

Cover photo:
Students take advantage of new bardware and software in the College's Anatomy Laboratory to enhance their studies. The new technologies are designed to complement traditional methods of teaching anatomy — dissection and textbook readings and renderings — while giving students improved tools to aid in the study and retention of anatomical course work.

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# W elcome to *Insight*

Welcome to the Fall 2003 edition of *Insight*. In this edition we introduce you to the five new members of the College's leadership team: Drs. David Lee, Paul Lunn, Barbara Sanborn, Jeffrey Wilusz, and John Zimbrick. They bring with them valued wisdom and experience as the College moves into a new era of scientific endeavor, teaching, and outreach. We welcome them and wish them the best of luck in their new positions.

You'll also have the opportunity to learn more about the College's research programs and new grant projects that will enable further investigations into important global diseases such as HIV/AIDS, tuberculosis, leprosy, and prion-related diseases. The emphasis in this edition of *Insight* is on the College's biomedical research programs and how they relate to the overall mission of the College.

We also honor several faculty members who recently have received prestigious awards for their work in teaching and research. These honors and awards reflect the overall excellence of the faculty at the College, and we congratulate the recipients – Drs. Ray Whalen, John Belisle, and Edward Dudek – on their achievements.

We welcome your questions and comments on *Insight* and its contents. If you'd like to get in touch with us, please send your correspondence to:

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You can e-mail *Insight* comments to Paul Maffey, Director of Development for the College, at pmaffey@cvmbs.colostate.edu. We also invite you to visit us at our Web site at www.cvmbs.colostate.edu.

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## M

### essage from the Dean

Dear Friends,

During the past year, we have witnessed a variety of new and old diseases coming to the fore, including Severe Acute Respiratory Syndrome (SARS), West Nile virus, and monkey pox. These, combined with previously existing disease threats, make us very aware of the continuing danger infectious diseases pose to human populations worldwide, including here in the United States, where we sometimes can feel removed from the diseases that threaten the rest of the planet.

At the College of Veterinary Medicine and Biomedical Sciences, we are heavily invested in research programs that address the diseases posing the greatest threat to humankind today - tuberculosis, cancer, HIV/AIDS, arthropod-borne infectious diseases, and more. Our newer studies in prion-based diseases are beginning to answer questions that five years ago hadn't even been asked. We are active in West Nile research and vaccine development. Although we are most well-known for our work in veterinary medical research, our biomedical programs are actually the larger of our two areas of expertise. What is perhaps unique to this College is how our dual focus - veterinary medicine and biomedical sciences – enhances the quality of both programs by bringing together experts and resources which, when combined, are able to fight enemies of the body with the powers of the mind.

The College is home to the Mycobacterium Research Laboratory, which has carved a global niche for itself as a center of excellence in tuberculosis and leprosy research. In 2003, tuberculosis claimed the lives of two million people. Worldwide, two billion people are infected with the bacterium that causes tuberculosis. Researchers at the laboratory are working at many levels to understand *M. tuberculosis*, assaying drugs used in the treatment of TB, and collaborating with scientists from around the world to develop more

effective vaccine and treatment programs. You can read more about this program and get an update on other innovative research enterprises in a related story looking at some current research at the College (see page 10).

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The College also is home to an innovative HIV research program that is looking at changing stem cells to make the body's immune system resistant to HIV infection (see related story on page 13). HIV/AIDS remains a pandemic of most frightening proportions. Worldwide, 65 million people are HIV-positive. United

Nations AIDS (UNAIDS) estimates that there are 5 million new cases of HIV each year. In 2002 alone, approximately 3.1 million people died of HIV/AIDS. When President Bush visited Africa this summer, we saw the face of AIDS on our televisions. The United States has committed \$15 billion over the next five years to fight AIDS in Africa. It will help, but our battle is just beginning.

At the College, we also house the Arthropod-Borne and Infectious Diseases Laboratory (AIDL). As West Nile virus once again took over headlines this summer, we were reminded of the intricate relationship between humans and the mosquitoes with which they share the earth. Researchers at AIDL not only study diseases transmitted by arthropods, they also study the arthropods themselves to see if they can unlock a door that one day will lead them to alter mosquitoes so they are not capable of spreading disease.

It seems at times that the diseases are getting ahead of us and we can do little to stop the death and destruction that comes in the wake of a major outbreak, but we are making progress. In August, scientists announced they had developed a high-speed vaccine for the dreaded Ebola virus. The vaccine



Dr. Lance Perryman

has been shown to give macaque monkeys protection from Ebola after one injection. Scientists from the Vaccine Research Center of the National Institute of Allergy and Infectious Diseases believe the vaccine will be safe and effective in humans as well, offering immunity in as little as four weeks after vaccination.

Breakthroughs such as this do not happen easily. Science must develop understanding to the point at which such an event is possible. This only happens through persistence, years of research, basic and applied scientific studies, and a bit of luck. At the College of Veterinary Medicine and Biomedical Sciences, we are proud to be a part of the global scientific community that is bringing hope to people the world over in the form of improved medicine, better vaccines, and lives filled with joy instead of suffering. As supporters of the College, each of you is a part of that as well.

Best Regards,

Lance Perryman, D.V.M., Ph.D.
Dean, College of Veterinary Medicine
and Biomedical Sciences



## V

### irtual Reality Goes to the Dogs in Anatomy Lab

The study of anatomy always has posed a unique set of problems for student and teacher alike. Two-dimensional images can hardly reveal the complexity of anatomical structure, while carting around dissected specimens for review of material is hardly sanitary or desirable. At the College's Anatomy Laboratory, students now have a third option – the use of virtual anatomy on portable software that enables students to review anatomy in a three-dimensional environment.

Virtual anatomy is part of an overall program to bring technology into the Anatomy Laboratory — technology that creates an innovative and effective learning environment in which students are better able to discern anatomical structures, commit details of anatomy to memory, and retrieve information for review at their convenience.

"In anatomy, we have had the textbook and written guides, work in laboratories, dissections, and a few other functional materials like plastinated organs," said Dr. Ray Whalen, a Professor in the Department of Biomedical Sciences and technology coordinator for the Anatomy Laboratory. "Dissections are the best way to learn anatomy, but once you're done, it's not easy to reproduce the material. If you forget something from a dissection, it's difficult to regain that knowledge."

Dr. Whalen and a team of veterinary students began to work on a software program to make a "virtual

canine" to aid students in their study of canine anatomy. The result of their work is an interactive software program that



The virtual canine software allows students to view images of canine anatomy in three-dimensional, multilayered detail.

prepares students for their laboratories, guides them through classroom activities, and provides a review of material



Dr. Mark Frasier, an Associate Professor in the Department of Biomedical Sciences, helps students working on their anatomy studies. New computers and software make teaching and learning anatomy more efficient and effective.

"Dissections are the best way to learn anatomy, but once you're done, it's not easy to reproduce the material. If you forget something from a dissection, it's difficult to regain that knowledge."

after laboratories so students can get a good grasp on the material they have covered.

The virtual canine allows students to view images of canine anatomy, specifically anatomy of the head, in three-dimensional detail. Using the program, they can rotate images on their computer screen and peel away layers of virtual skin, muscle, and fat to reveal hidden structures and bone. Dr. Whalen said students love the new software, the only complaint being that they would like to have additional software titles available featuring the remainder of the canine anatomy and other animals studied in the anatomy labs.

"The process of digitizing anatomical subjects is very time and labor intensive, and right now, time and money are our two primary constraints to developing additional software," said Dr. Whalen. "Our goal is to finish the canine model and then get started on an equine model as those constraints allow. I would add that it has been one of the highlights of my career to work with these veterinary students in the development of this software. They are so enthusiastic about this work and have such a level of dedication and professionalism that I have really enjoyed the whole process and I'm very proud of what they have been able to contribute and achieve."

One added feature of the software is that, over time, it may reduce the need

for animal cadavers for anatomy laboratories at Colorado State and other research institutions. It will become one more tool to support the College's 3-Rs policy of reduce, replace, and refine regarding the use of animals in teaching and research. Dr. Whalen eventually hopes to license the software and make the software development program self-sustaining.

In addition to the new imaging software, the students in anatomy are benefiting from a high-

tech retrofitting of the physical facility itself. The laboratory now provides a specialized computer workstation at each anatomy station to supplement teaching with computer models and streaming video. For example, students will be able to watch a surgery in progress at the Veterinary Teaching Hospital and relate it to what they are studying in anatomy. Distance learning, especially with continuing education courses, also is possible with the communications and video links provided at the laboratory.

"Our new technology enables us to

open up our venue," said Dr. Whalen. "We no longer are contained in just this building. That means we can provide education and outreach on a larger scale, incorporate distance learning into our curriculum, and provide support to students even after they have left the University."

Incorporating this type of technology into the teaching of anatomy has been Dr. Whalen's dream for the past 20 years. Pulling the money and resources together has been difficult, but with assistance

from the Department of Biomedical Sciences, the Office of the Dean, and funding from the Colorado Commission on Higher Education, Dr. Whalen has been able to make part of his dream a reality in the last 10 years. He is hoping additional private funding may help him complete the canine anatomy software and equine software, as well as continue upgrades in the anatomy laboratory.

"We would love to find some private support for our software development as well as the continued upgrading of the Anatomy Laboratory," said Dr. Whalen. "With additional funding, we really could make rapid progress on our objectives for a 'virtual' laboratory."

If you are interested in supporting the work of Dr. Whalen, contact Paul Maffey, Director of Development for the College. A special fund has been created to provide funding and support to Dr. Whalen's efforts in software development and technology investment. You can reach Maffey at (970) 491-3932, e-mail at rpmaffey@cvmbs.colostate.edu, or visit the Development Office's Web page at www.cvmbs.colostate.edu.



Dr. Ray Whalen makes a fine point in the Gross Anatomy Laboratory.

## N

### ew Leadership Team Set to Continue College's Tradition of Excellence



Drs. Jeffrey Wilusz, John Zimbrick, Barbara Sanborn, David Lee, and Paul Lunn.

Dr. David Lee

The past two years have seen many changes at the College of Veterinary Medicine and Biomedical Sciences. The College's departmental structure was dramatically altered, Dr. James L. Voss retired as dean and was replaced by Dr. Lance Perryman, administrative positions were shuffled, and five new individuals were brought on board to head up the four new departments and the James L. Voss Veterinary Teaching Hospital.

The new leadership team is now in place on campus, and proper introductions are in order.

#### Dr. David Lee

Director, James L. Voss Veterinary Teaching Hospital

In the *U.S. News* and World Report college rankings, Colorado State University's Professional Veterinary Medical Program is ranked second only to

Cornell University. The new director of the Veterinary Teaching Hospital could help change that, as he definitely has the insider's track on what is happening at Cornell and how the College might beat them next year. Dr. David Lee received his Bachelor of Science, D.V.M., and M.B.A. from Cornell and had worked since 1996 at Cornell where he was Executive Director of the College of

Veterinary Medicine's External Affairs and Marketing and previously Executive Director of Strategic Planning and Business Development.

"Cornell always has been an important part of my life — in my immediate family, we probably have 10 degrees from Cornell — but in the last few years, I have been looking for a change," said Dr. Lee. "There were only a handful of schools I would have considered, and Colorado State was one of them. The Veterinary Teaching Hospital is rich with tradition but also has a very dynamic and

invigorating atmosphere, and I am excited to be here."

Dr. Lee's own research interests focus on organizational behavior and how to motivate people, as well as practice management, and he hopes to help not only the hospital improve its business workings but also teach courses in practice management to students in the Pro-

fessional Veterinary Medical Program.

"The hospital is a very customer service-focused organization," said Dr. Lee. "But we have many customers including our clients, patients, students, veterinarians, alumni, and the state of Colorado. We need to understand and meet the special needs of each of these customers, realizing that just focusing on the financial aspects won't get us

to where we need to be. A balanced approach, looking at the internal and external stakeholders' perspectives, is key to making our constituents happy."

One of Dr. Lee's first objectives as director is to improve and update the hospital's internal processes, including moving from paper patient records to electronic records that can track care and be available throughout the hospital to faculty and students via PDAs or laptop computers. The goal is to have a paperless and wireless hospital, so everyone can communicate with ease, and patient records are updated real-time. Dr. Lee would like to tap the College's alumni base to support the College through development efforts and work within the 25-year plan to continue to improve hospital facilities. He also would like to undertake a survey of hospital customers to get a better idea of attitudes toward, and feelings about, the hospital.

#### Dr. D. Paul Lunn

Department of Clinical Sciences

Though a native of Great Britain, Dr. Lunn has spent most of his professional career in the United States, where he has enjoyed the research and teaching opportunities afforded



Dr. D. Paul Lunn

him particularly in equine medicine. Dr. Lunn joined the College on Aug. 15 as head of the Department of Clinical Sciences, coming to the College from the University of Wisconsin-Madison School of Veterinary Medicine, where he served as Associate Dean for Clinical Affairs and Director of the Veterinary Medical Teaching Hospital.

"We loved the idea of living in Colorado, and after my previous position as a hospital director, I wanted a position in departmental administration with the opportunities it afforded for working closely with faculty," said Dr. Lunn. "This is a very exciting position, and I am look-

ing forward to helping the faculty meet their goals and the goals of the Department."

Dr. Lunn is especially interested in growing the Department's programs in basic, applied, and clinical research. His own research interests are in large animal medicine with a focus on equine immunology and infectious disease.

"Although my focus here primarily will be my administrative responsibilities, I am looking forward to bringing my research program to Colorado and to the new collaborative opportunities that will result," said Dr. Lunn. "I also love to teach and hope to participate in the classroom whenever possible."

Dr. Lunn received his B.V.Sc. from the University of Liverpool in Great Britain in 1982 and then completed an internship in Large Animal Medicine and Surgery at Ontario Veterinary College. After a two-year period in general practice, Dr. Lunn completed a three-year Large Animal Medicine Residency and M.S. degree program at the University of Wisconsin-Madison. In 1991, he completed his Ph.D. work at the University of Cambridge, Great Britain. He is a Diplomate, 1992, of the American College of Veterinary Internal Medicine and a member of the Royal College of Veterinary Surgeons. Dr. Lunn joined the University of Wisconsin-Madison faculty in 1991 as an Assistant Professor in the Department of Medical Sciences, School of Veterinary Medicine.

### Dr. Barbara Sanborn

Department of Biomedical Sciences

Dr. Sanborn comes to Colorado State University from the University of Texas Medical School in Houston, where her career focused on molecular aspects of hormone action in the reproductive system

in the reproductive system and the development of women's health



Dr. Barbara Sanborn

programs. As new head of the Department of Biomedical Sciences, she'll draw from her Texas experience where, among other things, she ran a busy research program, served as Vice-Chair of the Department of Biochemistry, and was director of an NIH Training Grant and Research Director in the Office of Women's Health, University of Texas Health Science Center Women's Health Initiative. She also served as President of the Society for the Study of Reproduction.

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"I was looking for an administrative challenge and a department with growth potential and found both here at Colorado State," said Dr. Sanborn. "We have robust reproduction biology and neurobiology groups here and a strong core of people who are interested in ion channel physiology and biochemistry."

Dr. Sanborn received her Ph.D. from Boston University. From early in her career, she has been interested in reproductive hormone actions and how hormones work at the molecular level. Her work looks at signaling mechanisms and how these signals affect the biology of the cell. As her research progressed, she became more involved in women's health research and educational outreach for both the lay public and medical professionals. At the University of Texas Medical School at Houston, Dr. Sanborn held a primary appointment in the Department of Biochemistry and Molecular Biology and a joint appoint-

ment in the Department of Obstetrics, Gynecology and Reproductive Sciences. She had a very active research program, part of which she has moved to Colorado State. In addition to her administrative duties, Dr. Sanborn will continue as a researcher, something she feels gives her the ability to relate to the challenges

facing faculty within her department.

"I moved my two NIH grants here with me and now have my laboratory set up in the Animal Reproduction and Biotechnology Laboratory at the Foothills Campus," said Dr. Sanborn. "In addition to my research and administration duties, I also am interested in keeping a hand in teaching and working with our graduate students."

Dr. Sanborn has several priorities as new head of the Department of Biomedical Sciences. She would like to complete the integration of the Department and create a greater sense of collegiality as well as an integrated approach to graduate education. Dr. Sanborn is committed to enhancing career development opportunities for faculty and to developing a clear plan for future growth, including planning for a new basic sciences building. The Department is actively recruiting new faculty members for open positions to complement an already nationally rec-

ognized research and teaching program.

#### Dr. Jeffrey Wilusz Department of Microbiology, Immunology and Pathology

Dr. Jeffrey Wilusz took over as head of the Department of Microbiology, Immunology and Pathology on Aug. 1. Dr. Wilusz came to Colo-



Dr. Jeffrey Wilusz

rado State University from the University of Medicine and Dentistry of New Jersey-New Jersey Medical School, where he was a Professor in the Department of Microbiology and Molecular Genetics as well as that Department's Vice Chair, and was Assistant Dean for the medical school's M.D./Ph.D. program.

Dr. Wilusz said his first task is to learn the workings of the Department in order to clearly understand its missions in teaching, research, and outreach. From there, he has a number of topics of particular interest.

"I'm interested in developing new collaborative research projects," said



### N ew Leadership Team Set to Continue College's Tradition of Excellence

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Dr. Wilusz. "We have so many talented people within the Department, I think that wherever we aim our efforts we will be successful. Of course, in order to be successful, we have to make sure we have the equipment, resources, and personnel to get the job done, and that also will be a priority for my office."

On the teaching side, Dr. Wilusz would like to see an increase in the undergraduate research presence and the introduction of more technology into courses so that teachers can teach and students can learn more efficiently and effectively. He also wants to make sure that the Department is teaching the most up-to-date material possible.

"In a way, we need to work backwards," Dr. Wilusz said, "We need to understand what our students need to know when they graduate four years from now. The question we need to ask ourselves is what do our students need and how do we get there?"

Dr. Wilusz said he is looking forward to the challenges of being a department head. He enjoys working with people and the organizational work of being an administrator. He also hopes to keep a hand in teaching, something for which he has received numerous awards, as well as oversee an active research program. He has moved his own laboratory to Colorado State University from New Jersey, along with five people who had worked in his laboratory and two grants from the National Institutes of Health.

Dr. Wilusz is a graduate of Rutgers University (Cook College) in New Jersey, where he received a Bachelor of Science degree in animal sciences. He received his Ph.D. in molecular virology from Duke University and received postdoctoral training at Princeton University, Department of Biology. His major research interests revolve around the control of gene expression at the post-transcriptional level. These areas include a biochemical and molecular description of mechanisms, factors, and RNA elements involved in mRNA stability, polyadenylation signal recognition, and regulated messenger RNA-protein complexes.

#### Dr. John Zimbrick

**Department of Environmental and Radiological Health Sciences** 

Dr. John Zimbrick comes to the College from

Purdue University where he was a Professor of Health Sciences and member of the Purdue Cancer Center. Although he had not planned on leaving Purdue, the opportunity to come to Colorado and lead the nation's only combined environmental health/radiological health program was too tempting to pass up.

"When this job came up, it certainly got my attention," said Dr. Zimbrick. "I looked at the description and realized that this Department was unique in the United States. It is the only department that combines toxicology, epidemiology, industrial hygiene, radiation and cancer biology, and health physics. The Department's broad spectrum has a common theme of health effects of various physical, chemical, and biological agents, and there is not another place like it. We are in a position to do things as a Department that just can't be done anywhere else, and I am very excited about that."

As he familiarizes himself with the Department, Dr. Zimbrick already has developed objectives. Initially, he would like to bring faculty and staff together with a shared vision of the Department. He also would like to start a Department-wide research initiative to examine the effects of combined exposures to radiation and secondary agents on living systems. Dr. Zimbrick would like to complete the work required to establish undergraduate programs in health physics (also known as radiological health) and industrial hygiene. He also would like to update the Department's Web page and try to enhance alumni giving to departmental scholarships.



Dr. John Zimbrick

"We have started the process leading to accreditation of the health physics program," Dr. Zimbrick said. "We feel this will be a very positive development for the Department, as this degree is in high demand across the country, and just a handful of programs are available to meet industry

and government requests for graduates with degrees in health physics."

On the research side, Dr. Zimbrick currently has a National Institutes of Health grant focusing on spatial properties of radiation-produced clusters of damage in DNA. He also would like the Department to partner with the Animal Cancer Center in studies with specific interest in the use of the MRI, particularly using new magnetic resonance techniques to enhance images of tumors and study tumor metabolism.

"There is so much we can do here with the resources we have," said Dr. Zimbrick. "I would really like to see us take this Department up to the next level and make it preeminent in the fields of environmental and radiological health sciences. I think that we can provide education and leadership in these areas for the country and the world."

Dr. Zimbrick attended the University of Kansas, where he received his master's and Ph.D. in radiation biophysics. He was a member of the faculty there from 1969 until 1984 and also served as chair of the Radiation Biophysics Department. After KU, Dr. Zimbrick was a scientific review administrator with NIH and then joined Battelle-Pacific Northwest Laboratory, where he was Chair of the Biology and Chemistry Department and held a joint appointment at Washington State University. He then became Director of the Board on Radiation Effects Research of the National Academy of Sciences before joining Purdue University in 1997.



## B

### iomedical Research Programs Set CVMBS Apart

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When most people think of the College of Veterinary Medicine and Biomedical Sciences, they tend to focus on the veterinary medicine part. The College is, after all, home to the James L. Voss Veterinary Teaching Hospital and world-renowned research and treatment programs in animal cancer, equine orthopaedics, veterinary cardiology, critical care, and more. But it is the biomedical sciences, that last bit dangling onto the College's name, which truly makes the College a unique place to study, teach, and conduct research.

The College was the College of Veterinary Medicine until 1967, when the official name was changed to the College of Veterinary Medicine and Biomedical Sciences. During Dr. Rue Jensen's tenure as dean, from 1957-1966, the College actively was investing its resources in the biomedical sciences. This was in part to offset declines in state funding with greater federal dollars, in part to offer greater research and teaching opportunities to non-D.V.M. faculty, and in part to give the College a strong position in a number of growing and dynamic fields, including environmental health.

"The development of the biomedical sciences is a good example of the advantage that existed for the University in having a strong program in veterinary medicine and in having an opportunity with increased federal funding to develop an interest in the biomedical sciences," said Dr. Robert Phemister, former Dean of the College, in a 1982 interview. "Building on the faculty and the reputation of the College, the University did a smart thing to capitalize on it and make it become a further strength for the University. The biomedical-veterinary medicine combination is virtually unique among veterinary fields."

Biomedical sciences describes the interface between biology and medicine. It is a huge field that allows individuals at the College to participate not only in veterinary medical research but in human medical research, as well. Nearly 20

years ago, the College decided to focus its efforts in five areas of the biomedical sciences to compete more effectively for extramural funds. These areas included cancer biology, neuroscience, infectious disease, environmental toxicology, and animal reproduction. Each of these programs now is designated a University Program of Research and Scholarly Excellence (PRSE), five of the 14 so designated programs at the University.

In 2002/2003 the College received almost \$50 million in external funding for these and other research programs at the College, with 85 percent of that coming from the federal government, mainly the National Institutes of Health. the National Science Foundation, the Department of Agriculture, and the Department of Defense. The Homeland Security Act, established in response to the Sept. 11, 2001, terrorist attacks, dramatically increased funding for infectious disease research. While this is good for the College's program in infectious disease, it could make funding more difficult to obtain for other areas of research.

"The challenge will be maintaining the breadth of biomedical research we currently enjoy," said Dr. Terry Nett, Associate Dean for Biomedical Sciences with the College. "With the Homeland Security Act, the dollars are changing. The finite pool of funds available from the federal government is being shifted from general biomedical research into biodefense. That means that the funding for some other areas will suffer. We haven't seen the true impact yet because most research grants run two to five years, but in the next two to three years, we will begin to see the impact of these changes. Our goal will be to maintain our diversity and strengths with tightening dollars. A part of that is striving to maintain and recruit the best faculty available so that we have the best people competing for those limited funds."

The College's five PRSEs will continue to receive emphasis in terms of the

College's resources for the foreseeable future, but efforts also are being put into developing new programs, including a joint research and teaching program in orthopaedics with the College of Engineering, focusing primarily on humans and horses. Two other areas of emphasis are the scientific fields of proteomics and genomics.

In the coming decade, Dr. Nett also wants to keep the College at the forefront of what he says will be some dramatic changes in biomedical research.

"Technological innovation will enhance our ability to understand how organisms function," said Dr. Nett. "We will see dramatic advances in structural biology, specifically three-dimensional images of molecules that allow us to see how molecules interact with each other. This will allow us to better research and maybe even remedy diseases like Alzheimer's and cystic fibrosis that are based on interactions between molecular structures."

Another area Dr. Nett sees as critical to biomedical sciences is continued public support and public education — education that should begin in grammar school.

"We need to do a better job of instilling a sense of wonder in children when it comes to the scientific world," said Dr. Nett. "I don't think we do a very good job of educating the public about what it is we do. A number of scientific organizations are beginning to tackle this problem with programs directed at educating our vouth about the sciences and fields in scientific discovery and educating adults about the importance of science in everyday life. If you look at the television show CSI, this is one example of how education about science though perhaps not intentionally - is taking place in an effective and interesting way. But scientists need to be doing so much more if we want to maintain support from the populous and continue to attract the best and the brightest to scientific professions."



## R esearch Update

#### Microbiology Team Receives \$7 Million to Develop Early Test for Leprosy

A team of nine Colorado State microbiologists, led by University Distinguished Professor Patrick Brennan, has been awarded two grants from the



Dr. Patrick Brennan

National Institutes of Health to develop early tests for leprosy based on the recently completed genome of the bacterium responsible for the disease.

The Colorado State team, which received a total of \$7 million, is working with four international centers — in

Katmandu, Nepal; Cebu, Philippines; Rio de Janeiro, Brazil; and Medellin, Colombia – areas of the world where leprosy is still endemic.

Currently, there are no pre-clinical tests for leprosy. Diagnosis is based on physical examination for infected patches on the skin. Thanks to a successful application of multi-drug therapy, however, those diagnosed with leprosy can control the disease.

One of the few basic research programs on leprosy worldwide has been located at Colorado State University since 1980 in the Mycobacterium Research Laboratory. The laboratory, which also works to a large extent on the related disease of tuberculosis, is part of the College's Department of Microbiology, Immunology and Pathology.

Dr. Brennan's research team contributed to the discovery of the bacterial factors responsible for leprosy and the factors that can be used in an early diagnosis of the disease. For this discovery, Dr. Brennan's team was awarded an earlier grant from the National Institutes of Health.

With this current award, Dr. Brennan and colleagues have set a goal of one new early-testing tool per year of the seven-year grant. The team already is applying new tests to leprosy patients in clinical trials in Katmandu, Nepal.

### Prion Research Laboratory Awarded \$8.4 Million to Study CWD

The National Institutes of Health recently awarded an \$8.4 million grant to the College's Prion Research Laboratory to study

chronic wasting disease (CWD), including its mode of transmission, the potential for interspecies transmission, and a possible vaccine against the disease.

Dr. Edward Hoover

The research study will focus on four major objectives: assess how CWD is transmitted among deer, develop a transgenic mouse model for CWD, evaluate the potential for interspecies transmission of CWD, and test potential strategies for a CWD vaccine.

Dr. Edward Hoover, a Colorado State University Distinguished Professor and director of the laboratory, acknowledged that the objectives of the research are very ambitious but that he and his collaborators are looking forward to the challenge.

"Progress in the study of this disease has been difficult because the causative agent is a protein rather than a nucleic acid-containing agent," Dr. Hoover said. "Therefore, we can't use the kind of technology we use to detect and understand viruses and bacteria.

"Additionally, the incubation period is quite long — probably two to six years in nature. For this reason, we are working with Dr. Glenn Telling at the University of Kentucky to develop a transgenic mouse model to more easily study the pathogenesis, transmission, and intervention of CWD."

The team also will focus on detecting the CWD prion in body fluids and excretions of deer since, as Dr. Hoover explained, one of the most interesting

and important aspects of the disease is how the infection is transmitted among deer.

Chronic wasting disease was first detected in the late 1960s and is endemic in free-ranging deer and elk in northeastern Colorado and southeastern Wyoming. More recently, the disease has emerged as a threat to ranched elk in several western states and has been found

in the Midwest in areas of Wisconsin. It is one form of a group of fatal brain diseases called transmissible spongiform encephalopathies, or TSEs, which include bovine spongiform encephalopathy in cattle and Creutzfeldt-Jakob disease in humans. To date, there is no evidence that CWD is transmissible to humans.

### Research May Help Decrease Number of Serious Infections in Medical Patients

A collaborative research project conducted by a Colorado State University veterinarian and two Boulder



Dr. William Dernell

scientists with Rose Biomedical may lead to new medical technology for reducing the number of serious infections suffered each year by millions of both animal and human patients.

Dr. William Dernell, an Associate Professor in the Department of Clinical Sciences, and Drs. Steve Frank and Ammon Balaster, scientists working with Rose Biomedical in Denver, have the first study underway using a rat model. The project will test the efficacy of a new antimicrobial treatment for serious, established infections that are the result of major surgery or long-term medical treatment.

If successful in the initial study, the technology will be further tested at the College's Animal Cancer Center to assess how well it works in reducing infections

in dogs that have undergone limb spare surgery to remove and replace cancerous bones.

"To prolong their lives, dogs with bone cancer often require the removal of the cancerous bone and use of a replacement rod," said Dr. Dernell. "Unfortunately, about 50 percent of these dogs suffer postsurgical leg infections, for which systemic

antibiotics may have limited effectiveness. In human cancer patients, the rate is between 20 and 25 percent."

Dr. Dernell explained that, in these cases, most of the infections are deep in the tissues and are of mixed origin. Additionally, most dogs that have undergone cancer surgery already have been treated with a course of antibiotics while undergoing chemotherapy. "So there is already something of a resistance to some antibiotics," Dr. Dernell added.

The new method for treating these hardy, persistent infections involves driving the antibiotics deeper into the affected tissues so that they can attack the bacteria more directly.

Dr. Frank, who has spent years perfecting the technology, believes this new method will revolutionize this type of medical treatment.

The rat study model currently being used in this project simulates a previous study conducted by Dr. Dernell. In that test, antibiotic polymer beads were evaluated as a treatment for resistant infections. That study provided a very rigorous test model for antimicrobials

and offers a direct comparison of effectiveness.

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Dr. Barry Beaty

Dr. Dernell and his associates have applied for a grant from the National Institutes of Health to pursue additional pre-clinical studies at Colorado State and, eventually, develop a treatment application that can improve the quality and reduce the cost of health care.

### CDC Awards Training Grant in Vector-Borne Diseases to AIDL

The Centers for Disease Control and Prevention has awarded a Fellowship Training Program grant to the College's Arthropod-Borne and Infectious Diseases Laboratory.

The grant provides almost \$250,000 per year for five years to train graduate students in medical entomology, arbovirology, microbiology, and vector-borne diseases. The ultimate purpose of this funding is to improve the ability of the U.S. public health system to effectively respond to the problem of vector-borne infectious diseases by increasing the number of specialists with demonstrated field- and laboratory-based skills.

"We're very grateful to the CDC for this award. Being selected for one of these grants says quite a lot about the quality of our research, our facilities, and our scientists," said Dr. Barry Beaty, University Distinguished Professor and former head of the AIDL at Colorado State. "This award complements the funding we just received from NIH to form, in partnership with the University of Texas Medical Branch in Galveston, an Emerging Virus Disease Unit and demonstrates the importance of this kind of research."

Dr. Carol Blair, former chair of the Department of Microbiology, is co-program director on the grant, which also includes an illustrious roster of internationally recognized researchers and AIDL faculty, including Drs. William Black, Richard Bowen, Charles Calisher, Jon Carlson, Joel Hutcheson and the director of AIDL, Ken Olson.



Dr. Carol Blair

The more than 30 researchers at the Arthropod-Borne and Infectious Diseases Laboratory at Colorado State concentrate on the prevention, diagnosis, and control of mosquitoborne encephalitis, vellow fever, dengue, Hantaviruses, parasitic diseases, and Lyme disease. Researchers at AIDL regularly collaborate with researchers at the Fort Collins laboratory of the Centers for Disease Control and Prevention - Division of Vector-Borne Infectious Diseases: and the U.S. Department of Agriculture - Arthropod-Borne Animal Diseases Research Laboratory in Laramie, Wyo., which provides an unparalleled training experience in vector-borne diseases for the students at Colorado State University.

The CDC grants are part of the "Healthy People 2010" initiative, which is designed to make dramatic progress in improving the health of America's population over the next 10 years.

#### Mycobacterium Researchers Receive \$3 Million Grant to Study TB Vaccines

Drs. Ian Orme and Randy Basaraba in the Department of Microbiology, Immunology and Pathology have been awarded a five-year, \$3 million grant from the National Institutes of Health to conduct a pioneering study to examine the long-term effectiveness and safety of tuberculosis vaccines. The scientists are determining if the most promising new vaccines — those proven successful in short-term studies — can remain effective over the long term and if specific vaccines actually could be damaging to

### R esearch Update

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the lungs over time. The team is striving to provide the first fundamental scientific



Dr. Ian Orme

information regarding pathological changes in the lungs induced by tuberculosis vaccinations.

"This has not been looked at before and is the next important step in our tuberculosis vaccine research. We know that several tuberculosis vaccines

seem to be effective in the short term, but there is not a lot known about how these work at the basic pathology level," said Dr. Orme, principal investigator of the study. "However, we also are going a step further with our research to look at the long-term safety and effectiveness of TB vaccines, another area which has previously received very little attention."

The safety issue is currently of great concern to the researchers because of a newly emerging category of live vaccines derived from mutated TB bacteria. This new class of potential vaccines has great promise but also may carry big risks. Previous studies have provided no long-term

safety data about these types of vaccines. With more than 8 million verifiable new cases of tuberculosis each year, there is an urgent need for more effective vaccines. Recent data suggests that the current annual death rate of 3.3 million people per year due to the disease may be increasing. Nearly one-third of the world's population, approximately 2 billion people, is believed to be infected with TB.

Dr. Randy Basaraba

The College of Veterinary Medicine and Biomedical Sciences is home to

the world-renowned Mycobacterium Research Laboratory, which mainly focuses on studies of tuberculosis and leprosy. The laboratory's TB-related work has been supported by more than \$50 million in research grants and has led to several breakthroughs in the field.

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#### West Nile Virus Studies Released

Researchers at the College have released results from a research project that summarized the background

characterization of last year's outbreak of West Nile virus in equids from Colorado and Nebraska.

"The objective of the study was to describe the equine West Nile virus cases in Colorado and Nebraska in order to better understand the progression of clinical

disease, clinical signs, and clini-



vaccinated as well as their survival rate."
Study results indicate:

- The estimated case fatality rate for affected horses in Colorado and Nebraska was 28.6 percent, similar to reports from other regions.
- The age range for equine cases was from three months to 35 years.
- Only 13 cases in the study were fully vaccinated based on current manufacturer recommendations. Of these, the survival status of 12 is known and all 12 horses lived.

 The most common clinical sign associated with West Nile virus infection identified in the study was an altered gait, including reluctance to move, stumbling, perceived lameness, and ataxia or weakness.

The complete study report can be viewed and/or downloaded at ftp://ftp.communications.colostate.edu/westnile.doc or from the University's Animal Population Health Institute Web site at www.cvmbs.colostate.edu/aphi.

Dr. Josie Traub-Dargatz

In a second study released in May, Dr. Traub-Dargatz's team examined the economic impact of West Nile virus on the Colorado and Nebraska equine industries. The study showed that the disease cost equine owners more than \$1.25 million in 2002,

and prevention costs for WNV vaccinations likely exceeded an additional \$2.75 million. Colorado reported 378 and Nebraska 1,100 confirmed cases of WNV in equids.

"To date, no other comprehensive national or regional estimates of WNV's economic impact on the equine industry have been published," said Dr. Traub-Dargatz. "Determining the economic impact of the disease is important for prioritizing current and future research as well as management and control efforts."

The study, published by co-authors from the U.S. Department of Agriculture's Animal and Plant Health Inspection Service, was a cooperative effort among researchers from Colorado State University, the USDA, Colorado and Nebraska State veterinarians, and the veterinary schools at the University of Nebraska and the University of Pennsylvania. A complete copy of the report is available at <a href="https://www.aphis.usda.gov/vs/ceah/cahm/Equine/wnv-info-sheet.pdf">www.aphis.usda.gov/vs/ceah/cahm/Equine/wnv-info-sheet.pdf</a>.



## olorado State, City of Hope Researchers Use Phenomenon of RNA Interference to Improve Resistance to HIV Infection in Human Cells

Using what researchers are calling a "powerful tool," a scientific team at Colorado State University and City of Hope Cancer Center in California has successfully created HIV-resistant human immune system cells that have the promise of leading to new and potent treatments for HIV infection.

The powerful tool is "small interfering RNA," or siRNA, and it has the potential to change the face not only of HIV treatment, but also treatment for other illnesses including hepatitis, cancer, and a catalog of genetic diseases. In the Colorado State-City of Hope study, published in the July issue of *Molecular Therapy*, researchers designed a siRNA that gave T-cells and macrophages — the foundation of the human immune system — resistance to HIV infection.

The research team, led by Dr. Ramesh Akkina, a Professor in the Department of Microbiology, Immunology and Pathology, in collaboration with Dr. John Rossi from City of Hope, placed genetically engineered anti-HIV siRNAs into human blood-forming stem cells.

"These studies are the first in which siRNAs were introduced into bloodforming stem cells," said Dr. Akkina. "The blood-forming stem cells were

Researchers showed that genetically altered stem cells were able to differentiate into mature T-cells and macrophages, that these cells carried with them the siRNAs that provided resistance to HIV infection, and that the cells still were able to fully function as part of the immune system.

genetically altered with anti-HIV small interfering RNAs. The stem cells then were differentiated into macrophages and T-cells — the primary targets in HIV infection — and these immune system cells were shown to express the anti-HIV siRNAs introduced into the stem cells. When challenged with HIV infection, the immune cells showed sustained resistance."

Researchers showed that genetically altered stem cells were able to differentiate into mature T-cells and macrophages, that these cells carried with them the siRNAs that provided resistance to HIV infection, and that the cells still were able to fully function as part of the immune system.

"By genetically altering stem cells with the siRNAs, we hoped the many cells derived from stem cells would carry the new genetic information with them and be able to maintain HIV-resistance," said Dr. Rossi, Chair of the Division of Molecular Biology at City of Hope's Beckman Research Institute and co-investigator of the study. "We also hoped that the alterations would not negatively affect the ability of the stem cell to differentiate or of the immune cells to maintain their function as the body's first-response

medical team."

Dr. Akkina noted that when the collaborative research team began work on this study, they were not certain if siRNAs would have a harmful effect on the stem cells' ability to differentiate, a complication that would have increased the difficulty of developing siRNAs for therapeutic purposes.

"We were putting a foreign molecule into the stem cell and realized that at any point along the differentiation



Dr. Ramesh Akkina

pathway, we could have a negative effect. It was very exciting for us to see the stem cells still able to form immune cells and still express resistance to HIV," said Dr. Akkina. "This helps us get one very large step closer to a new way of treating HIV infection and perhaps gives new hope to the millions of people who are living with this disease."

In the study, the researchers first designed an anti-HIV siRNA that would shut down the virus's ability to replicate. The gene that was targeted in HIV, known as REV, is essential for HIV replication and also conserved throughout the many different HIV types. The gene encoding the anti-HIV siRNA then was inserted into a virus vector that could carry it into the stem cell. The virus, called a lentiviral vector, was derived originally from HIV but rendered non-pathogenic and safe with genetic engineering. Once the lentiviral vector was ready with its anti-HIV siRNA gene payload, researchers delivered it to purified stem cells, called CD34+ cells, which give rise to T-cells and macrophages.

From there, the stem cells took two different routes. Some of the stem cells were cultured in a test tube in the presence of the appropriate growth factors, known as cytokines, which caused the stem cells to differentiate and produce mature macrophages that expressed the anti-HIV siRNAs. Other stem cells were



### C olorado State, City of Hope Researchers

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The HIV research team in Dr. Akkina's lab includes, from left to right, Leila Remling, Dr. Akkina, Joseph Anderson, and Akhil Banerjea.

injected into mice with severe combined immunity deficiencies and implanted human thymus and liver tissue, known as SCID-hu mice. In these animals, the CD34+ cells matured into T-cells as they would in a human environment. These animals provided the scientists a unique and important opportunity to test their research on human tissue in a live animal model.

The macrophages and T-cells derived from the stem cells showed resistance to HIV infection, demonstrating that the procedure was effective both in the test tube and in human cells in living systems. When the virus hit the genetically engineered macrophage or T-cell, it was unable to replicate due to the anti-HIV siRNA with which the cell was now armed.

"Using a viral vector to introduce the anti-HIV siRNA into the stem cells means that the cells that manufacture immune system cells throughout an organism's life now will produce virus resistant cells that carry a copy of the anti-HIV siRNA," said Dr. Akkina. "Our goal is to protect cells that are the main targets for HIV, and that is what siRNA technology is allowing us to do. Stem cells are self-renewing and will continu-

ally produce HIV-resistant macrophages and T-cells, allowing the immune system to maintain its health in the face of HIV infection."

It usually is not HIV that causes death but opportunistic infections that take advantage of the suppressed immune system caused by HIV. Treatment with siRNAs may allow physicians to preserve a patient's immune system, thus helping to manage HIV as a lifelong illness in much the same way as diabetes. In addition, at this point, siRNA therapy seems to be nontoxic as it changes the stem cells themselves — without a detrimental effect — rather than acting upon the entire body.

"We now are poised for human clinical trials, but I don't yet see siRNA as a sole treatment for HIV," Dr. Akkina said. "I imagine that if all goes well, it most likely will be used in conjunction with combination therapy – added to the regimen, not replacing it. In the future though, as more research and clinical studies are completed, that may change. Therapies based on siRNAs certainly have a lot of potential, and we are very excited about what that might mean for the quality of life and longevity of HIV patients and others who suffer with other long-term illnesses."

RNA has long been secondary in science to DNA, the blueprint of life shaped like a twisting ladder in each cell's nucleus. RNAs are nucleic acids associated with control of cellular chemical activities, and for years, scientists believed that RNA was simply at the beck and call of DNA, assigned to shuffling about information from DNA as instructions to make proteins. Extra bits of RNA were thought to be simply excess production by the cell. However, recent studies - studies that some say will reshape the field of biology - have shown that cells also contain pieces of RNA that are not carrying instructions for making proteins. These RNA snippets in fact seem to play a role in gene regulation, while defects in small RNAs may be responsible for the onset of certain diseases such as Prader-Willi and Fragile X Syndrome. Small RNA also may offer new insights into infectious agents such as the hepatitis C virus, which has been tough for scientists to decipher. Small RNA also holds hope for cures.

"We have been looking at gene therapy for HIV in our laboratory for the past 10 years," said Dr. Akkina. "These therapies, using things like gene-silencing ribozymes, showed efficiency, but not at the levels we wanted. Last year, we started using siRNAs, and they proved to be much more powerful."

This study was funded by the National Institute of Allergy and Infectious Diseases of the National Institutes of Health. With the success of the animal model trial at Colorado State, Drs. Akkina and Rossi hope to secure funding soon for human clinical trials at City of Hope, where Dr. Rossi has participated in a number of RNA-based gene therapy studies in humans. Other study participants at Colorado State were Akhil Banerjea and Leila Remling and at City of Hope were Ming-Jie Li, Gerhard Bauer, and Nan-Sook Lee.



## C

### VMBS Faculty Members Receive Honors

Congratulations to faculty members at the College of Veterinary Medicine and Biomedical Sciences who have received numerous honors and awards including:

• Five professors, known for innovative teaching and research at Colorado State University, were announced in April as new University Distinguished Teaching Scholars at the Celebrate Colorado State! luncheon. Among them was Dr.



Dr. Ray Whalen

Lawrence Ray Whalen, a member of the faculty in the Department of Biomedical Sciences. Since joining the faculty of the College in 1982, Dr. Whalen has established a scientific research

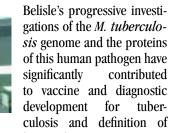
program with strong extramural funding

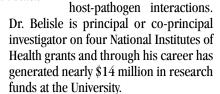
and has developed a career as an influential and creative teacher. His unique gift for using problembased learning and interactive presentations in working with undergraduate, graduate, and Professional Veterinary Medical

students has brought him distinction in local, national, and international venues. Dr. Whalen, whose doctorate and D.V.M. are from the University of California-Davis, received the Innovative Instructional Methodology Award from the College in 2002, the Provost's N. Preston

Davis Award for Instructional Innovation in 2000, and the College's Norden Distinguished Teacher Award in 1986.

• Dr. John Belisle, Associate Professor in the Department of Microbiology, Immunology and Pathology, was selected as one of two recipients of the prestigious Monfort Professor Award, an award established through a gift from the Monfort Family Foundation to help the University recruit and retain top-quality faculty. Dr. Belisle, a Colorado State alumnus, joined the University's faculty in 1999 and is director of the Mycobacterium Research Laboratory, one of the University's most active research facilities and an internationally recognized center of tuberculosis research. Dr.





• Dr. Ed Dudek, a Professor in the College's Department of Biomedical Sciences, has received the prestigious American Epilepsy Society/Milken Family Foundation Epilepsy Award for Basic Science Research. The award was presented in December at the American Epilepsy Society's annual meeting in Seattle, Wash. The



Dr. Ed Dudek

award honors individual pioneers in the field of epilepsy research who advance the Society's and Foundation's mutual goal of creating and carrying out lasting solutions to the challenges facing the 55 million people worldwide with epilepsy. Dr. Dudek has spent more than 25 years investigating the electrical signals transmitted between the neurons in the brain that are critical for information processing. He has focused specifically on studying the mechanisms that synchronize neurons and the alterations that occur during seizure activity, especially in individuals who have suffered an injury to the brain, one cause of epilepsy. Currently, Dr. Dudek is engaged in work on three inter-related projects, each funded by an NIH grant. These NIH grants will total more than \$5 million for the next four or five years and are focused on "translational research," research based on animal models of epilepsy that allow the neuroscientists to design treatments that can be further developed for study in humans.

## lass Agent Survey Shows Strong Support for Veterinary School

Dr. Iobn Belisle

As the College of Veterinary Medicine and Biomedical Sciences prepares to start a major building campaign to improve and expand the South Campus, class agents report they are firmly committed to the College and its desire to continue to offer one of the best veterinary medical educations in the country.

Recently, the College conducted a survey of class agents from the classes of 1940 through 2002. Class agents are

the representatives from their respective veterinary classes who act as liaisons between their class and the College. The survey asked agents to rate their education at Colorado State, as well as rank the importance of good facilities to good education, among other questions.

This fall, the College hopes to begin fundraising for the 25-year master plan to develop the College's South Campus, including the James L. Voss Veterinary Teaching Hospital. Because most of the funding for the new facilities will come from private donors, the College was interested in assessing how class agents felt on a number of issues regarding the College; its programs in teaching, research, and outreach; and the impact of existing and planned facilities. The overall result of the survey was strong support for expansion, especially regarding the positive effects these plans



### lass Agent Survey

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would have on the teaching and clinical programs. Highlights of the survey include:

- 90 percent of those surveyed were extremely pleased or very pleased with their education from Colorado State University.
- 89 percent believe it is extremely important or very important for the College to retain its role as one of the top veterinary colleges in the country.
- 94 percent believe it is important for D.V.M. alumni to be informed that funding from the state of Colorado provides less than 25 percent of the overall cost of operating the College. Continued excellence in education, service, and research can only come with private funds.
- 77 percent believe D.V.M. alumni would be willing to support the building of new facilities; 62 percent believe D.V.M. alumni would be willing to provide corporate sponsor contact information; and 71 percent believe D.V.M. alumni would be willing to provide contact names of potential donors.

"The responses indicate that it is important for the College to retain its role as one of the top veterinary colleges in the country, and there is almost unanimous agreement that the quality of educational facilities can significantly impact the quality of education and research," said Dr. Lance Perryman, Dean of the College. "The response as to how willing D.V.M. alumni would be to support the building of new facilities is encouraging and the suggestions for other avenues to solicit support are very helpful."

Dr. Perryman also noted that there was a strong message from many respondents that while new facilities and expansion for research are important, teaching and clinical training should remain a high priority for the College.

"In every aspect of our vision for the future, a key motivation is to enhance and expand our capacity to enrich the education and clinical training of our students," Dr. Perryman said. "The initial phase of the South Campus expansion is dedicated to improving the infrastructure of the Veterinary Teaching Hospital to create a better training environment, improve animal care, and allow for greater learning opportunities."

The College would like to thank all the class agents who took part in the survey. Your voices will help to shape our future. To learn more about the College's 25-year master plan, you can go to the College's Web site and read the article, "25-Year Plan Takes College into the Future," in the Spring 2003 edition of *Insight* at www.cvmbs.colostate.edu/insight.

College of Veterinary Medicine and Biomedical Sciences



Knowledge to Go Places

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