumni know where you are and what you're doing. We hope to hear from you!

FEATURE

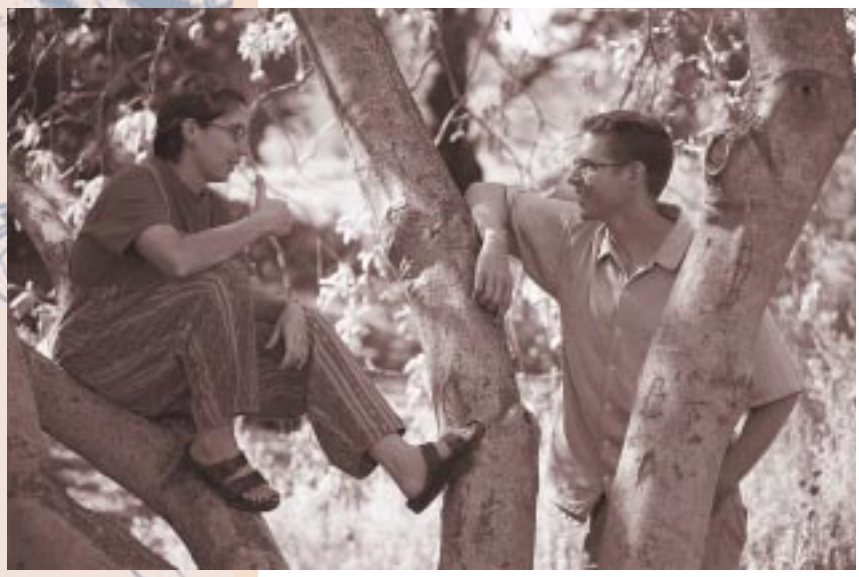
Students Review Endangered Species Recovery Plans

BY PHILLIP VAN MANTGEM, CHRISTY BRIGHAM, AND JOEL PAGEL*, STUDENTS IN THE GRADUATE GROUP IN ECOLOGY

The federal Endangered Species Act mandates that species recovery plans incorporate the best available scientific and commercial information regarding the current condition of threatened and endangered species, and establish conservation goals that private and public parties can use. Recently, however, recovery plans have been criticized because they often lack critical biological and ecological information (Tear et al. 1993, Clark 1997).

This past winter quarter, approximately 30 UC Davis graduate students and professors, led by Mark Schwartz, assistant professor of environmental science and policy, and member of the Center for Population Biology, participated in a national effort to critique recovery plans for threatened and endangered species. Twenty universities are involved in this national project.

Participants in the seminar, supported by the Society for Conservation Biology, U.S. Fish and Wildlife Service, and National Center for Ecological Analysis and Synthesis, evaluated endangered species recovery plans using a standardized questionnaire.This method allowed us to summarize critical aspects of the recovery plans by answering *yes/no* and multiple choice questions. Our data will be combined with results from 19 other universities participating in the study.



Jim von Rummelhoff

Ecology graduate students and authors Christy Brigham (left) and Phillip van Mantgem took part in a graduate seminar that analyzed endangered species recovery plans. (Author Joel Pagel is not pictured.)

Recovery plans primarily high quality

For each recovery plan, we answered more than 2,000 questions on areas such as threats, basic biology, recovery actions, costs of different actions, parties responsible for implementation, and current state of the species. This data may be used to answer questions concerning recovery plans such as: What are the recovery criteria for species? What actions are required to recover species? What are the threats that led to the species being listed? It is hoped that answering these and other questions will help us evaluate recovery plans and determine how we as university scientists might improve either the recovery planning process or other aspects of endangered species management.

Wyoming Game and Fish

The black-footed ferret is endangered because of habitat loss. Recovery plans for "charismatic" mammals such as the black-footed ferret tend to receive more funding.

Our impressions after reviewing the recovery plans were that they were generally of high quality. Most plans contained a careful attempt to document the threats posed to each species and developed a step-by-step outline to protect and manage the existing populations.

Short-term vs. long-term recovery strategies

It is clear, however, that major gaps exist in our knowledge of the basic biology of most endangered species (e.g., reproductive rates, geographic distribution, etc.), but the lack of this information may not hinder our ability to immediately protect these species.

For example, in a recovery plan for a group of 66 Hawaiian plants, it was apparent that almost nothing was known about the species' biology beyond location and current population sizes. However, the threats to these species were abundantly clear (in this case destruction by feral

pigs and competition by non-native weedy plants). Detailed biological knowledge isn't needed to understand these primary threats. Likewise, the recovery steps outlined in the plan called for straightforward interventions such as the construction of fences around known populations to keep out pigs and the removal of exotic plants. While these actions are short-term solutions, these steps prevent the immediate

Gerald D. Carr

Endangered species recovery plans may lack biological and ecological data critical to long-term conservation of endangered species such as the Hawaiian red-flowered geranium (above). But, as the article's authors point out, sometimes this information isn't needed for short-term solutions.

extinction of the species. More detailed biological information may be required to create self-perpetuating populations, but recovery plans must address short-term threats first.

Lack of funding constrains recovery plans

Probably the greatest threat to species survival is not lack of scientific knowledge, but lack of funding for relatively simple recovery actions. Each plan we reviewed contained cost projections to carry out recovery actions, but these budgets were almost never funded to levels that would ensure species recovery. Notable exceptions include recovery plans for the large, charismatic vertebrates (e.g., black-footed ferret and coho salmon). It seems we know what needs to be done, but lack the political will to see that these actions are carried out.

During the process of data collection, we realized the questionnaire was unable to address important qualitative questions regarding recovery plans. These include whether recovery goals are appropriate, or how recovery efforts are affected by federal agency actions, which may be contrary to species recovery.

A more synthetic view

A spring-quarter seminar therefore evolved from our concern about the questionnaire's focus on recovery plans and lack of subjective questions about recovery planning and endangered species management. For this second seminar, Mark Schwartz met with professors and students to write a survey that would create a more synthetic view of issues in endangered species management.

Another reason for the spring-quarter seminar emerged from winter-quarter participants' responses when asked, What is the most important step in endangered species management? The varied answers included getting a species on the endangered species list, writing the recovery plan, and implementing the recovery plan. The spring-quarter group therefore wanted the survey to be one they could give to both academics and agency personnel to assess their views on endangered species management. Consequently, the survey written by the spring-quarter group addresses what constitutes recovery and the role of recovery plans in endangered species management. The completed survey is currently being revised prior to being sent out.

Students from both seminars are looking forward to learning more about endangered species management through responses to the survey.

Clark, T.W. 1996. Appraising threatened species recovery efforts: Practical recommendations. S. Stephens and S. Maxwell (eds). Back from the brink: refining the threatened species recovery process. Surrey Beatty and Sons, Pty Ltd, New South Wales.

Tear, T.M., J.M.Scott, P.H. Hayward, and B.Griffith. 1995. Recovery plans and the endangered species act: are criticisms supported by data? *Conserv. Biol.* 9:182-195.

*Authors' note: Author order decided by game of "rock, paper, scissors."

For the past 25 years in the United States, the Endangered Species Act (ESA 1973 et seq.) has served as the legal mechanism to guide conservation efforts that prevent extinction of wild plants and animals. The ESA prevents private and public entities from killing or harming species (or habitat upon which they depend) designated by the federal government as "endangered" or "threatened" with imminent extinction. The law also directs the U.S. Department of Interior Fish and Wildlife Service and the U.S. Department of Commerce National Marine Fisheries Service to develop documents that guide conservation efforts to protect and ultimately "recover" listed species to population levels for which human assistance is no longer necessary.

People

Alumni

Clifford Siegfried, B.S., Zoology, 1969; Ph.D., Ecology, 1974, is assistant commissioner for museums and director of the New York State Museum, Albany, N.Y., a program of the New York State Education Department. "As a research scientist," says Siegfried, "I consider it an honor to lead the New York State Museum. The museum informs the public about New York and the world through more than 4.5 acres of permanent and temporary exhibits; its collections currently comprise more than 6 million specimens and artifacts. I'm now guiding a $15 million project to re-house and inventory the collections—this project includes the development of electronic database and digital image libraries to make information about the collections accessible at our Web site. We've nearly completed the master planning phase of a project to renovate our exhibit halls, which will incorporate new technology and interactives to bring New York stories alive for our visitors.

"I recently assisted with developing legislation that created the New York State Museum's Biodiversity Research Institute (BRI), a cooperative program between the museum and other agencies and conservation organizations in New York. I now serve as head of the interim scientific working group guiding operations of the Institute."

Michael Felder's, Ph.D., Genetics, 1970, major professor at Davis was Professor G. Ledyard Stebbins. "The world leader in plant evolutionary genetics," says Felder. In January 1972 Felder joined the Department of Biological Sciences, University of South Carolina, Columbia, S.C., where he teaches undergraduate genetics, introductory biology, and a graduate course on gene structure and function. His laboratory studies the regulation of genes involved in alcohol metabolism.

Felder also mentions that "Jim Price and Ann Bowling (née Trommerhausen) were good friends and labmates in Dr. Stebbins' lab. Jim is now a highly regarded professor at Texas A&M, and Ann is a renowned expert in horse genetics in Davis' veterinary school. In thinking about my stay at Davis, I must say that it was a tremendous experience; I can't think of anything that would have made it better. UC Davis is a world class institution, and I'm lucky I spent time there. The thing I remember most about the faculty at Davis was the casual and open atmosphere. Yet, all were devoted to both research and teaching."

A native of Oakland, Calif., **Mark Grathwohl**, B.S., Biological Sciences, 1975, is a physician with the Department of Pathology Laboratory, New York United Hospital Medical Center, Port Chester, N.Y. He received his medical degree from New York University and was trained in pathology at the Medical College of Virginia, Richmond, and UC Davis. He also trained in forensic pathology/legal medicine at the Medical College of Virginia and Virginia State Medical Examiner's Office. His research interests and expertise include general and clinical pathology, surgical pathology, hematopathology, and forensic pathology.

Elizabeth A. Caplener, B.A., Biological Sciences, 1992, wrote to tell us that in 1996 she received a Doctor of Pharmacy degree from University of the Pacific, Stockton, Calif. In 1996-1997 she completed a general practice pharmacy residency at David Grant Medical Center, Travis Air Force Base, Fairfield, Calif. In 1997 she commissioned as a captain in the U.S. Air Force and was stationed at the David Grant Medical Center. Caplener says, "I am currently the ambulatory care clinical pharmacist responsible for the following clinics: Coumadin Clinic, Asthma Education Clinic, and Medication Adherence Consultations. In addition, I have been a student preceptor for the University of Pacific School of Pharmacy's third-year students. At one time I thought I was going to teach high school biology, and now I have my chance to teach, which I very much enjoy!

"From June 21 to September 30, 1999, I was in Port-Au-Prince, Haiti, having been assigned to a 90-day deployment to support the 60th Air Transportable Hospital and weekly humanitarian assistance missions to the Haitians. In addition to supporting the healthcare of U.S. Armed Forces, U.N. personnel, and U.S. Embassy personnel in Haiti, our contingent has helped over 15,500 Haitians."

Originally from Mumbai, India, **Aparna Telang**, B.S., Zoology, 1988, has resided in the U.S. for most of her life. She says, "In addition to my formal education at Davis, I also interned at the Sacramento Zoo and Rockefeller University, New York City, during two separate summers, as well as volunteering at the UC Davis Raptor Rehabilitation Center during several terms.

"After graduating from UC Davis, I took some time off from school and traveled for three months through India, Nepal, and Spain. I then worked in the biotechnology industry for several years as a research associate, primarily in the areas of cell biology and protein chemistry. I realized Ph.D.s are having all the fun, so I entered graduate school and obtained an M.S. degree from California State University, Hayward, in biological science in 1995. My research adviser and master's degree mentor, Dr. Susan B. Opp, got me hooked on insect biology, and I am now continuing my entomological studies at the University of Arizona's Interdisciplinary Program in Insect Science, where I am currently working toward my doctoral degree. My current research, within the area of insect-plant interactions, focuses on the nutritional ecology of caterpillars at the level of both feeding behavior and post-ingestive physiology."

After graduation **Erica Wagner**, B.S., Biological Sciences, 1995, served an internship at the National Aeronautics and Space Administration (NASA) Ames Research Center, Moffett Field, Calif.

Following her internship, Wagner joined Lockheed Martin as an experiment support scientist in the Life Sciences Division of the Flight Payload Integration department. Wagner relates, "An experiment support scientist works collaboratively with research teams and NASA to translate science requirements into requirements for shuttle flights. I worked with research teams in the United States, France, and Japan—my experience with international teams was wonderful. In April of 1998, our payload, known as Neurolab, was launched into orbit. Watching the shuttle soar into the sky overhead, carrying experiments I had helped coordinate was amazing." Wagner recently received a promotion within Lockheed Martin and now works with the NASA chief veterinary officer developing animal welfare policies for the International Space Station.

Lance Larka, B.S., Genetics, 1995, is a research scientist at Operon Technologies, Alameda, Calif. He specializes in high-density DNA microarrays, liquid handling robotics, and bioinformatics. Prior to working at Operon, Lance was

instrumental in establishing a core sequencing facility to serve the Triticeae family of plants (wheat, oat, barley) with the U.S. Department of Agriculture in conjunction with the Genetic Resource Conservation Program at UC Davis. He also reviews entertainment software for the monthly publication "Computer Gaming World," is a contributing scientific writer for Alkami Biosystems, and is a consultant for high-throughput sequencing facilities around the globe. While a student at Davis, Lance played the sousaphone with the Cal Aggie Marching Band-uh! and he's now a member of the executive board of its alumni chapter. You can still find him marching, yelling, and playing at Homecoming, Break the Record Night, Picnic Day and at "as many other events as possible."

Students

Three evolution and ecology graduate students, **Tag Engstrom**, **Daniel Bolnick**, and **Grant Yamashita**, received research awards funded by The Daphne and Ted Pengelley Endowment for Research in Evolutionary Biology, which Professor Emeritus Ted Pengelley established in 1997 to honor his late wife. The endowment supports graduate research in the campus's Center for Population Biology. Bolnick will be using live samples of cichlids collected from crater lakes in Cameroon, Africa, to study the nature of sexual selection, mate choice, and reproductive compatibility between related species. Yamashita is in the initial stages of exploring chromosome diminution, a developmental phenomenon some species undergo in which fragmentation and elimination of chromosome regions occurs during early embryogenesis. Tag Engstrom focuses on the broad-scale patterns of genetic diversity in South American freshwater turtles.

Faculty

Section of Molecular and Cellular Biology Professor **Marilyn Etzler**, a 1962 graduate of Otterbein College, Westerville, Ohio, was honored with the Otterbein College National Alumni Association's Distinguished Alumna Award. Etzler is internationally renowned for her research on a class of plant proteins, lectins, that have broad biomedical applications and are distinguished by their ability to bind to specific carbohydrates. She joined the UC Davis faculty in 1969.

New Faculty

Sean Burgess joined the Section of Molecular and Cellular Biology as an

assistant professor in July. Her laboratory uses the yeast *Saccharomyces cerevisiae* to explore the mechanisms underlying recognition and pairing of homologous chromosomes during meiosis and in somatic cells, as well as how homolog pairing influences chromosome segregation in meiosis, gene expression, and the repair of damaged DNA. In addition, her laboratory is interested in the interplay between the cell cycle and chromosomal organization and function. Burgess received her Ph.D. in genetics from UC San Francisco in 1993. Prior to coming to UC Davis, she was a postdoctoral research fellow in molecular, cellular, and developmental biology at Harvard University, Cambridge, Mass.

Kenneth Kaplan, a new assistant professor in the Section of Molecular and Cellular Biology, studies the process of chromosome segregation in eukaryotes. His laboratory uses mam-

malian cells and the yeast *Saccharomyces cerevisiae* as models for analyzing the genetic, biochemical, and molecular characteristics of the kinetochore, a DNA-protein complex that selectively forms on centromeric DNA and is critical for the successful segregation of chromosomes during mitosis. He graduated with a Ph.D. in immunology from UC San Francisco in 1994. He then went to the Massachusetts Institute of Technology as a postdoctoral fellow.

Edward Powers, new assistant professor in the Section of Molecular and Cellular Biology, studies nutrient sensing and the control of cell growth in the yeast, *Saccharomyces cerevisiae*, with emphasis on the target of rapamycin transduction (TOR) pathway. Powers received his Ph.D. in biology from UC Santa Cruz, in 1992. From 1993 until he joined the UC Davis faculty in July, Powers was a postdoctoral fellow in Peter Walter's laboratory at UC San Francisco.

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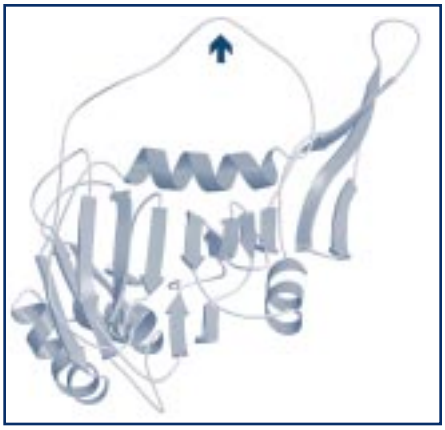
function, it's the first of its kind," says Fisher, who is an assistant professor in chemistry, and molecular and cellular biology working in the W.M. Keck Center for Structural Biology.

P35 inhibits a family of enzymes, caspases, that are critical for effecting programmed cell death. Once activated, the "death caspases" slice up proteins essential for a cell's survival, thus killing the cell.

A unique and remarkable attribute of P35 is its universal effect on caspases. Fisher explains, "The caspases are grouped into three families and P35 inhibits all of them as well as caspases from diverse organisms—from humans to insects. It's novel in that respect."

Now that the Fisher lab has determined P35's structure, it's investigating the molecular mechanism by which the protein inhibits death caspases. Fisher remarks, "The P35 system of inhibition is one of 'bait and trap.' Having a three-dimensional model of P35, we understand the bait. How it inhibits the caspases is the trap—that's what we're working on."



The striking feature of the anti-apoptic P35's structure is a large loop extending from the protein's body, designated the "reactive site loop" (arrow), which recognizes and cleaves "death caspases."

Once the trapping mechanism is understood, the door is opened for designing P35 molecules to use in anti-caspase therapies that could prevent the excessive cell death associated with diseases such as Alzheimer's, Parkinson's, Huntington's, and amyotrophic lateral sclerosis (Lou Gehrig's disease).

Reference: Fisher AJ, WD Cruz, SJ Zoog, CL Schneider, and PD Friesen. 1999. *The EMBO Journal* 18:2031-2039.

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