DEPARTMENT OF GENETICS, DEVELOPMENT AND CELL BIOLOGY

GDCB

IOWA STATE UNIVERSITY

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Alumnus: Lauro F. Cavazos

Lauro Cavazos' first day at Iowa State University was memorable.

And his most recent visit to campus this past April was just as memorable, although probably a little more comfortable.

"I came here from Texas to work under **Robert Melampy**, an internationally known physiologist in the Department of Zoology and Entomology," says Cavazos, who completed his PhD in physiology in 1954. "I showed up at Dr. Melampy's lab with my bag still in hand. I wasn't here 10 minutes, and he had me go to a seminar saying he wanted me to get off on the right foot," Cavazos recalls. "I spent my first night in Ames on a couch because I didn't even have time to find a place to live." That first night notwithstanding, Cavazos says his days at Iowa State gave him the confidence to succeed after graduation.

"Iowa State prepared me for a life of research and a life of teaching in the field of education," Cavazos explains. A recognized expert in several medical disciplines, he has been published widely in the physiology of reproduction, fine structure of cells and tissues, and medical education.

As significant as those contributions are, Cavazos' most important and lasting national impact has been in educational leadership. He served as a faculty member and administrator at the Medical College of Virginia and the Tufts University School of Medicine in Boston, where he was appointed dean in 1975. In 1980, Cavazos was appointed the 10th president of Texas Tech University, the school where he had earned his bachelor's and master's degrees in zoology.

When President Ronald Reagan nominated Cavazos for the position of U.S. Secretary of Education in 1988, he became the first Hispanic and the first Iowa State graduate to hold the nation's top education post. As secretary in the Reagan and the first Bush administrations, Cavazos concentrated on reforming U.S. education by raising expectations of students, teachers, and parents. He was a strong advocate of parental involvement in education, launched new programs to combat drug and alcohol use, and targeted federal resources to improve conditions and opportunities for the most needy school districts.

Cavazos has received numerous recognitions, including 22 honorary degrees and the "Most Influential Hispanic in the United States." During his recent trip back to Iowa State, Cavazos was honored yet again. This time his alma mater recognized him with the Iowa State Alumni Association's Distinguished Achievement Award, given in recognition of outstanding leadership in education and service to the youth of America.

> ""IOWA STATE PREPARED ME FOR A LIFE OF RESEARCH AND A LIFE OF TEACHING IN THE FIELD OF EDUCATION."
> — CAVAZOS

"I'm deeply touched and honored to be recognized in this way," Cavazos told the audience at the Distinguished Awards Celebration. "This is one of the great institutions in the nation."

During his visit, Cavazos was treated to presentations from some GDCB faculty about their exciting research programs in the biomedical field, as well as to some related hands-on research demonstrations in the Roy J. Carver Laboratory for Ultrahigh Resolution Biological Microscopy.

Currently a professor of family medicine and community health at Tufts University, Cavazos continues to work to expand opportunities for minority students in medical education.

Message from the department chair


MARTIN **SPALDING**

Dear Alumni and Friends,

Greetings from Iowa State and GDCB! We've had an exciting year as we've continued to enhance the framework of our new department. In last year's inaugural newsletter, we explained that the purpose of reorganizing the biological sciences at Iowa State was to strengthen undergraduate and graduate education and research. By bridging traditional subject and college boundaries, we promote interactions among faculty who study similar problems in different organisms, and we've expanded the educational and research opportunities for students.

In this newsletter, you'll learn about our interdepartmental undergraduate majors—Genetics and Biology (page 8). These majors provide students with tremendous opportunities to explore all aspects of their respective fields and then specialize in a specific area. Another article focuses on the Roy J. Carver Laboratory for Ultrahigh Resolution Biological Microscopy (page 3). State-of-the-art imaging tools help make this lab special, but more importantly, the lab facilitates interactions and collaborations between researchers in the physical and the life sciences.

You can also learn about the work of three of our GDCB faculty—Jeffrey Essner, Drena Dobbs, and Erik Vollbrecht. It's the dedication and enthusiasm of our faculty, students, and alumni that make our future so promising.

I'd be delighted to receive news about you and learn what you'd like to know about the department. Please feel free to call (515 294-1749) or e-mail me (mspalding@iastate.edu).

Sincerely,

Martin Spalding
Chair, Department of Genetics, Development and Cell Biology
mspalding@iastate.edu
515 294-1749

GDCB Undergraduate Scholarship Funds

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Please return to: The Iowa State University Foundation, 2505 Elwood, Ames, Iowa 50010-7164

Lab offers novel kind of workspace

Ask Bob Doyle about the Roy J. Carver Laboratory for Ultrahigh Resolution Biological Microscopy, and you'll learn about cross-fertilization. Of scientists, that is. Located in the basement of the Molecular Biology Building, the lab was conceived and built specifically as a place for physical and life scientists to work side by side.

"Before, when we had informal collaborations between an analytical chemist and a neurobiologist, it was apparent the life scientist didn't understand the way the physical scientist was thinking and vice versa," says Doyle, a GDCB associate scientist who manages the facility and who served on the lab's design team. "We decided if these scientists worked in the same place, they'd rub elbows, and they would learn by seeing how each other approached the problem."

Since imaging is a research technique common to both disciplines, the lab was developed as an imaging facility and equipped with state-of-the-art instrumentation. "This lab is set up to help researchers find new ways to address problems and questions," Doyle explains. "We put together multi-disciplinary teams and interact with the researchers to find solutions. Our goal is to foster research progress."

The Carver lab's instrumentation includes a wide range of computer-controlled imaging systems, including a confocal microscope, three atomic force microscopes, and an epifluoresecent digital imaging workstation. The physical setup of the facility enhances the research process as well. Features include a conference room where research teams develop proposals from initial brainstorming to final product, a room where scientists can analyze their data offline, a cell culture facility that has eliminated the need to carry live cells from building to building, and space dedicated to the design and development of new instrumentation.

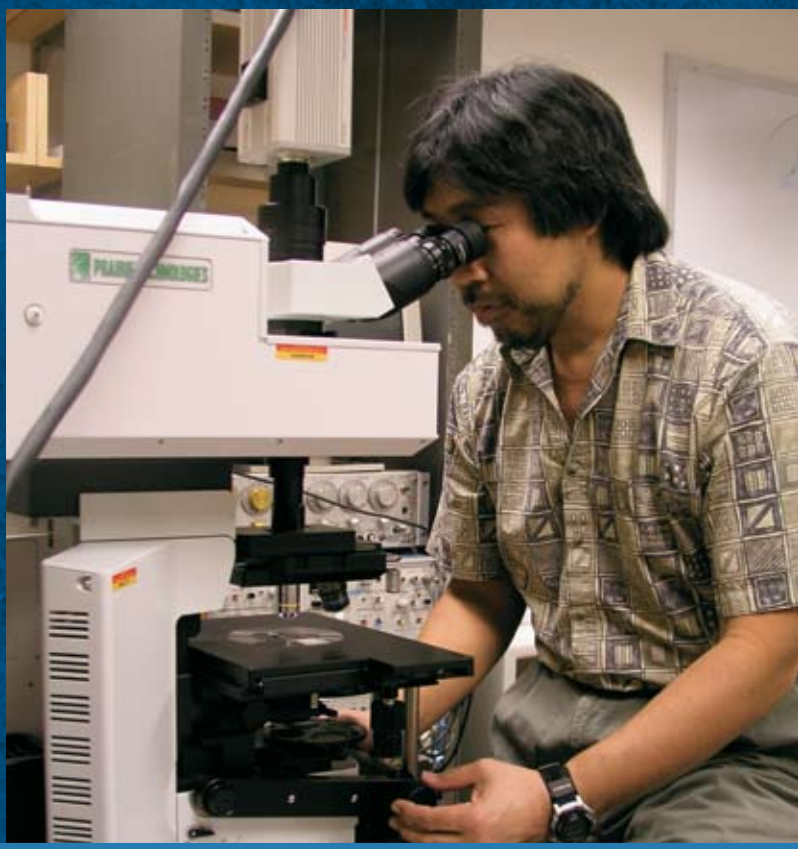
Doyle, whose own background is neurobiology, has managed the Carver lab since it opened in 2000. He's on constant lookout for ways to facilitate and enhance research.

In 2003, for example, space was converted to house the Affymetrix GeneChip® facility. "This is an autonomous lab from the biotechnology area," explains Doyle. "Traditionally, people doing imaging weren't thinking about gene chips or genomics, and people studying genomics weren't thinking of imaging. But with the research being done today, these areas are converging so it's very beneficial to have this facility on-site."

Last fall, with the help of several administrative units, the Biotechnology Council, the Plant Sciences Institute, and the Institute for Combinatorial Discovery, Doyle acquired a hyperspectral microscope workstation that he says will benefit many campus researchers. Since a lot of biology and life science imaging uses fluorescence for identifying specific targets, Doyle explored options that would solve limitations of traditional fluorescent microscopy. The hyperspectral microscope does the job by using a combination of digital imaging and spectroscopy.

"When fluorescent markers are used to identify cells, autofluorescence from the sample can cloud the picture," Doyle explains. "This system has the capability to spectrally unmix the original images and thus effectively leaves out the autofluorescence."

Work is now underway using the system to explore gene expression in plants, protein expression in transplanted cells, material deposition on polymer surfaces, and specific protein distribution in the brain. This new system allows researchers to ask questions that they haven't been able to ask before, so Doyle welcomes any and all "what if…" questions pertaining to fluorescence imaging.



› FOR MORE INFORMATION ABOUT THE ROY J. CARVER LABORATORY FOR ULTRAHIGH RESOLUTION BIOLOGICAL MICROSCOPY
Visit www.gdcb.iastate.edu/resources/facilities.html or call Bob Doyle at 515 294-6513.

Protein predictions

Understanding the structure of proteins and how proteins interact with each other is crucial to designing effective new drugs to treat specific diseases.

"There are two driving questions in our lab," says Drena Dobbs, GDCB associate professor. "One is, 'Can we predict the overall structure of a protein, given only its amino acid sequence?' And the other is, 'How do proteins recognize and interact with their correct partners (other proteins or DNA) in cells?'"

Using their experience in computational biology, Dobbs and her graduate students are looking for those answers by developing models based on data from biologists and other scientists. That data, she says, includes information about the interactions of specific proteins in a cell. Dobbs hopes scientists will eventually be able to understand the rules of nature that establish how amino acid sequences determine the structures of proteins and how proteins interact with other proteins to carry out their functions in cells.

"We understand the genetic code that translates information from genes in DNA through RNA to protein sequences," Dobbs explains. "But we don't yet understand the protein folding code that determines how a linear sequence of amino acids gives rise to a functional, folded three-dimensional protein."

Dobbs adds that the complexity of the problem is overwhelming because the number of ways that a protein can fold is astronomical—about 100 to the 20th power. "We're still a long way from understanding all the rules that determine folding," Dobbs admits, "but if we can, we'll also begin to answer the second question of how proteins interact with other macromolecules. When that happens we can begin to design new drugs that could be used to treat many diseases."

> "If we can predict how a tiny change in a sequence will change the shape of the protein, we can understand a lot more about how things really work in living cells."
> — Dobbs

Dobbs notes a few humans aren't susceptible to AIDS, so understanding which gene variants are responsible for protecting them from the HIV-1 virus could lead to new treatments or a vaccine for the disease. "We also know that people respond differently to drug treatments," she adds. "Medications for high blood pressure and heart disease are effective in certain individuals, but not in others; certain cancer treatments work great for some patients, but not for others."

Part of the reason that's true, Dobbs says, is the natural variations in human DNA that determine whether we are likely to get a disease, how we respond to treatment, and how rapidly the disease will progress. "Those variations, by and large, are expressed in protein structures," she explains. "If we can predict how a tiny change in a sequence will change the shape of the protein, we can understand a lot more about how things really work in living cells. And that would help us find treatments for many diseases.

"And that's our ultimate goal," Dobbs continues. "We want to understand how things work so we can develop models that will help us make better decisions about which experiments to do or which treatments to consider."

Dobbs considers collaborations with enthusiastic students and scientists from other disciplines as the most rewarding aspect of her research. "I like learning about other people's work and synthesizing information," she explains, "and computational biology allows me to do that. My students and I analyze large sets of data in our lab, generate hypotheses, and then we experiment to test our predictions. When our predictions are wrong, we go back, knowing that we need to improve our algorithms. If our experiments validate our computational predictions, we hope these approaches will ultimately lead to clinical therapies."

Slowly, but surely, Dobbs and her students are getting there. The number of tests to run is down to about 4 to the 100th power.

Chasing mutants

Studying mutant plants helps scientists determine and analyze the functions of specific genes.

Among the first things you notice when walking into Erik Vollbrecht's office are the funny looking ears of corn. He has a couple of shoeboxes full of them, and the ones that draw your attention right away have several small branches jutting out in different directions. Then you take a closer look and notice the kernels on these ears—some are discolored, while others are considerably misaligned. They're definitely not what you'd find at your local grocery store.

Follow Vollbrecht to the greenhouse on the third floor of the Molecular Biology Building or to his field at Curtis Farms near Ames, and you'll see him peeling back the husks on ears of corn, looking for defects. When he finds an anomaly, he pulls the ear from the stalk and takes it back to the lab to study. For Vollbrecht, a GDCB assistant professor, it's the mutated seeds from these malformed ears that help him learn how a gene functions in normal situations.

"In a mutant, the function of exactly one gene is removed," Vollbrecht explains. "We analyze how that removal changes the plant and consider the differences in the context of the molecule produced by that one gene. Looking at a collection of different mutants that cause similar visual changes allows us to catalog the parts that make up the system and the potential an organism might have."

> "In a mutant, the function of exactly one gene is removed. We analyze how that removal changes the plant and consider the differences in the context of the molecule produced by that one gene."
> — Vollbrecht

Vollbrecht focuses on corn because the ear is a good system for branching, which is his main area of study. Branching, he explains, is the main characteristic that controls the differences between the form and appearance of different plants—for example, trees and shrubs. Critical factors in branching include when and where branches are made and how long they grow.

"The traits I learn about in the ear of corn can also be applied to other plants," Vollbrecht offers. "In grasses and cereals such as rice, wheat, and sorghum, branching in the grain head is beneficial to yield. We're studying how subtle changes to a core gene set create the diverse architectures seen in grasses."

Vollbrecht's research has led to the identification of the gene ramosa1, which impacts the architecture of corn. In a normal ear of corn, each kernel is positioned on the end of a small branch. Ramosa1 tells those branches to grow short and in straight rows. The examples in Vollbrecht's office show how much of an effect a missing ramosa1 gene can have.

There's strong evidence that farmers, as far back as 10,000 years ago, realized the value of active ramosa1, Vollbrecht notes. "Our DNA sequence analysis shows that modern varieties of corn contain just a few versions of the ramosa1 gene, which is unusual for a maize gene," he says. "Early farmers bred maize from teosinte, a tall grass, over thousands of years, and we now know that they were careful to select corn that had lots of activity in this gene. That understanding pinpoints this gene as a master regulator of how the ear is constructed and implies that the ramosa genes may be manipulated to control ear or seed-head architecture in maize and other cereals."

Vollbrecht's research also focuses on functional genomics. He says new DNA sequencing and analysis technologies are critical because they essentially allow researchers to identify all of the more than 50,000 genes contained in the corn plant. "Simply identifying a gene, however, tells us very little about what it actually does," he says.

And that's why the mutants are so important. "We're knocking out 10,000 of those genes by making mutants," Vollbrecht explains, "which jumpstarts the analysis of the gene function."

Eventually, those mutant genes will be listed in a public database for use in a wide range of plant sciences. From basic research questions like the control of branching to biotechnology applications like biorenewables, this mutant collection will be used to determine the importance of each gene in the process being examined.

Fishing for answers

The National Center for Health Statistics reports cancer as the second leading cause of death in the United States. Cancer is a group of diseases characterized by uncontrolled growth and spread of abnormal cells.

Jeffrey Essner, GDCB assistant professor, is looking for genes in zebrafish that could lead to new treatments for humans that would stop the spread of abnormal cells.

Essner, who joined the faculty last fall, is setting up a zebrafish facility in Science II this summer. This facility, with a thousand plastic fish tanks holding thousands of fish, will introduce a new model system to Iowa State for researchers who are studying vertebrate development.

Zebrafish, as far as model systems go, are low maintenance and don't take up much space. Adults grow to about an inch, and a three-litre tank can hold up to 60 of them. They also develop quickly. Twenty-four hours into development, there is a beating heart. In addition, the embryos develop outside the mother. "The wonderful thing about these fish is that they give these optically clear embryos," Essner says. "You can simply look at them under a microscope and see what's going on inside."

Though these tiny fish might seem a far cry from humans, many genes in the zebrafish have the same function as their human counterparts.

In his research, Essner is working to find genes in the zebrafish related to angiogenesis, the development of new blood vessels formed by the budding of cells from existing vessels. Specifically, he wants to understand the genes that are required for tumor angiogenesis. These new blood vessels allow the tumor to receive nourishment for further growth and provide a route for cancer cells to metastasize to other parts of the body.

Once Essner finds the genes responsible for this vessel growth, he'll try to figure out how to turn them off and thus starve and kill tumors.

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> — Essner

Of some 30,000 zebrafish genes (roughly the same number as humans), about one of every 200 is important for blood vessel formation. To find those genes, Essner knocks down the expression of one gene at a time. Then he watches the development of the embryo to see if or how the gene would have affected blood vessel formation.

"We're really searching for that small subset of genes that are important for this process," says Essner. "By screening for these new genes, we hope to identify new candidates for anti-tumor agents." Once an anti-tumor agent is discovered, researchers will test it on other model systems. The hope is that it makes its way to a clinical trial stage for humans, and that it works.

Essner began using the zebrafish as a model while working on his PhD at the University of Minnesota. Following a postdoctoral appointment at the Scripps Research Institute in La Jolla, California, and a research faculty appointment at the Huntsman Cancer Institute, University of Utah, Essner became scientific director for Discovery Genomics Inc., a Minneapolis biotech company. That's where he began to see the applications of his research.

"It was my experience in industry that led me to believe I could make an impact on human disease; that you can easily transition basic research into therapeutic products," Essner says.

Essner's spouse, Maura McGrail, an associate scientist in GDCB, will also use the zebrafish facility. She is developing a cancer model in zebrafish embryos, essentially creating a fish that gets cancer. Often, cancer growth in zebrafish is quite similar to that in humans. McGrail's long-term goals are to find chemicals that will inhibit tumor formation and growth.

In another collaboration, veterinary specialist Dusan Palic will look at how the zebrafish immune system responds to different stimuli, in turn giving information about how the immune system functions. Essner is interested because cancers develop the ability to evade the immune system.

"We have become fairly proficient at curing mice of cancer," Essner explains. "However, when we go to the clinic with these same tools, they don't seem to work so well on humans. So it's really asking for a different kind of approach. Maybe screening more genes and understanding what those genes are doing will lead to more effective therapeutics."

From tragedy comes hope


DAVID **GLADSON**

As a marketing student at Iowa State in the 1980s, David Gladson had no connection to the disciplines that now comprise the Department of Genetics, Development and Cell Biology (GDCB). Today, however, an Iowa State scholarship firmly links this 1988 business graduate to GDCB.

The memorial brings together two dominant factors in Gladson's life—the university he loved and his 15-year battle with multiple sclerosis (MS), a disease that ravaged his body and led to his death in 2003. The fund is directed at enhancing the study of neurological disorders.

"David was so proud to be an Iowa Stater," says his brother, Steve Gladson. "He really enjoyed the time he spent in school, and he followed the Cyclones faithfully as an alum."

Known for his mild manner as he grew up in Cedar Falls, David Gladson found Ames to be full of good times. "Barney, that's what we called him because he looked just like Fred Flinstone's sidekick Barney Rubble, had a blast in school," recalls Todd Ortberg, who first roomed with Gladson in Friley Hall.

After a couple of years at Iowa State, Gladson buckled down and focused on his studies. The first sign that something was amiss happened on a hunting trip during Christmas break of his senior year. "We flushed some pheasants, but David didn't shoot," recalls Steve Gladson. "He said there were dark spots in his eyes, and he couldn't see the birds." David's vision returned after a few minutes, but over the next year the problem began to occur more frequently.

After numerous medical tests, he got the bad news. "His doctor told him he had the most aggressive case of MS he had ever seen," says Ortberg. Within a year, Gladson was declared legally blind, and he had to quit a marketing job he'd taken in Kentucky after graduation from Iowa State. He moved home to Cedar Falls. "David worked with the Iowa Department for the Blind to relearn how to do things," says Steve Gladson. "He was always looking for ways to increase his skills and to improve himself."

The disease progressed, and Gladson went to the Mayo Clinic in Rochester, Minnesota, for treatment. While there, he met his future wife, Jody, who had been paralyzed in a car accident. They were married May 24, 1997, and lived in a new home they had built in Rochester.

The MS, though, was relentless and eventually left Gladson incapable of taking care of himself. He initially received round-the-clock in-home care, but in February 2001 he moved to a nursing home. "David accepted that he had to move," says Steve Gladson, "but he didn't give up on living. He was very outgoing and interacted with as many people as he could."

David Gladson was just 39 when he passed away July 31, 2003. As the family prepared for the funeral, Ortberg proposed the scholarship in his friend's memory. "David's years at Iowa State were the best of his life," Ortberg asserts. "Putting money into an Iowa State scholarship that will be used to enhance the study of neurological disorders like MS is a way to make something positive come out of this tragedy."

> "David's years at Iowa State were the best of his life. Putting money into an Iowa State scholarship that will be used to enhance the study of neurological disorders like MS is a way to make something positive come out of this tragedy."
> — Ortberg

Working with the Iowa State Foundation, Ortberg and Steve Gladson have been raising money to create the scholarship. "David would be really proud to know this fund is in his name," says Steve Gladson. "He loved Iowa State, and it would be fantastic if some headway could be made to find a cure for MS and other diseases like it."

"We are very grateful to David's family and friends for honoring his memory with this scholarship," says Martin Spalding, GDCB professor and chair. "Our researchers study genetic, molecular, and chemical issues that could lead to improved treatment and cures for neurological diseases. Donald Sakaguchi, for example, is currently looking at ways to repair damaged nerve cells. (See article in the spring 2005 newsletter at www.gdcb.iastate.edu/events.) This fund will provide valuable support for research and for graduate students."

Interdepartmental majors.....continued from page 8

depth of expertise teaching and designing courses in a departmental major."

The second advantage for students is the opportunity to gain a variety of hands-on research experiences. "With 70-plus faculty involved in genetics research on campus, our students can explore different areas and really tailor their experiences to support their goals," Girton says. Faculty encourage and facilitate research experiences beginning with the students' freshman year.

The goal is to keep the genetics program small and well focused with between 80 and 100 majors. "This has been a very good recruiting year," Girton says. "I expect 20 freshmen coming in next fall, and with good retention we are on target to reach our enrollment goals."

With the increasing costs of education, scholarships are essential for attracting top students to the undergraduate Genetics and Biology Programs. To contribute to the GDCB scholarship funds, please use the form on page 2.

Interdepartmental majors offer breadth, flexibility

Undergraduate education in the Department of Genetics, Development and Cell Biology (GDCB) centers on two first-class interdepartmental majors—Biology and Genetics.

"An undergraduate degree in GDCB would be too narrow," explains Martin Spalding, GDCB professor and chair, "so we've taken an approach that allows students to take classes and interact with faculty from many different disciplines and across college boundaries." Both majors are available through either the College of Liberal Arts and Sciences or the College of Agriculture.

GDCB jointly administers the Biology major with the Department of Ecology, Evolution and Organismal Biology (EEOB). A popular program with over 450 students, Biology has always been an interdepartmental major at Iowa State. Last year's reorganization of the biological sciences means the Biology major is administered differently, but this should be transparent to students.

The interdepartmental structure offers Biology majors breadth and flexibility. "Six required courses provide students an overview and fundamental understanding of the major topics in biology and also helps them see the diverse career opportunities that are available," says Jim Colbert, EEOB associate professor and Biology Program coordinator. "Then, depending on their interests and goals, they choose from a wide variety of upper-level courses offered in 10 different departments." Graduates pursue careers in everything from human medicine and veterinary medicine to teaching to environmental professions.

Students complement their academic work with participation in BEST (Biology Education Success Team) and BETAL (Biology Education Teaching and Learning) learning communities, student organizations such as the Biological Sciences Club, and national and international field trips, which provide extensive opportunities for hands-on experiences. "Biology is a rapidly changing field," adds Colbert, "and we strive to help students identify and pursue the areas that intrigue them."

> "We've taken an approach that allows students to take classes and interact with faculty from many different disciplines and across college boundaries."
> — Spalding

As one of only six U.S. universities to offer an undergraduate Genetics major, the Iowa State Genetics Program attracts students from across the country. Jointly administered by GDCB, EEOB, and the Department of Biochemistry, Biophysics, and Molecular Biology (BBMB), the program's interdepartmental structure provides two key advantages.

"The genetics discipline at Iowa State includes faculty from 12 different departments specializing in the three areas of genetics—molecular, study of the gene as a physical unit of DNA; transmission, how genes are passed from one generation to the next; and population, how genes control the growth, development, and change in a species," says Jack Girton, BBMB associate professor and chair of the Genetics Curriculum Committee. "We wouldn't get this

continued on page 7

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