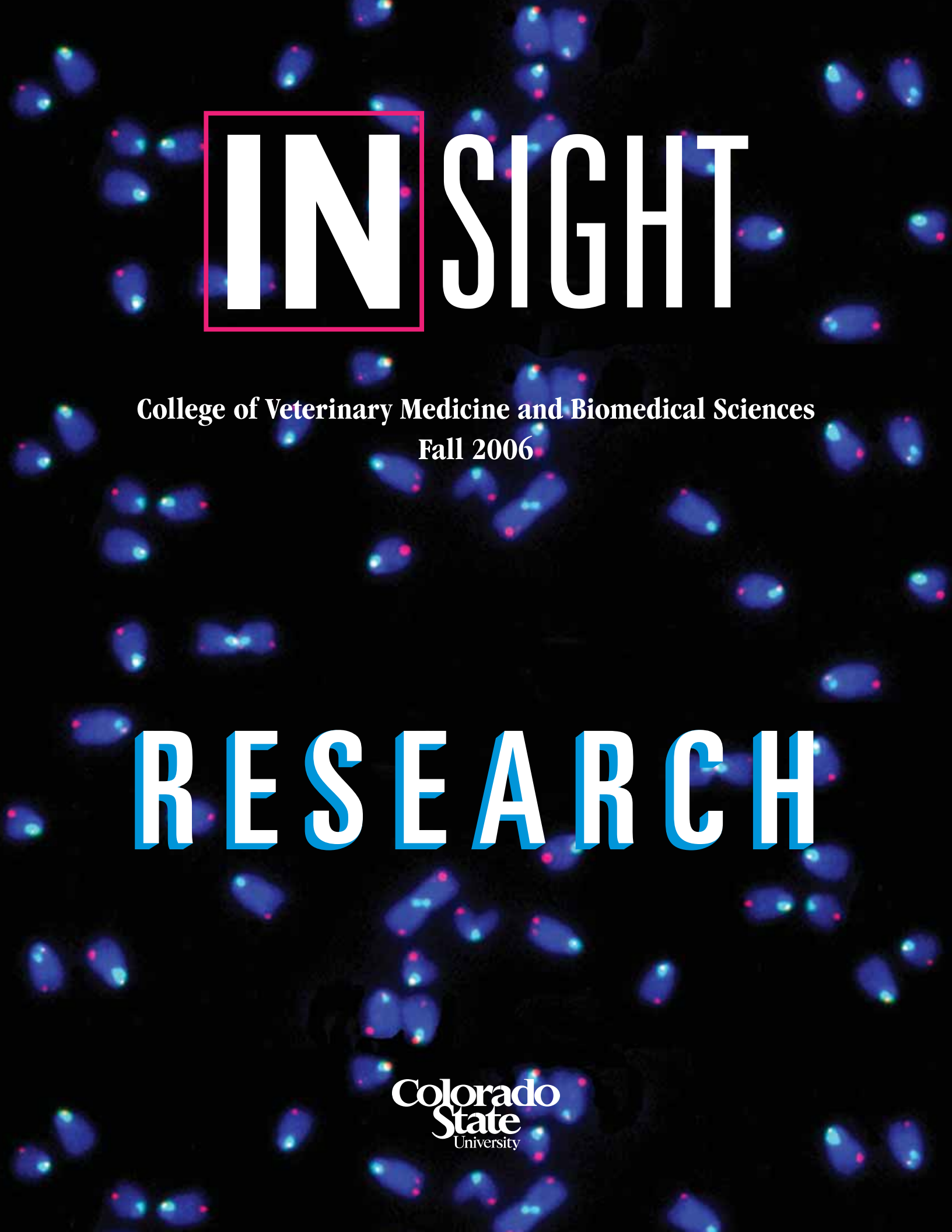

INSIGHT

College of Veterinary Medicine and Biomedical Sciences
Fall 2006

RESEARCH

Colorado State University

INSIGHT
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Fall 2006

College of Veterinary Medicine and Biomedical Sciences

On the cover:
Dr. Susan Bailey, with the Radiological Health Sciences and Cancer Research Program, uses the technique of chromosome orientation fluorescence in situ hybridization (CO-FISH) in her studies of telomeres. The cover image shows a mouse chromosome spread following CO-FISH with the mouse major satellite (green) and telomere (red) probes, two highly repetitive regions. CO-FISH signals split between the two chromatids indicate chromosome recombination events, a biological breakdown that can increase the risk of cancer.

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Production Coordinator: Colleen Rodriguez.

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Welcome to the Fall 2006 Research Edition of *Insight*

In this special edition of *Insight*, we focus on six research programs within the College of Veterinary Medicine and Biomedical Sciences that are exploring fields of study critical to understanding and improving human and animal health concerns.

You'll learn about the Infectious Disease Supercluster, the first such supercluster at CSU; the Animal Reproduction and Biotechnology Laboratory; the Orthopaedic Research Center, with its focus on equine and human orthopaedic disease and injury; the Radiological Health Sciences and Cancer Research Program, where clinical and basic research come together; the Veterinary Diagnostic Laboratory, one of the largest in the nation; and the High Plains Intermountain Center for Agricultural Health and Safety, where investigators are helping to improve farm safety.

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

Insight Correspondence
Office of the Dean
College of Veterinary Medicine and Biomedical Sciences
Colorado State University
1601 Campus Delivery
Fort Collins, CO 80523-1601

You can e-mail *Insight* comments to Carol Borchert, *Insight* Editor/Writer at: carol.borchert@colostate.edu. We also invite you to visit us at our Web site at: www.cvmbs.colostate.edu. ■

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Message from the Dean

Dear Friends,

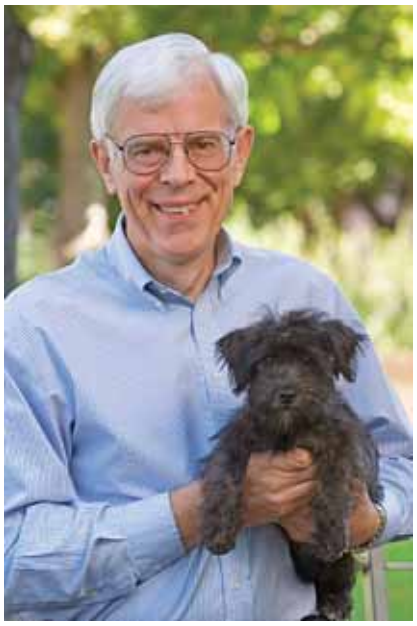
In the popular press, breakthroughs in medical science, the latest in cancer treatments and new, frightening diseases are processed through a sensationalist lens that often diminishes true concerns, oversells incremental advances, and scares a public all too vulnerable to the latest health threat (does anyone remember monkey pox?). Against this backdrop, scientists around the world and here at the College of Veterinary Medicine and Biomedical Sciences are busy doing the intricate work of science that rarely makes it into mainstream media, but is essential to the advancement of human and animal health.

In this edition of *Insight*, you'll have the opportunity to learn about research programs at the College that are tackling some of our society's greatest concerns including infectious diseases, debilitating injuries, cancer and radiation biology, worker health and safety, food safety, and bioterrorism. It is work that is slow and laborious, frustrating and rewarding, detailed and painstaking, with hard-won answers usually leading to more questions. Success is measured in small increments, as the sum of research programs from around the world lead to the "breakthroughs" gained, usually after countless years of supportive research.

I'm proud to report to you that the College has a number of internationally recognized research programs that are making a difference in the lives of people and animals today. Improvements in the treatment of osteosarcoma (bone cancer) in dogs have led to better treatment for human patients. Equine orthopaedic research is not only leading to healthier horses, but to advances in human orthopaedic care. Infectious disease research has exploded at Colorado State University, with realistic goals of developing and/or testing vaccines and treatments for globally important devastating illnesses including dengue fever, tularemia and tuberculosis. Our Veterinary Diagnostic Laboratory is an internationally renowned center of testing and test development for transmissible spongiform encephalopathies, including chronic wasting disease and bovine spongiform encephalopathy (mad cow disease), as well as a growing program in avian influenza testing and surveillance.

In our last fiscal year, the College's extramural research budget was close to $50 million. That not only means our scientists are able to conduct cutting-edge research, but our graduate and undergraduate students are benefiting from their experiences in some of the world's most advanced laboratories. Training new and inquisitive scientists who will be able to address current and future concerns is an important part of our mission.

"In our last fiscal year, the College's extramural research budget was close to $50 million. That not only means our scientists are able to conduct cutting-edge research, but our graduate and undergraduate students are benefiting from their experiences in some of the world's most advanced laboratories."



Dr. Lance Perryman and Lexi

I hope you enjoy this edition of *Insight* and come away with a favorable impression of the work underway at the College of Veterinary Medicine and Biomedical Sciences. Who knows, maybe one day, your life or the life of someone you love may be profoundly impacted by discoveries that originated at Colorado State University. ■

Best Regards,

Lance Perryman, DVM, PhD
Dean, College of Veterinary Medicine
and Biomedical Sciences

Infectious Disease Program Selected as First University Supercluster

When the Supercluster Request for Proposals went out April 14, the College of Veterinary Medicine and Biomedical Sciences was honored to have one of its Programs of Research and Scholarly Excellence – the Program in Infectious Disease – expanded and grandfathered in as Colorado State University's first designated research Supercluster.

"Designation as a Supercluster is a great tribute to all the individuals who have worked so hard to create an internationally renowned program in infectious disease here at Colorado State University," said Dr. Lance Perryman, Dean of the College of Veterinary Medicine and Biomedical Sciences.

Superclusters are specially sanctioned interdisciplinary alliances that will allow CSU to focus on key research initiatives in topical areas where the University has demonstrated globally competitive expertise and potential for growth. Annual budgets are provided by the University to enhance the Superclusters collaborative efforts to obtain project goals of global significance.

Dr. Perryman noted that during the past several years, the College has seen a huge investment in the Program in Infectious Disease by the University, the College and numerous federal programs. This includes a $40 million grant to establish the Rocky Mountain Regional Center of Excellence for Biodefense and Emerging Infectious Diseases at CSU, and funding for construction projects such as the $30 million Regional Biocontainment Laboratory, the Bioenvironmental Research Building, new laboratory facilities for the Veterinary Diagnostic Laboratory (D-Lab) and more. In the last Colorado legislative session, the D-Lab received $3.5 million in funds to initiate planning for the new Veterinary Diagnostic Center.

Exterior of the RBL.

"There is international concern over the re-emergence of infectious diseases, as well as drug-resistant infectious diseases such as tuberculosis," said Dr. Jeffrey Wilusz, Head of the Department of Microbiology, Immunology and Pathology, home to the majority of faculty members affiliated with the Infectious Disease Supercluster. "While Colorado State University has had a world-class program in infectious disease for many years, we are now seeing other entities – including government and private interests – take a renewed look at this issue and begin to put real resources behind it."

Interior of the RBL.

The overall mission of the Infectious Disease Supercluster is to "effectively mobilize CSU entities and resources to address major global challenges in the infectious disease arena." Major focuses of research include diseases caused by retroviruses, which cause AIDS and other diseases; mycobacterial infections including tuberculosis and leprosy; vector-borne diseases, which through insect transmission cause encephalitis, West Nile disease, dengue fever and other diseases; and blood parasites, which are a major cause of disease in developing countries. With the emergence of the potential for bioterrorism, additional urgency has been created in developing treatments and vaccines to many emerging infectious diseases with the potential to be weaponized.

Researchers with the Infectious Disease Supercluster collaborate closely with the Fort Collins-based branch of the Centers for Disease Control and Prevention. Funding for research is provided by the National Institutes of Health, Department of Defense, Homeland Security, USDA and other federal agencies. Researchers also are supported through private foundations, including the Bill and Melinda Gates Foundation.

For more information about the Infectious Disease Supercluster, visit the Department of Microbiology, Immunology and Pathology Web site at www.cvmbs.colostate.edu/mip/. ■

Dual Task of Understanding Select Agent Physiology While Developing New Therapeutics and Vaccines a Research Challenge

Researchers at the Rocky Mountain Regional Center of Excellence for Biodefense and Emerging Infectious Diseases (RMRCE) are charting new territory as they embark on investigations into infectious agents that have received little attention over the years. The factor creating the need for an infusion of resources into these diseases is that these agents can be turned into biological weapons.

The challenge for RMRCE researchers like Drs. Catharine Bosio and Steven Dow is that the National Institutes of Health is asking not just for basic science research, it wants research that will deliver viable treatments and effective vaccines. This applies to a lengthy list of infectious agents, many of which are poorly understood and, up until recently, have received little attention from the biomedical community due to limited threat and a lack of resources. Bioterrorism, however, is creating a new field of research into select agents that can be engineered into weapons.

"The need for vaccines is great, especially for first responders and for troops going into areas where some of these diseases, like tuleremia, are endemic," said Dr. Bosio, an Assistant Professor in the Department of Microbiology, Immunology and Pathology (MIP) and co-principal investigator and co-investigator on several RMRCE projects. "In a bioterrorism attack with these agents, which are typically found in nature, the agents can in some cases be engineered to increase their ability to cause disease, make them resistant to current medicines, or to increase their ability to be spread into the environment.

"One area of particular concern is pathogens that can be inhaled and potentially cause more severe disease and rapid disease. We want to understand the response in the lung – how it gets rid of a pathogen and what it considers benign. There are a lot of questions that need to be answered."

Bioterrorism agents can be separated into three categories depending on how easily they can be spread and the severity of illness or death they cause. Category A agents are considered the highest risk and Category C agents are those that are considered emerging threats for disease. Researchers with the RMRCE work with select agents in Category A and B, including *Yersinia pestis*, *Burkholderia mallei* and *B. pseudomallei*, *Francisella tularensis* and others.

"We are particularly interested in the development of new immunotherapeutic approaches for *Yersinia* and *Burkholderia*. We've previously developed immunotherapeutics for treatment of cancer and we now want to expand this platform to the treatment and prevention of infectious diseases," said Dr. Dow, an Associate Professor in the Department of Clinical Sciences and MIP, and principal investigator with Dr. Bosio on the RMRCE project *Role of Innate Immunity in Pulmonary Burkholderia Infection*. "We are looking at innate immune responses, the body's first line of defense against pathogens, and how we can give that a boost particularly in the lungs."

Dr. Dow noted that the first step in creating new immunotherapies is the development of a mouse model that will allow researchers to assess immunologic responses to infection with newer agents such as *Burkholderia*. Much of this work will build on recent studies done in the lab to develop a mucosal vaccine against pneumonic plague (*Yersinia pestis*) which also are being conducted by Drs. Dow and Bosio under a separate NIH grant. After the *Burkholderia* infection model is established, the research team then wants to determine the role of key cytokines and signaling molecules in controlling *Burholderia* infection in the lungs. The final step will be assessing the ability of a novel immunotherapeutic developed in their lab to elicit protection from infection. These studies will be conducted concurrently with plague vaccine studies which will involve the development and testing of new vaccine adjuvant platforms (substances added to vaccines that intensify the immune response to an antigen).

Drs. Steven Dow and Catharine Bosio

In the *Francisella tularensis* study, Dr. Bosio is co-investigator with Dr. John Belisle, and they are developing proteomic techniques to identify dominant antigens that may provide a set of vaccine candidates to evaluate in conjunction with new adjuvants. The goal of the study is to develop three or four vaccine formulations that will eventually enter clinical studies.

"Many of the diseases we are working with now have long been neglected because they weren't a major concern in the United States," said Dr. Bosio. "For example, we see maybe 100 cases of tularemia a year in the United States but it is potentially a real threat as a bioweapon because it is one of the most highly infective bacteria known. Just a few organisms, sometimes fewer that 10, can cause disease. With new funding from the NIH, we are exploring and learning so much about these pathogens, and we expect that what we discover here will apply to other infectious diseases that cause much suffering around the world." ■

Animal Reproduction and Biotechnology Laboratory Continues to Expand Boundaries

West of Fort Collins, at Colorado State University's Foothills Research Campus, are a series of ordinary-looking buildings where some extraordinary things are happening. Using the latest technology has to offer, from cloning and cryopreservation to immunochemistry and immunology, the Animal Reproduction and Biotechnology Laboratory (ARBL) is home to cutting-edge research programs that are leading to breakthroughs in human and animal reproductive health.

"Since the inception of the original Animal Reproduction Laboratory in 1972 (though the Bull Farm was established in 1941), the ARBL has contributed substantially to the advancement and understanding of reproductive health," said Dr. Thomas Hansen, Director of ARBL and a Professor in the Department of Biomedical Sciences. "Our faculty, staff and students are devoted to finding solutions to important problems in animal reproduction and human health."

Research programs within ARBL include hypothalamic-pituitary functions; ovarian function, gamete biology and embryology; uterine, placental and fetal physiology; assisted reproductive technologies; and reproductive toxicology and diseases. Faculty affiliated with ARBL come from the College of Veterinary Medicine and Biomedical Sciences and the College of Agricultural Sciences. Cross-departmental cooperation gives researchers a broader view and additional expertise from which to draw upon for research programs with a broader scope. Researchers also collaborate with colleagues from other academic and government institutions, including the University of Colorado Health Sciences Center and the U.S. Department of Agriculture, as well as private companies.

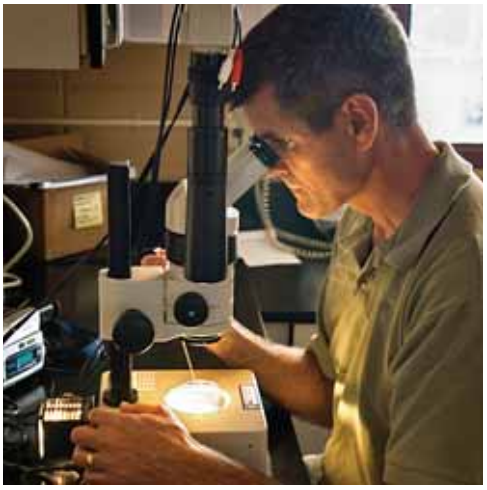
"Over the years, our faculty have been recognized for many firsts such as development of vaccines, contraceptives, reproductive hormones and antibodies, sexing sperm, test-tube fertilization to produce a live foal, and birth of a foal from frozen oocytes," said Dr. Hansen. "While advancing reproductive science, we also are learning basic reproductive biology including why things work the way they do and, more importantly, understanding why sometimes things don't work."

Many of ARBL's bovine assisted-reproductive technologies such as freezing and storing semen and embryo transfer have now been translated for use in horses. Also, the equine faculty has developed the technique of obtaining foals from mares that have recently died. Ovaries are sent to CSU, eggs are harvested and are either injected with sperm and transferred to recipient mares (ICSI) or are transferred to the fallopian tube for in vivo fertilization (GIFT). Researchers also are able to collect sperm from the epididymus of stallions that have recently passed away. In this case, sperm from the stallion is stored frozen until it is used in artificial insemination or it is injected into an egg from a donor mare, which is then transferred into the fallopian tube of a recipient mare. One of the first foals born using these technologies was for Cecilea Hylton. She was so excited about this foal that the Hylton Foundation provided ARBL more than $500,000 to support the research.

Enabling researchers in their reproductive studies at ARBL are specific facilities for cryopreservation of gametes and embryos, and cloning; DNA sequencing and characterization of genes; measurement of hormones, receptors and other compounds of biologic interest; transmission electron microscopy; isolation and culture of cells; immunology and immunochemistry; production of transgenic animals; analysis of semen, and embryo transfer. In addition to its research program, ARBL also is known worldwide for its short courses in animal reproduction and reproductive biology, and for its graduate and postdoctoral programs. Service units include the Reproductive Endocrinology Laboratory, Sperm Morphology Services, and Equine Reproductive Services.

In 1989, the Colorado Commission on Higher Education selected ARBL to be a state-supported Program of Excellence. The University named ARBL as one of 11 Programs of Research and Scholarly Excellence that same year. ARBL also has maintained a competitive National Institutes of Health Training Program in Mammalian Reproduction for postdoctoral fellows and PhD students. This federally funded program has continued for 30 consecutive years. The long-term objective of this program is to train young scientists in a broad approach to solving reproductive problems encompassing both molecular and organismic biology. Scientists trained in this manner will be able to use a broad array of approaches to address important basic and applied questions in modern reproductive biology.

For more information on the Animal Reproduction and Biotechnology Laboratory, visit their Web site at www.cvmbs.colostate.edu/bms/arbl.htm. ■



Dr. Patrick McCue, Associate Professor, Department of Clinical Sciences, in the Animal Reproduction and Biotechnology Lab (ARBL)

Collaborative Studies into Growth-Restricted Pregnancies Bring Researchers from CSU and UCHSC Together

At the University of Colorado's Health Sciences Center – Perinatal Research Facility in Denver, sheep are helping researchers understand some of the intricacies of fetal development, including how and why things go wrong. Dr. Russell Anthony, Colorado State University's Hill Professor of Animal Biotechnology in the College's Department of Biomedical Sciences, leads the collaborative effort between Colorado State University and the University of Colorado, capitalizing on both schools' strengths to more quickly push forward innovative research into growth-restricted pregnancies.

"More recently, our research has shifted from molecular/cellular aspects toward placental/fetal interactions, primarily in growth-restricted pregnancies," said Dr. Anthony, who has a joint appointment in the Department of Pediatrics at UCHSC and also is a faculty member with the College's Animal Reproduction and Biotechnology Laboratory. "In the United States, 8 to 10 percent of babies suffer from clinical fetal growth restriction. Worldwide the number is closer to 17 percent. In 80 percent of these growth-restricted infants, the underlying cause is a functional failure of the placenta to grow, develop and provide groceries to the baby in utero."

One of the focuses of Dr. Anthony's research is placental insufficiency. His research team is investigating the early stages of placental development, trying to understand what is going wrong that leads to low birth-weight babies who are small for their gestational age.

"Intrauterine growth restriction is a clinical diagnosis where the size of the head is maintained but the abdomen and trunk are proportionately smaller, displaying asymmetric growth," said Dr. Anthony. "And we are not only concerned about the developing infant. In the last 15 to 20 years, epidemiologists have been able to demonstrate that infants born at low birth weight have a higher predisposition to coronary heart disease, type 2 diabetes and hypertension as adults. We are finding that fetal organ systems, if not nourished at the right time, can suffer impaired development that can create lifelong health concerns."

Some causes of growth-restricted pregnancies, such as smoking, drug abuse and high altitude, are apparent. But, Dr. Anthony noted, most growth-restricted pregnancies are idiopathic cases with no apparent external or environmental cause.

"We are using sheep as a model and have developed various ways to set up growth-restricted pregnancies where we can assess oxygen, glucose and amino acids transfer to the fetus, and examine uterine and umbilical or fetal organ blood flow," said Dr. Anthony. "We are trying to look at the same end points that are examined in human cases, while we monitor pregnancies and verify that what we are seeing is truly mimicking what we know about growth-restricted pregnancies in humans."

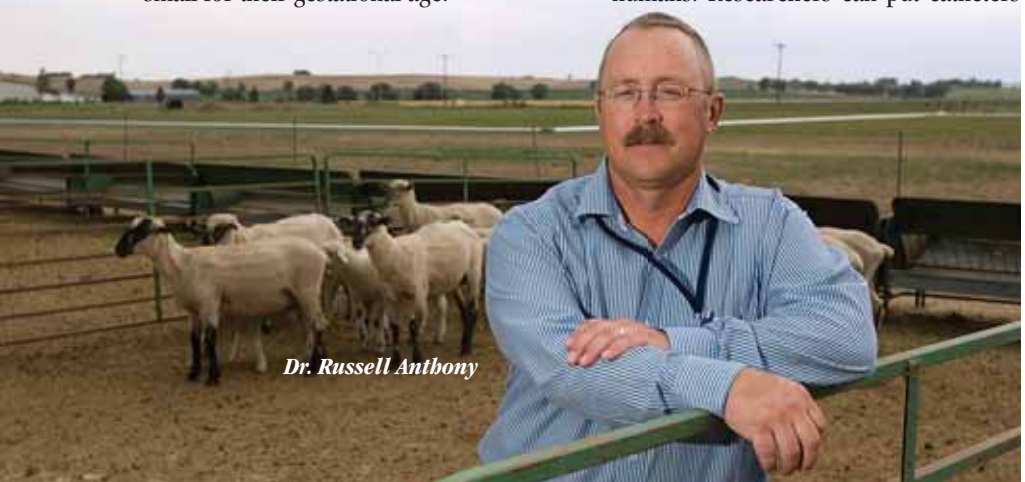
Using sheep as a model, researchers can take the next step, going further and looking at things that can't be done in humans. Researchers can put catheters into the fetus mid-gestation and not disrupt the pregnancy. With the catheters, they are able to look at nutrient transfer, oxygen transfer, and other markers of fetal growth and development.

Collaborating with researchers in Italy, where ultrasound monitoring of pregnancies is more routine, the CSU and UC team has good guidance on what to look at and where to focus. They are also looking at stable isoptomers of amino acids and glucose that can be tracked across the placenta into the fetus.

"A lot of development of methodology is done here at CSU," said Dr. Anthony. "As we develop new approaches, we transfer that technology to Denver. There are a lot of things we can do here much more cost-effectively than there. For example, the CSU team has a grant to look at a gene called peri-attachment factor. It is expressed early in gestation and during the period of maternal recognition of pregnancy in cattle and sheep. The gene also is expressed later in gestation and researchers are working to determine the role it plays then as well. They are using *in vivo* RNA interference to examine the function of this protein, and that technology may be applied to growth-restricted pregnancies in the future.

"We also do a lot of cross-training of researchers and physicians from both institutions. The physicians get a good appreciation of how basic research is impacting clinical practice, and our graduate students get to see the big picture of why the work they are doing is so important."

Dr. Anthony hopes that through the work of the CSU-CU team, scientists can better understand the aspects of placental development that are problematic, including key developmental mechanisms, and begin to look at early treatments that may prevent or reduce conditions leading to growth-restricted pregnancies and the associated long-term health risks. ■



Dr. Russell Anthony

Orthopaedic Research Center Advances Treatment of Joint Disease/ Musculoskeletal Injury

Dr. Wayne McIlwraith is sometimes described as a horse's best friend. A pioneer in orthopaedic research, many of the advances in technique, technology and treatment made by the Orthopaedic Research Center (ORC) have greatly benefited both the recreational and athletic horse. But Dr. McIlwraith, Director of the ORC and a Professor in the Department of Clinical Sciences, also has a special bond with the horses whose lives he hopes to improve.

For years following an injury sustained while rock climbing, Dr. McIlwraith dealt with joint pain in his left hip. Determined to avoid surgery as long as possible so he could keep climbing, Dr. McIlwraith finally underwent hip replacement surgery last year – but only after finding a doctor who would agree to help him keep climbing (and he still is). His struggle with injury and joint pain has brought home the importance of the work done at the Orthopaedic Research Center, not only from the viewpoint of helping equine patients, but also the importance of using what is learned to improve the quality of human life.

"It's pretty incredible when we look at the advances that have been made just in the past 30 years," said Dr. McIlwraith. "Injuries that would have been career-ending for the equine athlete are now routinely treated, this is especially so since the advent of arthroscopic surgery. But there is still so much we are trying to do, and so many areas for improvement in prevention, diagnosis and treatment. This is a very exciting time to be in this field, when new technologies and innovative techniques are truly making a difference in the lives of horses."

The ORC is part of the interdisciplinary Musculoskeletal Research Program which is comprised of three units: the Orthopaedic Research Center; the Orthopaedic Bioengineering Laboratory, focusing on the treatment and prevention of muscular, neuromuscular and skeletal injury and disease; and the Comparative Ruminant Orthopaedic Laboratory where sheep provide a model for researching important orthopaedic problems, including osteoporosis and bone implants for cancer patients.

Today, the ORC has four major areas of research:

- **Joint Tissue Healing** – This addresses principally articular cartilage healing, but has been expanded to include other tissues such as tendons.
- **Early Diagnosis of Bone and Joint Disease** – This includes the development of novel imaging techniques (present and future), body fluid markers and also molecular monitoring. The use of these early diagnostic techniques includes: evaluation of the pathogenisis of bone and joint disease; early detection of disease processes; and monitoring of therapy with the long-term goal of preventing severe arthritis or failure.
- **Improvement in the Understanding of the Pathogenesis of Exercise-Induced Traumatic Disease** – These investigations use both molecular tools such as reverse transcriptase PCR evaluation of tissues in various stages of disease as well as biomechanical studies in joint modeling. The imaging and biomarker techniques are critical here to try and find ways of diagnosing early microdamage.
- **Continued Development of Novel Therapies for Traumatic Synovitis, Capsulitis and Osteoarthritis in the Horse** – These include evaluation of biological inhibitors of critical mediators in joint disease including the use of gene therapy techniques.

Dr. Wayne McIlwraith

"The focus of our research is, of course, the horse, but one of the great

Researchers Hope Studies Will Lead to Prevention of Catastrophic Injuries in Horses

aspects of what we do is that our discoveries are advancing human orthopaedic medicine as well," said Dr. McIlwraith. "Over the years, we have worked with human orthopaedic researchers and physicians, including those at the Steadman-Hawkins Clinic in Vail, one of the finest orthopaedic centers in the world, and researchers from institutions across the nation and around the world. These are productive and beneficial collaborations that we hope will help to alleviate the suffering of both the equine and human patient."

For more information on the Orthopaedic Research Center at Colorado State University, visit their Web site at www.equineortho.colostate.edu. ■

> "Injuries that would have been career-ending for the equine athlete are now routinely treated, this is especially so since the advent of arthroscopic surgery. But there is still so much we are trying to do, and so many areas for improvement in prevention, diagnosis and treatment."

At the start of the Preakness Stakes last May, excitement was in the air. The horses were edgy, anticipating the race's start, including Kentucky Derby winner Barbaro, the horse many thought might be the one to take home the Triple Crown nearly 30 years after the last winner (Affirmed in 1978). Once they were off, within seconds, excitement turned to horror as Barbaro's right rear leg twisted at a sickening angle and it became clear that he had suffered a life-threatening injury.

Veterinarians later confirmed that Barbaro had experienced a break to his cannon bone above the ankle, a broken sesamoid bone behind the ankle, and a shattered pastern, as well as a dislocation in the ankle joint, or fetlock – all without warning. Dr. Wayne McIlwraith, Director of the Orthopaedic Research Center (ORC) at the College of Veterinary Medicine and Biomedical Sciences, has watched the race tape, as well as seen and treated such catastrophic injuries in many other horses. It's something that he and his research team are hoping they can prevent from happening to other horses through the development of new diagnostic imaging techniques and fluid biomarkers that will predict and prevent catastrophic injuries before they happen.

"The challenge with many of these horses is there is no obvious evidence before a race that something is wrong," said Dr. McIlwraith. "In the United States, race track veterinarians evaluate horses before events to determine the fitness of the horse to race. At big races, like the Breeder's Cup, an inspection team of four veterinarians watches and examines the horses for four days before the Cup. If a horse is lame, it's pretty easy to see. Jockeys and trainers also monitor their horse's health. But horses may have other degrees of disease we know occur and lead to these catastrophic injuries, but aren't apparent at a clinical level."

Dr. McIlwraith's group is attacking the problem from multiple angles, including diagnostic imaging techniques, fluid biomarkers and racetrack surface evaluation. Advances in imaging are improving the early diagnosis of injury to soft tissues, articular cartilage and bone. The ORC uses digital radiography, nuclear scintigraphy, computed tomography (CT) and magnetic resonance imaging (MRI) for clinical cases and research projects. Drs. McIlwraith, Chris Kawcak, Natasha Werpy, David Frisbie and Richard Park are all involved with this work.

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Julia Stangel, a research associate in the Molecular Biology Laboratory at the ORC.

Research Program Goes from Laboratory Bench to Clinical Setting in Search of Answers

In the Molecular and Radiological Biosciences Building (MRB) on Colorado State University's main campus, research is underway on a gene defect that may make women more susceptible to breast cancer, on energetic heavy ions that may make astronauts more prone to cancers like leukemia, and on radiation damage to the protective buffers on chromosomes. Meanwhile, at the Flint Animal Cancer Center, veterinarians are applying new treatment modalities to patients with bone cancer, lymphoma, soft-tissue sarcomas and more.

While distinct in their focus, what brings these two groups together – the basic research side and the clinical research side – is that investigators work together under the umbrella of the Radiological Health Sciences and Cancer Research (RHSCR) Program of Research and Scholarly Excellence to advance cancer prevention, diagnosis and treatment for animals and humans.

"It seems too easy for many scientists to get bogged down in the details of their research work, some losing track of the bigger picture and what is really at stake," said Dr. Robert Ullrich, Director of the RHSCR. "When basic and applied researchers work side by side, we can accomplish so much more because we have a greater understanding of what it is we are working to accomplish. At the Animal Cancer Center, every day we see cancer patients who may be one breakthrough away from being cured. Also, at the MRB Building, so much of what we do relates to human cancer using animal models provided by the Animal Cancer Center, based on naturally occurring animal tumors."

Melinda Wilhelm and Chana Fuller prepare a patient for an MRI at the Animal Cancer Center.

The Radiological Health Sciences and Cancer Research Program provides education, research and service related to carcinogenesis, cancer prevention, radiation protection, cancer diagnosis and experimental therapeutics. The multi-departmental and multi-college program collaborates on many projects with researchers at the Flint Animal Cancer Center at the James L. Voss Veterinary Teaching Hospital, using animal models with naturally-occurring tumors to advance the diagnosis and treatment of cancer in humans and animals.

> "When basic and applied researchers work side by side, we can accomplish so much more because we have a greater understanding of what it is we are working to accomplish."

In 2003, the Cancer Biology Group, housed within the Department of Environmental and Radiological Health Sciences, received a competitive grant from the National Aeronautics and Space Administration. The five-year, $9.7 million grant is helping researchers develop a better understanding of radiation risks to astronauts during deep-space travel and prolonged stays in space. But the grant also is helping researchers understand the pathology of acute myelogenous leukemia (AML), one of the most common types of radiation-induced leukemia.

Additional areas of focus for researchers at the RHSCR include: cellular radiation biology, DNA repair, radiation genetics, cancer genetics, molecular cytogenetics, spontaneous animal tumors as models for human medicine, radiation therapy for cancer, cancer imaging, prediction of tumor response to therapy via cellular assays, novel cancer treatments, nuclear medicine, cell immortalization, chromosome instability, viral carcinogenesis, radiation-induced mammary cancer.

For more information on the Flint Animal Cancer Center and the Radiological Health Sciences and Cancer Research group, visit their Web sites at www.cvmbs.colostate.edu/erhs and www.csuanimalcancercenter.org. ■

Protective Caps on Chromosomes Show Scientists How Variation Can Affect Cancer Risk

Dr. Susan Bailey studies the images gaily lighting up her computer screen and notes the total state of disarray. In bright reds, yellows and greens, this picture of chromosomes may look beautiful, but it shows a system that is failing to protect the most basic structure of life – the genome.

In humans, as well as in every other eukaryotic organism (organisms with a complex cell or cells), chromosomes are arranged in a linear fashion. The physical ends of the chromosomes, or telomeres (literally meaning "end-part") were first described by scientists almost 70 years ago based on the telomere's end-protection function. Telomeres consist of highly repetitive DNA that preserves chromosomal stability, including protecting the ends of chromosomes from degradation and preventing chromosomal ends from improperly fusing. Every time the cell divides, the telomere erodes a little bit so that over time, with aging, exposure to carcinogens, or genetic disease, telomeres shorten and eventually malfunction. Telomeres can be extended by telomerases, a specialized enzyme involved in the synthesis of telomeres. Telomerase, however, is active only in germ line and stem cells, and certain white blood cells, but is repressed in most cells of the body. A notable exception is cancer cells, where high telomerase activity creates "immortal" cells, capable of dividing forever (which is why they can form tumors).

"We are investigating relationships between DNA repair and telomere biology – specifically we are looking at the role of dysfunctional telomeres in carcinogenesis," said Dr. Bailey, an Assistant Professor in the Department of Environmental and Radiological Health Sciences and investigator with the Cancer Biology Group. "Through the Flint Animal Cancer Center (ACC), we have the opportunity to evaluate canine tumors and determine telomere length and telomerase status, which are more similar to human than the mouse, thus using dogs as a model for human cancer to better understand the role telomeres play in the development of cancer."

When telomeres aren't functioning properly, researchers see rearrangement and misjoining of chromosomes. This chromosome instability can contribute to increased cancer risk. Also, some individuals are more prone to chromosomal instability than others. From a practical point of view, understanding this vulnerability and how it impacts DNA repair capability may help these people make better decisions regarding exposures to carcinogens and cancer therapy options.

Understanding telomerase and telomeres, said Dr. Bailey, will not only help to define risk; it will also help to develop more refined treatments of cancer.

"Telomerase is very active in cancer cells, with the vast majority of tumors being telomerase positive," said Dr. Bailey. "By developing telomerase inhibitors, we may be able to target cancer cells specifically. Combining this strategy with reducing DNA repair may speed up the process and kill tumors faster. This is a very exciting area of research."

Working with many collaborators over the years, including Dr. Maria A. Blasco, a researcher in Spain who developed the telomerase knock-out mouse, Dr. Bailey and her team continue to examine telomere function and carcinogenesis. Dr. Bailey is working with Drs. Sue Lana and Kelvin Kow at the ACC on canine osteosarcomas. She is establishing collaborative efforts with researchers in the lab of Dr. Thomas Cech at the University of Colorado's Health Sciences Center. Her research team works closely with Dr. Robert Ullrich's (Department of Environmental and Radiological Health Sciences) laboratory and is currently examining the role of telomeric proteins in the DNA damage response in collaboration with Dr. Jacob A. Aten, a researcher in the Netherlands. Her team is examining the role of telomere instability in human breast cancer, collaborating with Dr. Alice Sigurdson of the Radiation Epidemiology Branch of the National Cancer Institute. They also are modeling the role of telomeric vs. genomic recombination in collaboration with Dr. Edwin H. Goodwin of Los Alamos National Laboratory. Dr. Bailey's work on mouse Pot1, in collaboration with Dr. Sandy Chang at the M.D. Anderson Cancer Center, was recently accepted for publication in *Cell*. ■

Assistant Professor Susan Bailey, Department of Environmental and Radiological Health Sciences

Nuclear Medicine Offering Novel Options for Difficult-to-Treat Cancers

In cancer therapy, there is a fine line between helping a patient and hurting a patient. Many drugs and technologies that can effectively kill cancer cells also cause irreparable harm to the patient, and so have been put on the back shelf. Today, thanks to advances in drug delivery systems and creative thinking, some of those shelved options are giving cancer patients new hope.

Researchers at Colorado State University's Diagnostic Imaging Group's Nuclear Medicine Section and the Flint Animal Cancer Center are at the forefront of efforts to develop and test viable cancer treatments using radioactive nucleotides including Indium-111 and samarium. Indium-111 studies are targeted towards cancers that are diffused throughout the body, for example, malignant lymphoma, while the samarium studies are focused on osteosarcoma (bone cancer). Dr. Phillip Steyn is principal investigator on the Indium-111 project, collaborating with colleagues from the Mayo Clinic, and Dr. Nicole Ehrhart is leading the samarium study.

"Bone cancer is commonly diagnosed in pet animals," said Dr. Ehrhart, an Associate Professor in the Department of Clinical Sciences. "Veterinarians at the Animal Cancer Center diagnose and care for hundreds of new cases of canine osteosarcoma (OSA) every year. Unfortunately, it is a disease that also affects humans, most commonly children."

Treatment for osteosarcoma consists of surgery to remove the tumor, followed by chemotherapy to delay the spread. Loss of limb and/or function is still a relatively common occurrence for OSA patients, despite the increase in limb salvage procedures performed, and decisions about treatment and amputation can be agonizing for patients, parents and owners. Despite continuing improvements in treatment, approximately 40 percent of children with OSA die of their disease. In dogs, more than 90 percent of patients eventually die of OSA.

"Although radiation therapy is not part of the current standard of care for OSA in people, recent evidence in human patients suggests that radiation improves progression-free interval and quality of life in patients with extremity OSA who have refused surgical therapy or in whom surgery is not possible," said Dr. Ehrhart, an ACVS board-certified surgeon. "In addition, existing evidence in dogs suggests that the use of radiation in combination with chemotherapy increased tumor kill to clinically favorable levels over either treatment alone. We believe the beneficial role of radiation for treatment of OSA in children and dogs has likely been underestimated. New radiation treatments are available that can minimize radiation effects to normal adjacent tissues, yet provide improved tumor kill over standard OSA treatment."

Dr. Ehrhart is studying a new method of delivering samarium to avoid dangerous side effects that restrict its potential as a cancer therapy. It involves isolating the circulation to the leg with the tumor from the rest of the body's circulation by placing the leg on a heart-lung machine. The drug can then be delivered safely to the tumor, without exposing the rest of the body to its potentially toxic effects. The amount of samarium left in the tumor bone isn't enough to cause the harmful side effects, but because it's delivered directly to the tumor, it reaches high enough concentrations to kill the tumor. After the drug is delivered to the tumor, the drug is flushed out of the perfusion circuit and the body's own circulation to the leg takes over again. If successful, veterinary surgeons will make a huge impact on the care of both dogs and children with bone cancer.

Dr. Steyn is taking another approach, looking at more of a Trojan Horse delivery system, for cancers that are difficult to treat because they have spread throughout the system.

Dr. Phillip Steyn

"What we have found is that tumor cells, with their high metabolic rate, have an affinity for Vitamin B-12," said Dr. Steyn. "Vitamin B-12 on its own won't do any damage, but when we attach radioactive material to it, we are in essence making a smart bomb that can potentially destroy the tumor cell. Labeling with radioactive material basically produces internal radiation as opposed to an accelerator beam, which has an external source, and we hope this approach lessens the damage inflicted on healthy tissue."

Dr. Steyn's research team is currently conducting dose escalation studies to evaluate dose efficacy. So far, he notes, the levels of Indium-111 delivered to canine patients have not been shown to kill tumors nor harm the body (the patients go on to receive standard OSA treatment). The project, which is privately funded, will likely expand to look at other labeling candidates that may be effective against other cancer types.

"The exciting part of these research projects in nuclear medicine is that they may offer one more tool for oncologists to reach for when they are devising treatment programs for their patients – and one more tool may make the difference between life and death," said Dr. Steyn. "I envision that these types of treatments, using radioactive materials, will not stand alone but will be part of a comprehensive treatment program for any given patient, giving them greater hope for a positive outcome." ■

D-Lab's Mission Reflects Changing Times and Technology

As veterinary medicine has progressed in treatment modalities, the need for more specific and accurate diagnoses has exploded. Twenty years ago, tumors were categorized as benign or malignant and animals treated accordingly. Today, cancer treatments are tailored to patients so clinicians need detailed, specific diagnoses in order to map the best treatment plan for the best prognosis.

"Cancer is only one area of veterinary medicine where we have seen unbelievable advances in diagnosis and treatment," said Dr. Barbara Powers, Director of the Colorado State University Veterinary Diagnostic Laboratory System (D-Lab). "We are challenged daily to provide the highest level of service possible, while developing and testing new diagnostic methods and learning new technologies to provide our clients with the very best in diagnostic medicine."

In the case of cancer treatment, the D-Lab not only provides testing, but has conducted studies in collaboration with the Flint Animal Cancer Center that were used to develop tumor grading systems that are in use across the country.

It is the mission of the Colorado State University Veterinary Diagnostic Laboratory System to provide timely, accurate and pertinent animal disease diagnostic services and educational outreach to veterinarians, animal industries and animal interests. As part of the University and College of Veterinary Medicine and Biomedical Sciences, the D-Lab contributes to research through the development of new approaches to disease identification, investigation, prevention and to contribute to the education of professional veterinary medical, graduate, undergraduate, and post-doctoral students. The D-Lab also has branch facilities in Grand Junction and Rocky Ford.

During the last several years, the D-Lab has experienced rapid growth in the number of tests it performs, thanks in large part to its designation in 2004 as one of seven U.S. Department of Agriculture BSE laboratories, established to increase testing for bovine spongiform encephalopathy. In fiscal year 2004/2005, nearly 350,000 tests were performed by the D-Lab, an increase of 45.3 percent in the number of tests performed during the previous year. The D-Lab also saw an increase of 75.7 percent of the number of animals tested (nearly 240,000 in 2004/2005) over the previous year. But BSE testing is not the only thing driving growth at the D-Lab.

"Testing technology has really changed during the last 10 years, driving forward the abilities of the veterinary diagnostician to provide more accurate and complete diagnostic services," said Dr. Powers. "Advances in molecular diagnostics, including polymerase chain reaction and immunohistochemistry, are creating a whole new diagnostic field that not only requires highly specialized equipment, but we had to build a whole new laboratory section to house the equipment. The testing is so sensitive that it is highly susceptible to cross-contamination and must be physically isolated from other diagnostic sections."

The D-Lab is part of the National Animal Health Laboratory Network and, in 2002, received $2 million to enhance Biosecurity-Level 3 laboratory space for foreign animal disease testing. In May, the D-Lab received $3.5 million in state funding to begin planning and architectural work on the new Diagnostic Medicine Center which will provide state-of-the-art facilities and plenty of new space to accommodate the rapidly expanding D-Lab.

The D-Lab already needs the additional space, so far managing to get along in very cramped quarters by renting modular units. Dr. Powers notes that a number of areas are growing rapidly in the diagnostic area including avian influenza testing; concerns about vaccination which are leading to evaluation of titers before vaccination; an increase in work with the Division of Wildlife as it pertains to the interactions of wildlife with humans and domestic animals; continuing development of the Colorado BVD (bovine virus diarrhea) Control Program (developed by Dr. Jim Kennedy at the Rocky Ford Diagnostic Laboratory); and advances in data transmission so that animal disease information can be confidentially, easily and rapidly shared among concerned agencies.

Dr. Powers also noted that the D-Lab has led the way in a less glamorous area of diagnostic work, but extraordinarily important, that of the disposal of carcasses.

"We have been a leader in alternative methods of disposal of carcasses and were one of the first laboratories to use alkaline hydrolysis," said Dr. Powers. "We are now in the second generation of this technology, and are even exploring methods of making the end-product useful as an energy source. I think it is just one more place that we are thinking ahead and looking to improve what we do to the best of our abilities."

To learn more about the Colorado State University Veterinary Diagnostic Laboratory System, visit their Web site at www.dlab.colostate.edu. ■

It is the mission of the Colorado State University Veterinary Diagnostic Laboratory System to provide timely, accurate and pertinent animal disease diagnostic services and educational outreach to veterinarians, animal industries and animal interests.

D-Lab Leader in TSE Diagnostics

At the Colorado State University Veterinary Diagnostic Laboratory (D-Lab), the largest single testing program is for transmissible spongiform encephalopathies (TSEs) such as chronic wasting disease (CWD), scrapie, and bovine spongiform encephalopathy (BSE). TSEs account for 40 percent of the D-Lab's nearly 350,000 tests performed in 2004/2005, and almost one-third of those are done as part of the national BSE testing program.

> The University's Veterinary Diagnostic Laboratory was chosen as one of seven laboratories nationwide for high-throughput BSE testing.

"The D-Lab has led the way in TSE testing, largely as a result of our work with chronic wasting disease," said Dr. Barbara Powers, Director of the D-Lab. "We did the validation of the rapid test for CWD, developed by Bio-Rad, and that is now the test used for BSE."

Bovine spongiform encephalopathy is a progressive neurological disorder in cattle. The disease attacks the central nervous system and brain. Cattle lose weight, have difficulty with balance, act skittish and eventually die. In cattle, BSE is believed to be caused by an abnormal protein called a prion. A similar disease in humans, called new variant Creutzfeld-Jakob disease, is thought to be linked with BSE. Concerns were raised worldwide about the spread of BSE and the potential exposure of humans to the BSE agent. Testing programs were put in place as governments sought to determine the prevalence of the disease in cattle herds.

In 2004, Colorado State University was selected to be part of the U.S. Department of Agriculture's national BSE laboratory network established to increase testing for bovine spongiform encephalopathy. The University's Veterinary Diagnostic Laboratory was chosen as one of seven laboratories nationwide for high-throughput BSE testing.

The Diagnostic Laboratory was the only one of the facilities selected that was already equipped with the high-throughput equipment needed to conduct the necessary volume of testing. The equipment was installed in 2002 when the Diagnostic Laboratory, in conjunction with the Colorado Department of Wildlife, tested and validated a rapid robotic system for chronic wasting disease testing developed by Bio-Rad Laboratories.

The robotic system automates a portion of the testing procedure, speeding sample preparation and enabling laboratories to provide faster results using fewer technicians.

Colorado State's laboratory alone has the capacity to conduct more than 150,000 tests per year. Because of the D-Lab's capabilities, it now conducts approximately 28 percent of all national BSE testing.

"As we look to the future, I can see similar things happening with emerging diseases, especially as we look at avian flu or animal diseases that could be used for bioterrorism or agraterrorism," said Dr. Powers. "Our challenge here is to not only focus on today's animal health issues, but predict and plan for what tomorrow will bring."

Colorado State University's Veterinary Diagnostic Laboratory System's responsibilities include monitoring and testing for animal diseases. The Colorado State laboratory also is accredited by the American Association of Veterinary Laboratory Diagnosticians as a full service laboratory for all species of animals. ■

Dr. Barbara Powers, Director of the Diagnostic Lab and Professor in the Department of Microbiology, Imunology and Pathology.

HICAHS Programs Help Address Major Health and Safety Issues in Agriculture

The American family farm is idealized in our culture as a simple way of life. The fact of the matter is, it also is a dangerous way of life. Farmers and their families are exposed to a unique set of work-related hazards that often create an environment ripe for injury, illness and even death. The High Plains Intermountain Center for Agricultural Health and Safety (HICAHS) at Colorado State University is dedicated to reducing and, ideally, eliminating accidents, injuries, diseases and deaths resulting from agricultural operations through education, intervention and research.

"Agriculture is one of the most hazardous occupations in the United States, based on statistics from the National Institute of Safety and Health (NIOSH)," said Dr. Stephen Reynolds, Director of HICAHS since 2002 and a Professor in the Department of Environmental and Radiological Health Sciences. "In a typical year, approximately 800 individuals lose their lives while working in U.S. agriculture. An additional 150,000 people suffer debilitating injuries and illnesses, and a large number of deaths due to occupational disease go unreported. Alarmingly, large numbers of farm accidents involve children. All of these deaths and disabilities greatly affect the social and economic well-being of rural communities nationwide."

> "All of these deaths and disabilities greatly affect the social and economic well-being of rural communities nationwide."

HICAHS was established in 1991 by Dr. Roy Buchan through a grant from the National Institute of Health and Safety, a research and service arm of the Centers for Disease Control and Prevention. HICAHS is a multi-disciplinary organization incorporating the fields of engineering, industrial hygiene, education, toxicology, social work, epidemiology, environmental health and agricultural sciences. The center is one of 10 NIOSH centers nationwide dedicated to agricultural health and safety.

"When HICAHS was established initially, we were best known for our outreach programs," said Dr. Reynolds. "We did a lot of work with Cooperative Extension and emphasized consulting work with individual producers and organizations. In 2000, we saw a shift in emphasis at NIOSH toward research and away from outreach, so we have had to re-tool our program to focus on research to a greater extent, while still providing education and outreach services."

In 2003, HICAHS received a $2.5 million, three-year grant to continue its work. Today, HICAHS has three core programs: prevention and intervention, multi-disciplinary research, and education and outreach. Each core program has a number of ongoing projects.

Dr. Stephen Reynolds

Prevention and Intervention Core

1. Roll-over Protective Structures (ROPS) Design and Testing for Agricultural Vehicles. (In 2006, HICAHS received additional funding from NIOSH to institute programs that would reduce tractor-related accidents.)
2. Reduction of Exposures from Dairies and Cattle Feedlots

Education/Outreach Core

1. Agricultural Health and Safety Curriculum Evaluation
2. Interactive Agricultural Health and Safety CD: 4-H Youth
3. Regional Education Through State Extension Agents

Multi-Disciplinary Research Core

1. Development of Novel Biomarkers for Pesticides
2. Endotoxin and Genetics in Organic Dust Lung Disease
3. Improved Methods of Obtaining Injury Information from Migrant Farmworkers

HICAHS works in collaboration with a number of institutions on its various projects, and networks with others to ensure comprehensive efforts and good communication to improve agricultural safety and health. These organizations include the North American Agrimedicine Consortium, National Institutes for Farm Safety, National Children's Center for Rural and Agricultural Health and Safety in Wisconsin, other NIOSH centers throughout the country and others.

For more information on the High Plains Intermountain Center for Agricultural Health and Safety, visit them at www.hicahs.colostate.edu. ■

Adduct Biomarkers May Help Scientists Pinpoint Risk of Pesticide Exposure

The debate over the benefits and dangers of agricultural chemicals is one fraught with differing opinions, conflicting scientific studies and raw emotionalism. At the High Plains Intermountain Center for Agricultural Health and Safety, research is underway to better understand the effects of these environmental chemicals on humans and animals, and to develop biomarkers that can help predict health risks.

Dr. John Tessari, an Associate Professor in the Department of Environmental and Radiological Health Sciences, and his team are focusing their studies on Atrazine, one of the most commonly used herbicides in the United States and worldwide. In 2003, according to the Environmental Protection Agency, more than 77 million pounds of Atrazine were used on major crops in agricultural operations.

"The health effects of Atrazine are still being researched and debated," said Dr. Tessari, whose analytical lab focuses on environmental chemicals. "There is a lot of controversy about cancer risks, but what we do know is that Atrazine affects reproduction by impacting the luteinizing hormone (LH) and follicle stimulating hormone (FSH). Our laboratory is researching the use of biomarkers, in this case an Atrazine adduct formed in albumin, as an early warning system of exposure in individuals who may be susceptible to long- and/or short-term health problems due to the chemical."

An adduct is a complex that forms when a chemical, such as Atrazine, binds to a biological molecule, such as DNA or protein. Atrazine is a parent molecule that is metabolized within 24 hours in the body. It is actually one of Atrazine's metabolites, DACT, that forms the adduct being studied. The advantage of using these protein adducts, is that they are chemically stable, have a long half-life in the body, and are not subject to repair as is DNA. Using the rat as a model, Dr. Tessari's research team has identified the specific bound adduct to use as an "exposure biomarker" – biomarkers used to measure actual absorbed dose or internal dose and the extent of actual environmental chemical (or metabolite) in the body. His team has also identified the peptide sequence containing the adduct peptide, and is now in the verification stage of their research.

> "We are extraordinarily fortunate to be one of the few universities in the nation to have the instrumentation and expertise that enables this type of proteomic work."

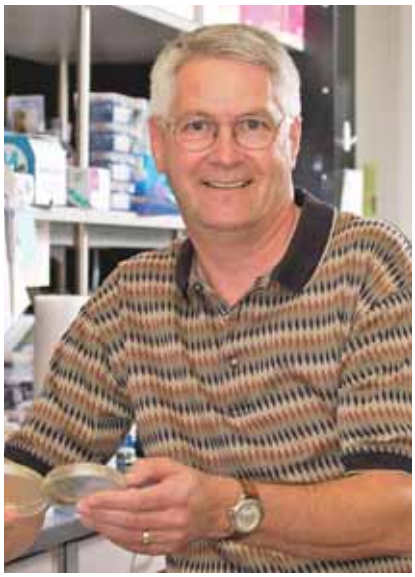
"We are extraordinarily fortunate to be one of the few universities in the nation to have the instrumentation and expertise that enables this type of proteomic work," said Dr. Tessari. "Our Macromolecular Resource Facility allows us to do mass spectrometry analysis using the MALDI-TOF-TOF mass spectrometer (Matrix-Assisted Laser Desorption/Ionization Time-of-Flight/Time-of-Flight), truly cutting edge technology. That, combined with the sequencing databases available via the Web, and the mapping of the human genome, is enabling us to do things we didn't think possible five years ago.

"It's really exciting to be a part of this and look back at how our work has completely changed – how much more we are able to do to advance human health – thanks to the technical and procedural advances that are enabling us to analyze cellular interaction."

Working on a five-year grant from the Environmental Protection Agency, Dr. Tessari eventually hopes to move the research program in novel biomarkers for pesticides from animal to human studies. ■

John Tessari (center), Associate Professor in the Department of Environmental and Radiological Health Sciences with staff (left to right) Rena Saito, Fred Whitecotton, Gregg Dooley and Brian Cranmer in Dr. Tessari's Gas Chromatograph Instrumentation Lab.

VMBS Faculty Receive Prestigious Honors and Awards

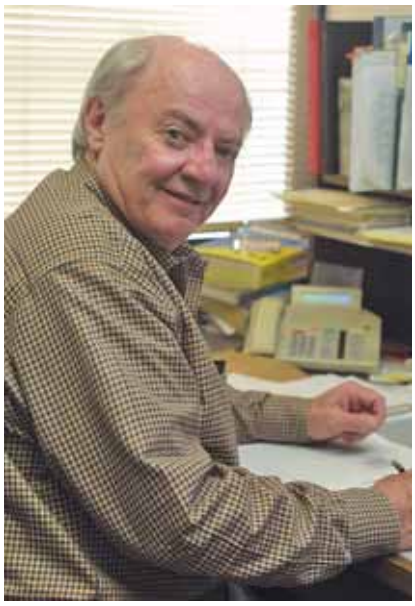


Dr. Herbert Schweizer Elected to Fellowship in the American Academy of Microbiology

Dr. Herbert Schweizer, a Professor in the Department of Microbiology, Immunology and Pathology, has been elected to Fellowship in the American Academy of Microbiology. As a newly elected fellow, he was recognized at the Academy Fellows Luncheon and Meeting during the 106th American Society for Microbiology's General Meeting in Orlando, Fla., held in May. During the luncheon, the American Academy of Microbiology welcomed 54 new Fellows, elected through a highly selective, peer-reviewed process in recognition of their scientific achievement and original contributions that have advanced microbiology.

Dr. Schweizer, who joined Colorado State University in 1995, focuses his research on new drug targets and mechanisms underlying drug resistance, and understanding resistance mechanisms, most notably efflux pumps. Clinical bacterial isolates often are characterized by their resistance to established antibiotics, Dr. Schweizer noted, and an understanding of the underlying resistance mechanisms has important implications for therapy and the drug discovery process.

Dr. Schweizer's research team is working to define specific metabolic pathways, the key enzymes involved and their regulation at the molecular level. Biochemical and genetic studies are being employed to study the molecular architecture and regulation of efflux pumps in *P. aeruginosa* and related bacteria. To support these studies, the research team is developing new genetic tools for pathogenic bacteria, especially those of interest because of their potential use as biowarfare agents, including *Burkholderia pseudomallei* and *B. mallei*, which cause the diseases melioidosis and glanders, respectively.



Dr. Joel Bedford Receives Excellence in Mentoring Award

Dr. Joel Bedford, a Professor in the Department of Environmental and Radiological Health Sciences, has been selected by the Radiation Research Society to receive the organization's Excellence in Mentoring Award. Dr. Bedford is the fourth recipient of the award, which was established in 2002. The Radiation Research Society (RRS) requested letters of nomination for the award, which were reviewed by a 10-member panel charged with selecting the recipient. Dr. Bedford will receive the Excellence in Mentoring Award at the business meeting of the RRS in Philadelphia, Penn, at the organization's 53rd Annual Meeting to be held jointly Nov. 5-8 with the American Society for Therapeutic Radiology and Oncology.

Dr. Bedford became interested in radiological sciences after graduating from the University of Colorado with a degree in chemistry. He then worked in the Biochemistry Department at the University of Colorado's Health Sciences Center and eventually enrolled in the master's program in radiology. After completing his master's degree, he went to Oxford where he completed his PhD degree in 1966, studying radiation effect.

Dr. Bedford then returned to the United States where he joined the faculty at Vanderbilt University as an instructor, earning tenure in 1971 as an Associate Professor. In 1975, Dr. Bedford gave up his tenured position for what seemed to be a good opportunity at Colorado State University, a chance to join an entire department devoted to his field of study, the Department of Radiology and Radiation Biology.

Through the years, Dr. Bedford has found his work in radiation sciences challenging and rewarding, but he says that what really keeps him going is his students.

"In my mind, the best part of this work is having students who get really interested in the scientific aspects, and they come up with their own ideas that we can discuss and explore," said Dr. Bedford. "Helping our students and our postdoctoral fellows is the most rewarding aspect of this entire enterprise."

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CVMBS Faculty Receive Prestigious Honors and Awards

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Epidemiology Professor Selected to Serve on Advisory Panel

Dr. Mo Salman, a Professor in the Department of Clinical Sciences and Director of the Animal Population Health Institute (APHI) at Colorado State University, has been selected to serve on a panel of scientific advisors to the European Food Safety Authority (EFSA).

Dr. Salman began his three-year tenure June 1 as a member of the Panel on Animal Health and Welfare. The EFSA provides objective scientific advice on all matters with a direct or indirect impact on food and feed safety. It is an agency of the European Union, established in 2002 following a series of food-related crises including an outbreak of bovine spongiform encephalopathy and concerns of dioxin contamination in the food supply. The authority has a Scientific Committee and nine scientific Panels which advise the EFSA.

Dr. Salman is the only North American among the 191 scientists who are serving on the panels. A rigorous selection procedure was coordinated by EFSA scientists and reviewed by an external Evaluation Committee.

"I am very pleased that EFSA has been able to attract such highly qualified scientific experts for its Scientific Committee and Panels, which form the backbone of its work in providing scientific opinions and advice on matters related to food and feed safety," said Stuart Slorach, Chairman of the Board.

CVMBS Dean Installed as 41st President of AAVMC

Dr. Lance Perryman, Dean of the College of Veterinary Medicine and Biomedical Sciences, became the 41st president of the Association of American Veterinary Medical Colleges (AAVMC) on March 13. Dr. Perryman's installation as president was the culmination of the AAVMC's annual meeting held in Washington, D.C.

"I am very proud to have the honor to provide leadership and work with such well respected experts and leaders in the field of veterinary medical education," said Dr. Perryman. "The AAVMC has an aggressive agenda of issues that are important not only to veterinarians and veterinary students, but to society as a whole. As educators we must step up to the plate and provide leadership and set examples for our colleagues and veterinary students."

As president, Dr. Perryman is carrying out an aggressive agenda including the DiVersity Matters Initiative which focuses on the importance to the profession and society of having veterinarians in communities reflect the people they serve; passage of the Veterinary Workforce Expansion Act to alleviate the shortage of veterinarians working in public health, public practice and research; and development of a long-range plan that will shape veterinary medical education to meet the demands and challenges of a changing society.

Dr. Perryman has a distinguished career in academic veterinary medicine. He received his Doctor of Veterinary Medicine degree from Washington State University (WSU) and is a diplomate of the American College of Veterinary Pathologists. He served as Assistant Professor, Associate Professor, and Professor in the Department of Veterinary Microbiology and Pathology at WSU, and also as Associate Dean for Research and Graduate Studies. He received a MS degree from The Ohio State University and a PhD from WSU. He served as Department Head for seven years at the Department of Clinical Sciences, College of Veterinary Medicine, at North Carolina State University before taking over as Dean of the College of Veterinary Medicine and Biomedical Sciences at Colorado State University in 2001. ■

College of Veterinary Medicine and Biomedical Sciences

Researchers Hope Studies Will Lead to Prevention of Catastrophic Injuries in Horses

continued from page 9

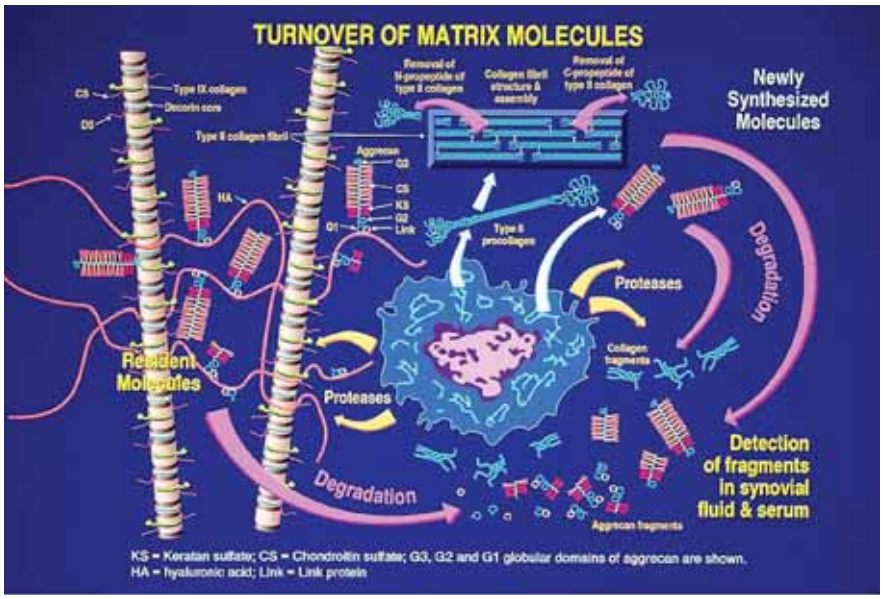
Dr. Chris Kawcak

"These imaging tools, with the exception of digital radiography and scintigraphy, are not routinely used at the track, so our interest is in developing standards that will allow veterinarians to use something like CT to discern microdamage and injury potential, as well as working to make CT more practical for use at the track," said Dr. McIlwraith. "We are using CT to identify bone density patterns associated with various joint injuries, and we hope this work will one day offer veterinarians another tool to improve decision making regarding a horse's fitness to race."

The ORC also is actively developing fluid biomarkers, particularly changes in synovial fluid that indicate the presence of early disease, to predict injury. In research sponsored by the Grayson Jockey Club Research Foundation, the ORC has been working in collaboration with racetrack veterinarians in Southern California to evaluate the efficacy of fluid biomarkers in predicting injury. In the California study, Dr. David Frisbie followed 200 horses for 10 months, collecting fluids, serum and blood along the way and correlated biomarker information to incidence of injury. Dr. Frisbie is still processing data from the study, but early results show that biomarkers have real potential as a predictor of injury.

"Our hope is that biomarkers will become part of the routine screening of horses, especially if we have a horse that is suspicious clinically," said Dr. McIlwraith. "We can use this type of test to confirm that a horse needs to be laid off, sometimes reinforcing the suspicions of the jockey or trainer."

A third area of research is racetrack surfaces. Dr. McIlwraith is working with



Biomarker principles

Dr. David Frisbie

Dr. Mick Peterson of the University of Maine and Dr. Raoul Riser of the Department of Health and Exercise Science at CSU to evaluate racetracks with a biomechanical hoof track tester. The tester is used to identify track problems that could potentially cause injury to racehorses. At one particular track in California, the results of track testing were lifesaving. In one six-week period, 24 horses were euthanized and 240 taken off the track because of injury. After testing the track and recommending some changes to how the track was worked, the result was that only two horses were euthanized in the following six weeks.

"Ultimately, we want to improve the overall health of horses, while reducing the incidence of catastrophic injuries," said Dr. McIlwraith. "Barbaro brought much of the work we do to light, with all the publicity surrounding his injury, and we are hopeful that we can prevent such heartbreaking injuries in the future."

Barbaro, now more than three months out from surgery to repair his hind leg, continues to recover. He will never be able to race again, but his veterinarians hope he will have a second career as a sire. To learn more about the Orthopaedic Research Center, visit their Web site at www.equineortho.colostate.edu. ■

CVMBS 100th Anniversary Celebration to Commence at Annual Conference in January

Although the first veterinary class at the Colorado Agricultural College was listed in the College's 1879 brochure, it wasn't until 1907 that the State Board of Agriculture begrudgingly agreed to the creation of the Department of Veterinary Science with Dr. George Glover as the head. Nearly 100 years of Hope Care Cures later, the College of Veterinary Medicine and Biomedical Sciences is preparing to celebrate its Centennial Anniversary.

"Throughout 2007 we are planning many special events to commemorate the College's 100th anniversary," said Dr. Lance Perryman, Dean of the College (Dr. Perryman is the College's ninth dean in 100 years). "This will not only be a time of celebration, but a time of reflection as we look back on how far we have come, and look forward to what the future holds for us."

The 100 Year Celebration will kick off at the CVMBS Annual Conference on Jan. 6, 2007, with a Hope Care Cures Centennial Banquet featuring a number of distinctive guests. More information will be available on the Hope Care Cures Web page coming online soon at www.cvmbs.colostate.edu. ■

College of Veterinary Medicine and Biomedical Sciences
1601 Campus Delivery
Fort Collins, Colorado 80523-1601

Colorado State University