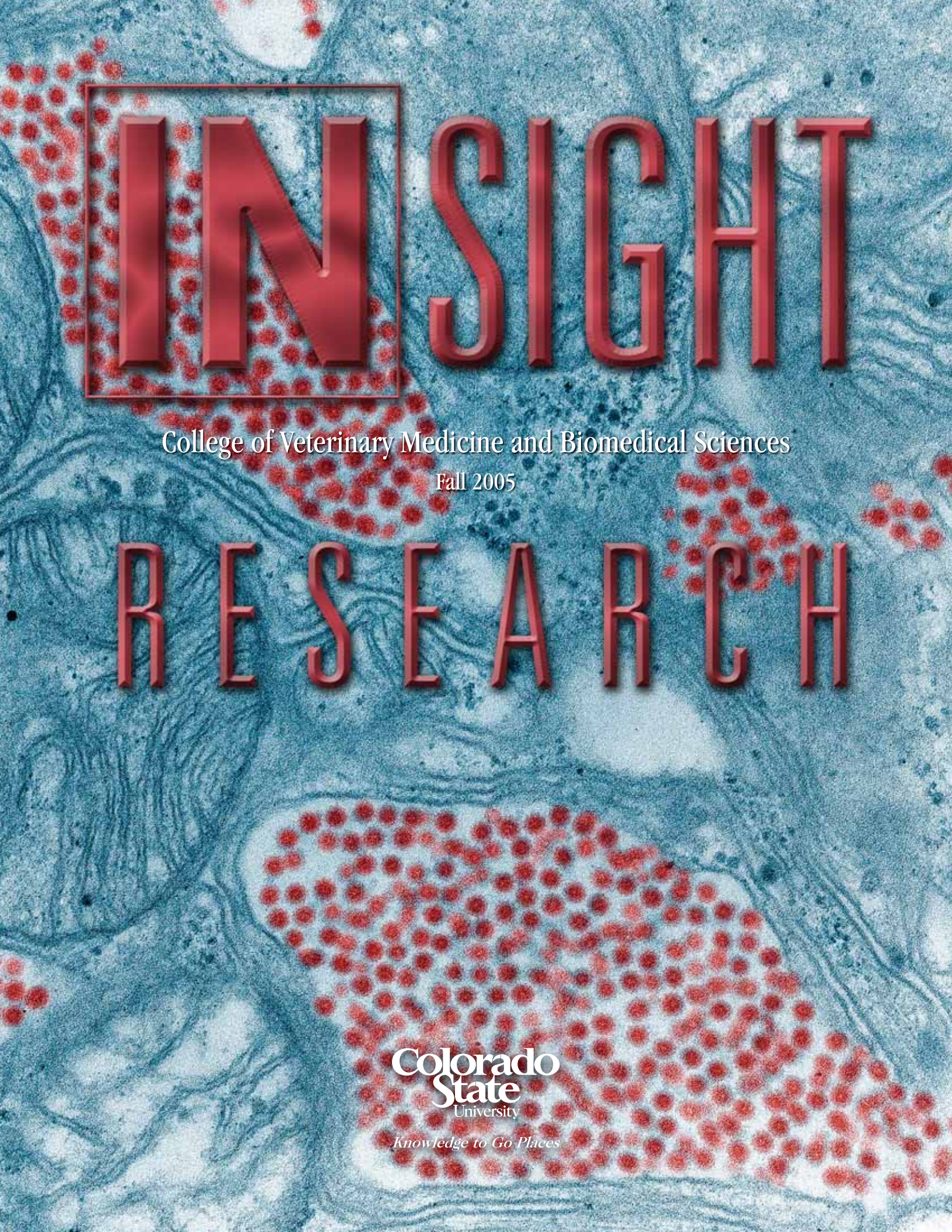
INSIGHT
College of Veterinary Medicine and Biomedical Sciences
Fall 2005
RESEARCH
Colorado State University
Knowledge to Go Places

INSIGHT

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College of Veterinary Medicine and Biomedical Sciences

On the cover:
This colorized transmission electron micrograph (TEM) shows a salivary gland extracted from a mosquito infected with the Eastern equine encephalitis (EEE) virus. The virus has been colorized red and magnified 83,900 times. EEE virus is one of a number of "select agents" researchers at the Regional Center of Excellence for Biodefense and Emerging Infectious Diseases are studying.

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Welcome to the Fall 2005 Research Edition of *Insight*

In this special edition of *Insight*, we focus on research activities within the College of Veterinary Medicine and Biomedical Sciences. We'll take an in-depth look at the new Regional Center of Excellence (RCE) for Biodefense and Emerging Infectious Diseases research and training. The RCE, funded with a $40 million grant from the National Institute of Allergy and Infectious Diseases, is one of 10 in the nation charged with enhancing biodefense.

In this edition, you'll also learn about the Program in Molecular, Cellular and Integrative Neurosciences, a multi-college research and teaching program designed to expand our understanding of the human neuronal system and conduct research that helps those suffering from diseases or injuries that affect normal function. Researchers here are using state-of-the-art technology to look deep within neuronal cells, seeking answers to some of the most complex questions of the mind.

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:

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

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Message from the Dean

Dear Friends,

The terrorist attacks of September 11, 2001, and the dissemination of anthrax spores through the U.S. mail a month later, brought many changes to our world. Americans, most of whom felt largely immune to the bombings and senseless killings that beleaguered much of the planet, were suddenly thrust into a world where planes could bring down buildings and letters could deliver death.

In response to those attacks, and concerns over the potential for future attacks, the government moved to dramatically increase spending on biodefense research with the goal of developing accurate and rapid diagnostic tools, therapeutic medications and effective vaccines that would protect the public against agents of bioterror.

In June, Colorado State University was selected by the National Institute of Allergy and Infectious Diseases (NIAID) to establish a Regional Center of Excellence (RCE) for Biodefense and Emerging Infectious Diseases research and training. This four-year, $40 million grant is part of a $400 million effort by the NIAID to establish 10 regional centers of excellence to address national biodefense research needs. We are extremely proud that our programs at the College of Veterinary Medicine and Biomedical Sciences, especially the Infectious Diseases Program, have been entrusted with a task so vital to our nation and the world.

It's also important to note that this grant would not have been successful without the work of so many of our faculty and staff who have developed a body of work that was worthy of an RCE, who worked diligently to develop and submit a comprehensive grant application, and who are now putting in long hours to get the RCE up and running.

In this research edition of *Insight*, you'll read about the RCE and some of the research projects that are already underway. This fascinating work has implications not only for biodefense, but also for the advancement of health care around the world. Our researchers are tackling some of the most devastating diseases known to humankind, and increased funding from NIAID means that we will be able to save lives all the sooner.

You'll also read about research projects in the Program in Molecular, Cellular and Integrative Neurosciences. This exciting program, a University Program of Research and Scholarly Excellence, is helping us to develop a better understanding of the human nervous system with research that examines the inner workings of the neuron. Researchers in this program have come together across departmental and college boundaries to explore the normal and abnormal function of the nervous system with the hope of one day being able to help people who suffer from debilitating disease or injury.

The College of Veterinary Medicine and Biomedical Sciences is proud to be home to academic excellence in our undergraduate and graduate programs, to outreach and service programs that touch the lives of many, and to research endeavors that may one day lead to a cure for cancer or a vaccine against tuberculosis. Among schools of veterinary medicine in the country, in 2004 we led in total extramural research expenditures with $52.9 million. We also led all veterinary schools in terms of total National Institutes of Health research expenditures with $34.15 million. Our faculty is held in high esteem nationally and internationally, and we are so very proud of the important work that they do.

Our research programs are not only important to the creation of knowledge and advancement of science and medicine, they contribute so much to the College and to the University. Thanks to our research programs, we are able to provide state-of-the-art laboratories and invaluable research experience for undergraduate and graduate students. We are able to add highly qualified faculty and research associates who enrich the University with their knowledge and experience. Research dollars help build new buildings and outfit laboratories with the latest equipment.

Dr. Lance Perryman

I hope you enjoy this research edition of *Insight* magazine. In these pages, you are getting a glimpse of the future of biomedical sciences. You are getting an insider's look at the Regional Center of Excellence and examining neurons with our researchers at the Program in Molecular, Cellular and Integrative Neurosciences. We are proud of who we are and what we do, and hope that you will join us as we share just a few of our past accomplishments and preview what we hope will be our future ones. ■

With Best Regards,

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

NIAID REGIONAL CENTER OF EXCELLENCE FOR BIODEFENSE AND EMERGING INFECTIOUS DISEASES

CSU Selected to Establish Regional Center of Excellence

The terrorist attacks of September 11, 2001, and the anthrax scare that followed in October of that year set in motion a chain of events that radically changed the research focus of many in the scientific community and ignited the little known and often ignored field of biodefense. Four years later, in June 2005, the College of Veterinary Medicine and Biomedical Sciences' Infectious Diseases Program brought the University into the biodefense arena in a big way. Based on research programs already in place, and with ambitious plans to expand infectious diseases programs in the future, the University was awarded a four-year, $40 million grant to establish a Regional Center of Excellence, or RCE, for Biodefense and Emerging Infectious Diseases research and training.

CSU and the University of California-Irvine, were the ninth and tenth RCEs established by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health. NIAID established the RCE network in 2003 with grants to eight institutions. With CSU and University of California-Irvine, the RCE network is now complete. Each institution leads an RCE consortium made up of universities and other research institutions within its geographic region. Network members are charged with the task of conducting research that will lead to next-generation treatments, vaccines and diagnostic tools for diseases such as equine encephalitis, anthrax, plague, melioidosis, tularemia, botulism and West Nile fever.

Principal investigator Dr. Barry J. Beaty, a Professor in the Department of Microbiology, Immunology and Pathology, is leading the Rocky Mountain RCE, whose members include five other universities and small business partners. It also includes substantial collaboration with the Centers for Disease Control and Prevention. The Rocky Mountain RCE will develop new vaccines, drugs and diagnostics for emerging diseases; provide training in emerging diseases and biosecurity to scientists, physicians, veterinarians and other public health personnel throughout the region; and assist state and federal agencies in responding to emerging diseases.

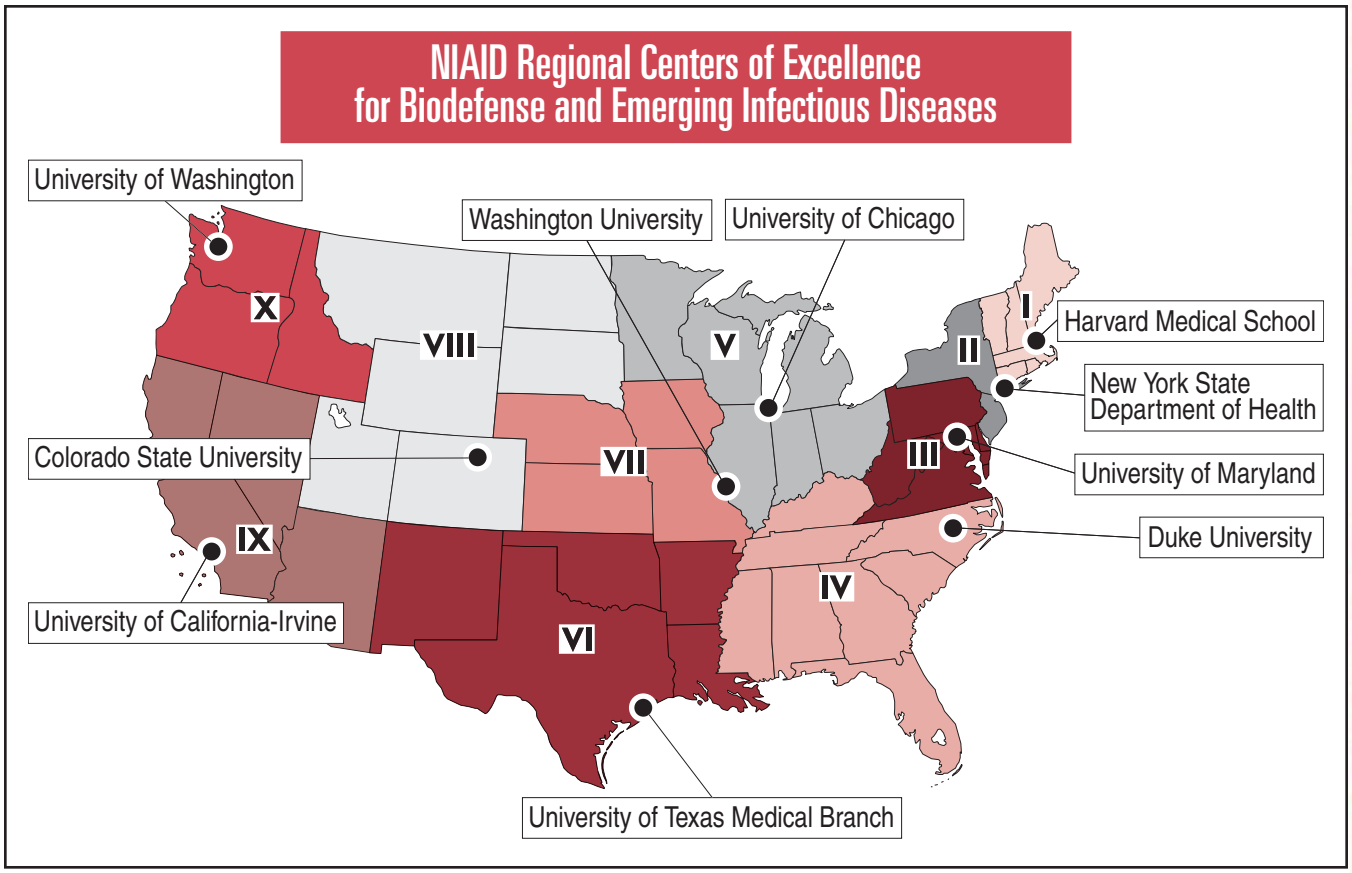
Dr. Barry J. Beaty

Based on research programs already in place, and with ambitious plans to expand infectious diseases programs in the future, the University was awarded a four-year, $40 million grant to establish a Regional Center of Excellence, or RCE, for Biodefense and Emerging Infectious Diseases research and training.

The Rocky Mountain RCE will focus on zoonotic emerging diseases, which are diseases of animals that are transmissible to humans. Zoonotic pathogens have been the source of almost all emerging diseases throughout the world such as West Nile virus and Sin Nombre Hantavirus that have emerged in the Rocky Mountain region in recent years. The Rocky Mountain RCE will provide a national and regional resource focusing on the diagnosis, prevention and control of these types of diseases.

"There are critical needs to develop new vaccines, drugs and diagnostics to counter these important diseases," said Dr. Beaty, a Colorado State University Distinguished Professor and member of the National Academy of Sciences. "A unique aspect of the Rocky Mountain RCE is to encourage partnerships with industry to develop expeditiously the tools and products needed to counter emerging diseases and bioterrorism events."

Industrial partners and other collaborators will be able to use the state-of-the-art facilities and expertise provided by the RCE and Colorado State's advanced research laboratories to move their discoveries into commercial products quickly and safely, providing



new products for biosecurity and positively impacting economic growth in the region.

The RCE complements and enhances similar research already underway at the College's Arthropod-Borne and Infectious Disease Laboratory and at the CDC's Division of Vector-Borne Infectious Diseases.

In August 2004, the CDC broke ground on a new $80 million, 156,000-square-foot facility dedicated to infectious disease research. In late 2003, the College was awarded a $17 million grant from NIAID to construct a 33,850-square-foot Regional Biocontainment Laboratory to expand the College's ongoing, world-recognized work in infectious disease and biosecurity research. The RCE will be housed primarily at this new laboratory which is expected to be completed in 2007. Additionally, Colorado State recently invested $10 million to enhance its Infectious Diseases Program. Until these buildings are complete, much of the RCE work will take place in the Bioenvironmental Hazards Research Building and other Foothills Research Campus facilities as well as BioSafety Level 2 laboratories on the Main Campus.

The Rocky Mountain RCE is comprised of scientists, public health practitioners and staff from Colorado State University, Centers for Disease Control – Division of Vector-Borne Infectious Diseases, United States Department of Agriculture – Arthropod-Borne Animal Diseases Research Laboratory, University of Colorado Health Sciences Center, Denver Health and Hospital Authority, Children's Hospital, Colorado School of Mines, Montana State University, University of Montana, University of North Dakota, University of South Dakota, University of Utah, Utah State University, Brigham Young University and the University of Wyoming. Companies participating in the RCE include Precision Photronics Corporation in Boulder, Alexion Antibodies Technologies in San Diego and DeltaNU LLC in Laramie. Additional universities, agencies and companies will participate in the RCE in the future.

The other consortia-leading institutions in the national RCE network are Duke University, Harvard Medical School, New York State Department of Health, University of Chicago, University of Maryland, University of Texas Medical Branch (Galveston), University of Washington in Seattle and Washington University in St. Louis. ■

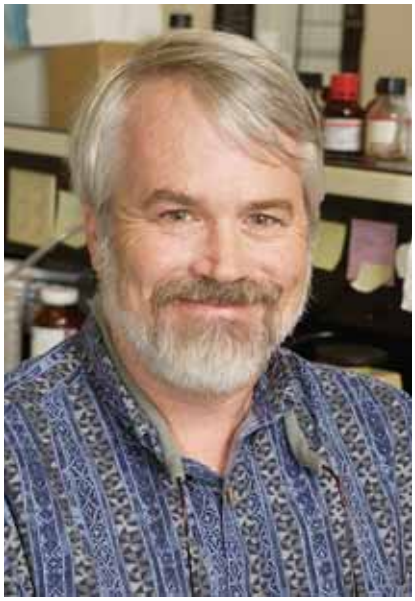
Alphaviruses Under Microscope as Concerns Rise Over Biodefense

When the United States and the Soviet Union were at the height of the Cold War, the USSR was aggressively pursuing the weaponization of biological agents that could be used in time of war to cause death and illness, create mayhem and instill fear in target populations. One such group of agents, known as alphaviruses, showed great potential in being successful at all three mainly because some of the alphaviruses can readily be transmitted to human and animal hosts by the aerosol route of infection – a prerequisite for use as bioweapons.

When the Soviet Union broke apart and the hostilities between the United States and the former Soviet Bloc turned to cooperation, concerns over alphaviruses faded like a bad memory. The urgency to develop effective vaccines and therapeutic agents diminished as the Cold War drew to an end. However, alphaviruses – including Venezuelan equine encephalitis (VEE) virus, Eastern equine encephalitis (EEE) virus and Western equine encephalitis (WEE) virus – are normally transmitted to their hosts by the bite of an infected mosquito and still presented a public health problem on a regional basis.

Fast forward to 2001 and the anthrax mailings that followed the terrorist attacks of September 11 – a paradigm shift was in the offing. Bioterrorism was the new catch phrase and the Department of Homeland Security wanted to make sure that research into select agents that could be weaponized, including alphaviruses, was re-energized and given greater national priority.

"We are concerned about these alphaviruses not only from a biodefense need, but also because of emerging disease implications," said Dr. Kenneth Olson, Director of the College's Arthropod-Borne and Infectious Disease Laboratory. "In the 1930s and 1940s, WEE was devastating. Tens of thousands of horses died or were killed in the western United States and the disease took a toll on humans who can contract the virus as well. In the 1960s and 1970s, VEE moved from Mexico into Texas and caused a lot of problems. Right now, EEE virus is being focally transmitted in the eastern United States and is associated with high morbidity and mortality rates. Experimental VEE vaccines for use in human have been produced in limited quantities, but there are still no good human vaccines for Eastern or Western equine encephalitis."



Dr. Kenneth Olson

"We will be looking at how the virus infects and how efficient it is in causing disease when delivered by aerosol or some other method, as when compared to transmission by mosquitoes."

The difficulty in battling these mosquito-borne viruses is that they are RNA viruses. That is, the genome is RNA and RNA genomes can't be manipulated. However, when researchers convert the RNA genome to cDNA (complementary DNA), they can then play with the genome, adding mutations to try to weaken the virus which can then be used as a vaccine. The virus will still be able to do some replication, but won't have a disease outcome.

"Our primary goal here is to help move the process along so we can learn about the pathogenesis of the virus in a mouse model, and use that model to test vaccines or anti-viral therapies that might become available down the road," said Dr. Olson. "The other aspect of our work is to look at the potential for infection when these alphaviruses are aerosolized. Today, we don't know what would happen if these aerosolized viruses get into the ecosystem – how efficiently would local mosquito populations pick up the virus and begin transmitting disease? With our mouse model, we will be looking at how the virus infects and how efficient it is in causing disease when delivered by aerosol or some other method, as when compared to transmission by mosquitoes."

Dr. Olson said the Regional Center of Excellence grant and the new Regional Biocontainment Laboratory will give his research group the facilities and means to move forward.

"We will now have the funds to hire the right people and provide them with the supplies they need to pursue this important work," said Dr. Olson. "We will take what we have learned to date about arthropod-borne diseases and move that into the field of alphaviruses; not only to address the threat of bioterrorism, but also to make progress in the battle against these devastating diseases that affect humans and animals in so many parts of the world." ■

PDM Core Helps Researchers Develop Vaccines, Therapeutics and Diagnostics

Twelve years ago, Dr. Patrick Brennan's laboratory was looking to produce a small sample size of leprosy skin test antigens to send to Nepal for a clinical study. Such a skin test showed little upside for biomedical companies to manufacture. As leprosy is not a disease found in the United States but typically in poor countries, making a small sample of skin test antigens for early clinical trials didn't seem economically feasible.

Dr. Brennan's research group, based in the Mycobacteria Research Laboratories, decided that the only option was to manufacture the skin test antigens themselves, a bit of naiveté, said Becky Rivoire, a Senior Research Associate, that turned out to be their saving grace.

"Had we known at the time how difficult it was going to be to negotiate all the government regulations, and just how much time and effort this would all take, I'm not so sure we would have signed on," said Rivoire. "But we didn't know and, 12 years later, here we are."

And "here we are" is a good place to be. When Colorado State University applied for a grant to become a Regional Center of Excellence, the proposed Product Development and Manufacturing Core, an extension of the Pilot Plant manufacturing facility at the Mycobacteria Research Laboratories, was a key component of the grant's approval by the National Institute of Allergy and Infectious Diseases (NIAID), a National Institutes of Health (NIH) agency. Because the focus of the grant is the development of vaccines, therapeutics and diagnostics, already having an existing facility to produce small quantities of these products for initial pre-clinical studies in animal subjects followed by clinical studies in human populations was critical.

"The NIH charge to us was to develop vaccines, therapeutics and diagnostics for translational research," said Rivoire, who is Co-Director of the PDM Core. "We proposed to be the bridge – to bridge the gap between research and clinical trials. We may have to work with some products start to finish, and others at different stages, depending on other public and private partnerships. We hope we can help move products through the development and manufacturing process which are not economically viable for pharmaceutical companies to produce."

Rivoire said one of the challenges for creating a successful PDM is that Current Good Manufacturing Practices (CGMP) must be followed. That means more documentation of procedures, more federal regulations to follow, and increased reporting of process and results. It also means extensive training for the PDM staff who must learn the ins-and-outs of small-scale pharmacological manufacturing.

Senior Research Associate Becky Rivoire

"We are getting assistance from pharmaceutical companies, and that is helping us to shorten our learning curve," said Rivoire. "We also are getting incredible support and encouragement from NIH and from CSU. It's a huge endeavor, but the challenges are not insurmountable."

Rivoire needs only to point to the success of the leprosy skin test antigen produced at the Mycobacteria Research Laboratories to support her convictions. The research group successfully completed a Phase 1 non-endemic safety study of the test products on volunteer students at Colorado State University. The skin test antigens then entered Phase 2 of the study, which was conducted in Nepal, an endemic area with significant levels of leprosy as determined by the World Health Organization. The researchers are now at Stage C of Phase 2 where they are testing the skin test antigens on patients. The eventual goal is to show that the leprosy skin test antigens can be used to diagnose leprosy early in the course of the disease thus improving treatment and reducing long-term health risks.

"In the course of generating these leprosy skin test antigens over these many years, Ms. Rivoire educated and trained herself, often at her own expense, in the arts of CGMP, the Code of Federal Regulations and other government policies and practices pertaining to human research, such that she was perfectly poised for the opportunity presented by the RCE initiative," said Dr. Brennan. "She is very much admired and respected by such bodies as the Regulatory Section within the National Institute of Infectious Diseases. The special attributes of Ms. Rivoire were a major factor in the acquisition of the RCE and in its future success."

The PDM Core, which requires Bio-Safety Level 3 (BSL3) facilities, will be located at the Bioenvironmental Health Research Building while non-BSL3 facilities will be located at the Microbiology Building until construction of the Regional Biocontainment Laboratory is completed in 2007. ■

Researcher Has Vision of Pan-Arthropod Vaccine

Despite its best efforts during the last 50 years, the World Health Organization has not been able to realize its dreams of vaccinations against some of humankinds' most ancient and devastating diseases including malaria, yellow fever, dengue fever, plague, Rift Valley fever and other arthropod-borne infectious diseases. A research team at Colorado State University is hoping that its work will one day help WHO make its dream come true.

A novel idea, which has taken more than a decade to achieve scientific acceptance, focuses on creating a vaccine not against the pathogens that cause disease, but against the saliva in the arthropods that transmit the pathogens – saliva that researchers now believe is critically important to the successful transmission of disease.

The laboratory of Dr. Richard Titus, a Professor in the Department of Microbiology, Immunology and Pathology, along with research partners in the College's Arthropod-Borne and Infectious Disease Laboratory (AIDL), and with other international research efforts, has been instrumental in understanding how saliva in arthropods creates ideal conditions in the vertebrate host when pathogens, for example *Leishmania*, are introduced into the host when the arthropod takes a blood meal.

"When sand flies inject *Leishmania* into the vertebrate host, they inject the parasite within their saliva," said Dr. Titus. "Sand fly saliva contains many proteins which help the fly obtain a blood meal. In addition, the saliva contains potent immunosuppressive proteins which can be critical to survival of the parasite within the host. We are looking at an alternative approach for vaccinating against *Leishmania* that involves developing vaccines against salivary proteins in an attempt to block the action of these proteins when the fly bites and thus prevent infection with *Leishmania*."

Dr. Titus first became involved with salivary studies when he was at Harvard Medical School. A colleague, Dr. José Ribeiro, was interested in sand flies and Dr. Titus was interested in leishmaniasis. Dr. Ribeiro was investigating the pharmacological properties of the sand fly's saliva, while Dr. Titus was curious as to how the sand fly transmitted disease. Later on, Dr. Titus became aware of the work of Dr. Peter Willadsen of Australia who devised a new way of protecting cattle from ticks. Rather than vaccinating against the tick, Dr. Willadsen created a vaccine that immunized the cow against a component of the tick's digestive track – a protein called Bm86. When vaccinated, cows develop antibodies to the protein so when a tick feeds, the tick gets a bad case of indigestion since the cow's blood basically attacks the tick's intestines.

"Dr. Willadsen was really thinking outside the box and it got me thinking outside the box, too," said Dr. Titus.

Arthropods, which include mosquitoes, sand flies, ticks, black flies and biting midges, transmit some of the most devastating and deadly diseases in the world. If researchers are successful in identifying a common protein denominator in saliva that has been preserved across evolutionary time in the different species of arthropods, they may be able to develop a single vaccine that would provide protection against all diseases transmitted by arthropods – a pan-arthropod vaccine. Dr. Titus concedes that the possibility of such a vaccine is in the distant future, but it is an enticing goal to work toward.

"We have a beautiful model here at CSU of how important saliva is to disease transmission," said Dr. Titus. "Dr. Barry Beaty and his group at AIDL have done fascinating work that shows how transmission of the LaCrosse virus is enhanced by the presence of saliva from the host mosquito. Using this as our model, and with increased funding and facilities from the Regional Center of Excellence, we hope to make rapid progress."

Dr. Beaty's research showed that when adult mice were injected with the LaCrosse virus alone, they did not develop disease. When they were injected with the virus accompanied by

If researchers are successful in identifying a common protein denominator in saliva that has been preserved across evolutionary time in the different species of arthropods, they may be able to develop a single vaccine that would provide protection against all diseases transmitted by arthropods – a pan-arthropod vaccine.

Dr. Richard Titus' Research Team: Tess Brodie, Jeanette Bishop, Richard Titus, Robin Morris, Santiago Mejia

saliva, as would occur through normal infection through the mosquito host, the mice died.

"It's an amazingly clean finding with no shades of gray," said Dr. Titus. "With just the virus, the mice lived – with the virus and saliva, the mice died. If we can immunize against one component of the saliva that modifies the immune system, we may be able to offer protection against infection."

Dr. Titus' work has implications for a diverse set of concerns. First and foremost, because of the RCE's objectives for biodefense, he is working to develop vaccines that offer protection to targeted populations in case of attack by a biological weapon. His work also has implications for military personnel who are increasingly deployed in areas where they have little natural immunity to regional diseases, such as leishmaniasis, which soldiers stationed in Afghanistan and Iraq are contracting in increasing numbers. Third, emerging infectious diseases are posing a greater threat to global populations with little available in terms of vaccines, therapeutics and diagnostics. Fourth, and perhaps most important, a viable vaccine against arthropod-borne diseases would alleviate unbelievable levels of suffering and change the course of human history.

"We don't expect that our work will provide the complete answer, but it is part of a new way of thinking about how to protect against these diseases," said Dr. Titus. "Our discoveries might become one component of a comprehensive vaccine to prevent infection. But this type of thinking represents a huge shift in how we approach infectious disease and it's very rewarding to be a part of that." ■

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Past Biological Weapons Raise Concerns

In the Australian outback, in the rice paddies of Thailand and in the fields of Cambodia, a deadly bacterium awaits the rainy season to begin its killing spree. No vaccine can protect its human victims. It can lie dormant in human cells for decades. It can take a life within 48 hours without ever being detected and, even when diagnosed properly, it is resistant to many of the most powerful antibiotics known to man.

If the disease melioidosis doesn't sound familiar, don't feel alone. This tropical infection has largely been off the radar of researchers in the United States. But that is changing. Dr. Herbert Schweizer, a Professor in the Department of Microbiology, Immunology and Pathology, is at the scientific front lines of research into the pathogen that causes melioidosis, thanks in large part to its identification as a "select agent" for bioterror by the National Institute of Allergy and Infectious Diseases.

"*Burkholderia pseudomallei* is on the select agent list because of its potential for use as a biological weapon," said Dr. Schweizer. "A close relative, *B. mallei*, has been used in biowarfare before, so there is a precedent. NIAID is concerned that *B. pseudomallei* could be targeted for weaponization and wants to take steps to protect public health by developing better diagnostic tools and therapeutic agents."

During World War I, horses and mules were the primary mode of military and civilian transport. If you could take out your enemy's transportation, you had a better chance of taking out your enemy and that is just what the Central Powers attempted to do. Glanders, which is caused by the bacterium *B. mallei*, is a disease that kills horses and, more rarely, people. The disease was spread by German troops to infect large numbers of Russian horses and mules on the Eastern Front. But that was only the beginning. The bacterium was used by the Japanese during WWII to infect civilians, horses and prisoners of war. The United States and the former Soviet Union also studied *B. mallei* as a potential weapon of biological warfare during and shortly after the war. Because of its persistence in the environment and its much greater drug resistance, *B. pseudomallei* is now seen by many as an equal or perhaps even likelier tool of terror.

Today, Dr. Schweizer is conducting research to develop a better understanding of *B. pseudomallei's* resistance to antibacterials, and how new drugs may overcome that resistance enabling melioidosis to be effectively treated with existing antibiotics. Because *B. pseudomallei* evolved in the soil with organisms that secrete antibacterial compounds, it has developed mechanisms to protect itself.

"What we are looking at is the function of efflux pumps that basically work to pump antibacterials, which include many of the commonly used antibiotics, out of the bacterium before the compounds can do any damage," said Dr. Schweizer. "If antibiotics can't stay in the bacterium, they won't be effective in stopping infection. If we can find inhibitors that will stop the action of these pumps, we may be able to develop an inhibitor-drug cotherapy that will allow use of many of the antibiotics that currently cannot be used because they are effluxed."

In addition to work on efflux pumps, researchers at the Regional Center of Excellence for Biodefense and Emerging Infectious Diseases are developing vaccines and rapid diagnostic tools to either prevent the disease altogether or at least improve the outcomes of medioidosis treatments. They also will develop public health programs to create awareness of the disease and its symptoms. The focus on *B. pseudomallei* can't come soon enough for regions of the world that have struggled in isolation to fund even basic research into melioidosis, let alone develop effective drug therapies.

Dr. Herbert Schweizer

Australia, because of a medical infrastructure that allows for quick diagnosis and intensive long-term treatment with high compliance rates, has reduced the death rate from the disease to less than 20 percent. But in developing countries, with few medical facilities and even fewer monetary resources to sustain expensive treatment, the death rate remains at 50 percent. Now, thanks to NIAID funding, that picture could change. Dr. Schweizer notes that some have criticized the government's investment in bioterrorism as a drain on biosciences, but researchers will be learning a lot and that is a good thing.

"Even if we never have a bioterror attack using *B. pseudomallei*, this research will benefit so many who suffer from the consequences of infection by this pathogen," said Dr. Schweizer, who has traveled to Australia and Singapore to conduct field research and develop a greater understanding of melioidosis. "People who have worked with the disease for so many years have felt that they were alone in the wilderness. Now, with NIAID funding and the resources of the Regional Center of Excellence at CSU, they finally have hope that they one day can offer their patients readily accessible and much more affordable life-saving therapy." ■

Rural Disease Makes Jump to Select Agent

When Dr. John Belisle was in junior high school, he remembers going hunting with his cousins in Nebraska. After they killed and skinned a rabbit, the reaction from his grandmother, whose parents had emigrated from Russia, was anger and fear. She associated rabbits with tularemia, a disease more commonly feared in her parents' home country. She yelled at the boys and made them scrub down. Tularemia, also known as rabbit fever, can be fatal.

Dr. Belisle didn't think too much more about tularemia over the course of his education and ensuing career in the biomedical sciences, but today tularemia is very much on his mind. As a faculty affiliate with the Regional Center of Excellence (RCE) for Biodefense and Emerging Infectious Diseases research and training, Dr. Belisle has undertaken a research project that he hopes will one day lead to an effective vaccine against tularemia.

"Tularemia is a disease most often associated with rural areas and hunting," said Dr. Belisle, who is a Professor in the Department of Microbiology, Immunology and Pathology. "People become infected through the bite of infected insects or by handling sick or dead animals. Hunters usually get the disease from fleas found on rabbits or other small rodents."

According to the Centers for Disease Control and Prevention (CDC), about 200 human cases of tularemia are reported each year in the United States. Symptoms are similar to the flu and include fever, chills, headache, respiratory problems, joint pain and dry cough. Skin ulcers also can develop if the source of infection is a bite, rather than inhalation. Tularemia can be treated with antibiotics when diagnosed properly.

"The reason we are concerned about tularemia is because of its potential for use as a bioweapon," said Dr. Belisle. "The bacterium that causes tularemia, *Francisella tularensis*, is highly virulent – only a few organisms can cause infection – and it can be very acute. Also, the precedent has already been set. The disease was weaponized by the Soviet Union during the Cold War. If tularemia were used as a bioweapon today, the bacteria would likely be aerosolized and could potentially infect large numbers of people. People who inhaled the bacteria could develop severe respiratory illness and our health care system would be rapidly overwhelmed."

Dr. John Belisle

Dr. Belisle noted that *Francisella tularensis*, while not a mycobacterium, shares several traits with the bacterium that causes tuberculosis, which is the primary research focus of his laboratory. The bacterium is intracellular and lives in the host's macrophages.

"We hope that by applying the methodologies and approaches we've developed with *Mycobacterium tuberculosis*, we will be able to move quickly in our studies of *Francisella tularensis*," said Dr. Belisle. "Our goal is to develop vaccine candidates ready for clinical trials in four years."

The research team will first look at various sub-cellular fractions of the bacterium that are able to induce a protective T-cell response in the host. They will then look at specific proteins within the fractions, and then at individual proteins that induce a protective response. After identifying several candidates, these will be formulated into clinical vaccines and used in clinical trials. Dr. Belisle said the greatest challenge for the team, because of the bacteria's highly virulent nature, will be developing good models that show a protective response. On the plus side, because the bacterium grows much faster than the tuberculosis bacterium, studies should be able to, theoretically, progress much more quickly.

"We also are adding additional personnel to assist in this project and, of course, we already have great expertise available to us here on campus, " said Dr. Belisle. "A great thing about CSU and the College is the ability to find highly qualified collaborators. We are working with two immunologists, Drs. Steve Dow and Catherine Bosio, who will help us with their expertise in animal models and evaluation of immune response."

Dr. Dow is an Associate Professor in Clinical Sciences and Dr. Bosio is an Assistant Professor in the Department of Microbiology, Immunology and Pathology. Dr. Belisle's team also is working closely with Dr. Jeannine Peterson at the CDC's Division of Vector-Borne Infectious Diseases in Fort Collins.

Dr. Belisle and his cousins didn't contract rabbit fever those many years ago in Nebraska – he doubts the rabbit was infected. But, for his grandmother, old fears take a long time to die. And, in today's new world of biodefense, bioweapons and bioterrorism, old fears have taken on a new life. This time though, scientists are hoping their research will lead to a better preventive approach to rabbit fever that will take away the potential threat of a weaponized tularemia bacterium. ■

Animal Cancer Center Selected to Receive Academic Enrichment Funds

The Robert H. and Mary G. Flint Animal Cancer Center (ACC) has been selected to receive a $2 million grant from the Colorado State University Academic Enrichment Program (AEP). The grant will help make the center an international leader in basic cancer biology and translational research used in the discovery and application of novel cancer diagnosis and treatment.

The grant complements a recent $1 million gift to create a graduate Cancer Biology program of study within the University's College of Veterinary Medicine and Biomedical Sciences. The graduate program, the first of its kind in the nation, will train scientists whose focus is on the basic science of the causes and prevention of cancer, in addition to cancer diagnosis, therapies and risk assessment. The anonymous donor requested that the gift be used to fund curriculum development with an emphasis on veterinary postdoctorate education and be administered through the Morris Animal Foundation.

The AEP grant will fund three specific areas at the ACC: experimental therapeutics, functional imaging, and the molecular signatures of cancer. Experimental therapeutics encompasses new chemotherapy drugs, specially designed therapies that target specific pathways in cancer cells, immunotherapy, cancer vaccines and more. Functional imaging permits veterinarians to look at tumors in non-invasive ways and to examine the biological differences between cancerous tumors and normal surrounding tissues. Molecular signatures involves looking at cancer on a molecular level including studying the DNA, RNA or proteins to better understand what makes each cancer cell different from normal cells and from other cancer cells.

"The program was designed by Dr. Robert Ullrich, Director of Research; Dr. Ed Gillette, Assistant Director; and myself," said Dr. Stephen Withrow, Director of the Animal Cancer Center. "Between the three of us, we have almost a century of experience in battling cancer with surgery, radiation and chemotherapy. In envisioning the program's structure, we saw a way of both increasing and expanding our knowledge of cancer and having a greater impact on the search for new answers to old questions."

The Academic Enrichment Program at Colorado State is a source of one-time funds to support unique, high quality academic programs at the University during the next 5 to 10 years. Quality and pursuit of excellence were the features that took precedence over all other considerations when the selection committee looked at the various programs competing for the funds. For more information about the Animal Cancer Center, visit their Web site at www.csuanimalcancercenter.org. ■

Consortium to Receive $19.7 Million Grant from Grand Challenges

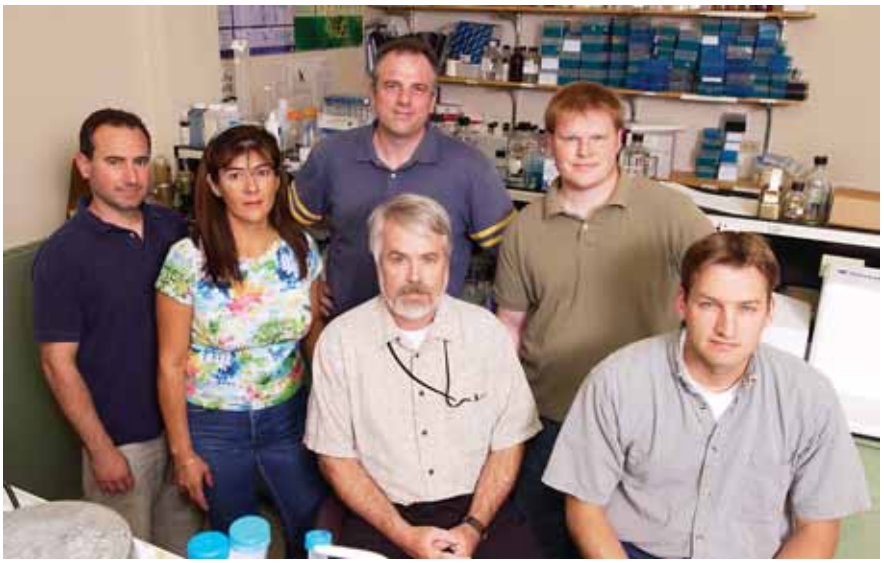
Researchers at Colorado State University are collaborating with others around the globe on a dengue virus research project as part of the $436 million Grand Challenges in Global Health initiative funded primarily by the Bill and Melinda Gates Foundation. The endeavor is among 43 groundbreaking research projects to improve health in developing countries.

Drs. Kenneth Olson, William Black IV and Jonathan Carlson are part of the Colorado State University group working with Dr. Anthony James, Principal Investigator, University of California-Irvine, on a $19.7 million Grand Challenges award to develop technologies to control dengue virus. The Colorado State subcontract is approximately $5 million. There are nine universities and one biotechnology company involved in this Grand Challenge 7 grant titled "Genetic Strategies for Control of Dengue Virus Transmission."

Dr. Olson is a Professor in the Department of Microbiology, Immunology and Pathology (MIP), and Director of the Arthropod-Borne and Infectious Disease Laboratory.

Dr. Carlson is Director of the Infectious Diseases Program, a University Program of Research and Scholarly Excellence, and a Professor in MIP. Dr. Black also is a Professor in MIP and one of his laboratory's research focuses is on mapping genes in the target mosquito that condition susceptibility to dengue viruses.

Dengue fever has been known for more than 200 years. The disease is caused by a group of viruses transmitted to people by mosquitoes of the species *Aedes aegypti*. The global prevalence of dengue has grown dramatically in recent decades with the disease now endemic in more than 100 countries. The World Health Organization estimates 50 million cases of dengue infection each year with approximately 20,000 people dying from dengue annually.



Dr. Kenneth Olson's research team: Christopher Bosio, Irma Sanchez, Alexander Franz, Dr. Olson, Brian Geiss, Dennis Pierro

The multinational dengue team will employ a combination of molecular, field and social science research to advance genetics-based strategies for preventing mosquitoes from transmitting dengue viruses. The project will examine approaches that could help inhibit viral development within the mosquito, reduce the ability of infected mosquitoes to successfully transmit the virus, and reduce or eliminate mosquito populations.

In addition to Colorado State University, other institutions joining UC-Irvine in the study are University of California-Davis, Texas A&M, University of Notre Dame, North Carolina State University, Cornell University, the Fiocruz Instituto de Tecnologia em Imunobiologicos in Brazil, the Eubios Ethics Institute in Thailand and Oxitec, a biotechnology company based in Great Britain that specializes in biological insect control.

The grant for the consortium adds to the rapidly expanding programs in infectious diseases at the College. In June, the College of Veterinary Medicine and Biomedical Sciences' Infectious Diseases Program brought the University into the biodefense arena. Based on research programs already in place, and with ambitious plans to expand infectious diseases programs in the future, the University was awarded a four-year, $40 million grant to establish a Regional Center of Excellence (RCE) for Biodefense and Emerging Infectious Diseases research and training.

The Grand Challenges initiative was launched by the Bill and Melinda Gates Foundation in 2003, in partnership with the National Institutes of Health, with a $200 million grant to the Foundation for the National Institutes of Health (FNIH). It is an international effort to achieve scientific breakthroughs against diseases that kill millions of people each year in the world's poorest countries. It is funded with a $450 commitment from the Gates Foundation with additional funding by the Wellcome Trust and the Canadian Institutes of Health Research (CIHR). The initiative is managed by global health experts at FNIH, the Gates Foundation, the Wellcome Trust and CIHR. For additional information on funded projects, go to www.grandchallengesgh.org. ■

MCIN Program Celebrates 20 Years of Groundbreaking Research

In 1986, Dr. Stanley B. Kater launched the Program in Neuronal Growth and Development as a seminar series designed to bring nationally and internationally recognized scientists to the Colorado State University campus. Twenty years later the program, now known as the Program in Molecular, Cellular and Integrative Neurosciences (MCIN), is a University Program of Research and Scholarly Excellence with a global reputation for outstanding research and innovative graduate education.

Today, MCIN has 25 neuroscience faculty affiliates in four colleges and eight departments including Biomedical Sciences, Biology, Biochemistry and Molecular Biology, Psychology, Occupational Therapy, Computer Science, and the Department of Environmental and Radiological Health Sciences, as well as the Department of Music, Theatre and Dance. The diversity of the faculty members reflects a range of research interests linked together by one common element – the neuron.

"The neuron is what brings us together at the Program in Molecular, Cellular and Integrative Neurosciences," said Dr. Jim Bamburg, Director of the MCIN and a Professor in the Department of Biochemistry and Molecular Biology in the College of Natural Sciences. "We are all working on aspects of the nervous system – muscle regulation, development, degenerative diseases, sensory perception, function and more. We are working to understand the neuron from the outside in, and the inside out."

In 1990, Dr. Bamburg was elected as the program's director and the group decided to establish a graduate program. The graduate program is unique in its approach in that it is not a degree-granting program. Enrolled students spend their first year rotating through MCIN laboratories and complete a core curriculum in the neurosciences. In their second year, the students select a mentor and a department (though the mentor is not necessarily in the same the department as the student), and the graduate degree they will pursue. They graduate from the University with a strong research background in neurosciences and a graduate degree that further defines their expertise. The student's transcript notes that they have successfully completed the requirements of the interdisciplinary MCIN program.

Dr. Jim Bamburg

In 1992, the University created the Programs of Research and Scholarly Excellence (PRSE) to encourage the growth and development of programs with a proven record and great potential. MCIN received PRSE recognition in the first year the program was established and has retained that status. Because of that designation, MCIN received budgetary increases all of which was earmarked for student support and stipends. In addition, in 2002 a subgroup of MCIN faculty received a training grant from the National Institutes of Health to support graduate students and postdoctoral researchers.

In the years since its inception, the research focus of the MCIN has evolved as faculty members have left the group, joined the group, or changed research interests. Today, faculty research interests are focused in areas related to neuronal differentiation, degeneration and regeneration; ion channels and membrane physiology; synaptic mechanisms; neuronal circuitry and chronobiology; sensory biology; artificial neural networks; cognitive neuroscience; and neurotoxicology.

"We have faculty working on just about every aspect of the nervous system," said Dr. Bamburg. "We work at the cellular and molecular levels and, with the addition of faculty affiliates in the Department of Psychology, on cognitive function as well. Our faculty is supported by state-of-the-art research facilities that support the latest technological advances in microscopy, imaging, freeze-fracture, protein sequencing and more."

Faculty members also have been instrumental in establishing a local branch of the Society for Neuroscience – the Front Range Neuroscience Group. The group, created in 2003, now hosts the premier neurosciences meeting in the Rocky Mountain region bringing in world-renowned speakers, a large and diverse group of vendors, and a poster session with the most recent breakthroughs in neurosciences.

"Dr. Stuart Tobet deserves much of the credit for establishing and maintaining this vibrant group," said Dr. Bamburg. "It brings much deserved recognition to the efforts of the MCIN faculty and highlights their research work as well as our graduate program. It's very exciting to host this meeting and bring so many amazing researchers here to Fort Collins. Our students benefit greatly from these interactions, and also they get a sneak preview of what to expect at the national conference."

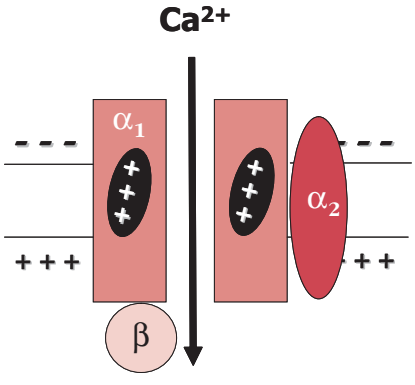
The next 20 years are sure to bring even more recognition to the Program in Molecular, Cellular and Integrative Neurosciences at Colorado State University as students and faculty redefine and refine our understanding of the complexities innate to the human nervous system. To learn more about the MCIN program, or the Front Range Neurosciences group, visit their Web site at www.cvmbs.colostate.edu/mcin. ■

Understanding Protein Structures May Help Improve Pain Medications

Whether working on patients in a clinical setting, working on elephants in the wilds of Cameroon, or working on calcium channels in his laboratory at Colorado State University, Dr. William Horne's overarching mission is to alleviate pain and suffering.

Dr. Horne, an Associate Professor in the Department of Biomedical Sciences, is a member of the Program in Molecular, Cellular and Integrative Neurosciences, and is Co-Director of the Center for Comparative Pain Medicine. His basic research into voltage-gated calcium channels and the protein complexes of which they are comprised is a far cry from the operating rooms where he has worked as an anesthesiologist helping patients through surgeries and administering post-operative pain relief. But the two are intertwined as Dr. Horne is able to see in a clinical setting where his laboratory research may one day lead – to improved analgesics that shut down pain more effectively and with fewer side effects.

"Our laboratory is looking at calcium channel structures, in particular the structure of a subunit referred to as beta 4 which seems to have dramatic effects on the gating kinetics (opening and closing) of the calcium channel," said Dr. Horne. "These voltage-gated calcium channels coordinate a variety of calcium-dependent processes in excitable cells (such as nerve and cardiac cells) including gene expression, signal propagation and neurotransmitter release."



A graphic depiction of an ion channel. Dr. Horne's laboratory is focusing on the sub-unit beta 4, as shown in the bottom of the figure with the Latin letter ß.

Neurotransmitters enable the transmission of pain so blocking the release of neurotransmitters inhibits pain. Before researchers can look to improve pain treatment by regulating the actions of calcium channels, they have to understand the molecular structure of these channels and the protein-protein interactions that occur between channel proteins and signaling molecules. The target protein Dr. Horne's laboratory studies is modular and typically has three subunits – alpha 1, alpha 2/delta and beta. All three subunits have been shown to play a major role in regulating pain transmission. His current work focuses on the alpha 2/delta and beta subunits.

"We want to understand what these protein subunits do when they combine with alpha 1 (the pore-forming subunit) to form a channel complex," said Dr. Horne. "Our research shows that the beta 4 subunit definitely affects gating kinetics and may have a critical role as director of channel modulation by somehow coordinating all molecular and electrical signaling events. Defining the structure of this important subunit will answer some critical questions as to its role in calcium channel function and pain."

Once researchers understand how the alpha and beta subunits interact, it may be possible to use this information to help create the next generation of pain relieving drugs.

Dr. Horne, who is board certified in veterinary anesthesiology, first became interested in calcium channels when he was a resident at Cornell University.

"I became fascinated with the target protein," said Dr. Horne. "When I started my PhD, I worked on the actual structure of the protein complex. At the time I was publishing several papers focused on the global structure of these proteins, powerful techniques in molecular biology exploded onto the research scene. I went on to Stanford to do a post-doc and became heavily involved with cloning multiple types of calcium channels from the brain and spinal cord."

Once researchers understand how the alpha and beta subunits interact, it may be possible to use this information to help create the next generation of pain relieving drugs.

The collective efforts of many researchers led to the discovery of 10 genes that code for calcium channel alpha 1 subunits: Dr. Horne was the first to discover one of them. After finishing his post-doc, Dr. Horne went to work for Neurex Corp. where he worked with a team that studied the use of a marine snail toxin as an analgesic agent. The toxin acts as a calcium channel blocker to prevent transmission of pain. The company eventually developed the toxin into a drug that was just recently approved by the Federal Drug Administration. Dr. Horne said he enjoyed working at Neurex but came to miss veterinary medicine. He took a position at North Carolina State and then joined the faculty at Colorado State in 2003. In addition to his laboratory and clinical work, Dr. Horne is involved as a veterinary anesthesiologist in a program in Cameroon to equip elephants with satellite tracking collars to aid in population studies and herd control. ■

Migration Studies Help Researchers Understand Brain Structures

When we think of migration, we often imagine birds flying thousands of miles south to escape winter's cold, salmon swimming upstream to spawn and die, or massive caribou herds heading across the tundra to bear their young. We don't often think of migration in terms of human cells, with migratory distances measured in microns, not miles. But the migration of cells – particularly neuronal cells – is critically important to the normal functioning of the human nervous system.

An extreme example of this is Kallman's syndrome with symptoms including gonadotrophin releasing hormone (GnRH) deficiency and accompanying effects, and a diminished or non-existent sense of smell. Kallman's syndrome arises when GnRH secreting neurons in a developing fetus fail to migrate from their site of origin in the nose into the basal forebrain. The syndrome is usually inherited and, for some forms, affects more males than females.

Kallman's syndrome, Prader-Willi and Rubenstein-Taybi are all rare genetic conditions that affect neuroendocrine structures. While unknown to most of us, these conditions are an area of interest to Dr. Stuart Tobet, an Associate Professor in the Department of Biomedical Sciences and a member of the Program in Molecular, Cellular and Integrative Neurosciences. Dr. Tobet's laboratory is examining how multiple signal types affect migration and cell position in the developing nervous system, and is using innovative tracking systems and video microscopy to image these migrations.

"Neurons form communities from which they can gather information and communicate about their environments," said Dr. Tobet. "Our brains evolved with the ability to compartmentalize and have cell groups that integrate and carry out different functions. We are studying the migration of cells into groups and what affects their movements. Differences between the two sexes in how functions are carried out, and in the ability to protect and recover from internal and external assaults including strokes and brain injury that occur during development, are areas of interest for the laboratory. There are differences in neuronal function between the two sexes that are above and beyond the more commonly thought of differences due to hormones."

Dr. Stuart Tobet, center, research associate, Michelle Edelmann and undergraduate student Brandon Wadas are researching estrogen receptors and their relationship to neuronal development.

Dr. Tobet's laboratory is using the ventromedial nucleus of the hypothalamus (VMH) and the proptic area as model systems for his group's research. These regions are critical components of the brain regulating homeostatic, neuroendocrine and behavioral functions. Cells in these regions migrate to specific positions according to the chemical environment around them, the types of neighboring cells, and potential anatomical connections. In his research, Dr. Tobet is able to follow the formation of nuclei in vitro using video microscopy – very elaborate home movies of cells on the move.

It takes many investigators to carry out modern-day neuroscience research and Dr. Tobet's collaborations stretch from Oregon on the West Coast to Boston and Virginia on the East Coast and includes Colorado, Texas and Kansas in between. Recently, Dr. Tobet was joined in his research efforts by Dr. Gregor Majdic, Assistant Professor, Department of Veterinary Faculty, Center for Animal Genomics, at the University of Ljubljana in Slovenia. Earlier this year, Colorado State University and the University of Ljubljana formalized their relationship with a Memorandum of Understanding that will allow the two laboratories to work together in a way that will improve cooperation and speed up progress in studies of hormone-independent sex differences in the brain.

"Research into the workings of the brain is exceptionally challenging, so working with Dr. Majdic in a team effort means we can meet the challenges more creatively and with better results," said Dr. Tobet. "The more we learn the better we are able to put some of the pieces together, and the greater our understanding of ourselves."

To view video images of cellular migrations in a mouse model, go to www.cvmbs.colostate.edu/bms/tobet.htm. ■

Dr. Tobet's laboratory is examining how multiple signal types affect migration and cell position in the developing nervous system, and is using innovative tracking systems and video microscopy to image these migrations.

Researchers Hope Tracking Ion Channels Will Give Clues to Cells' Function

Dr. Michael Tamkun

As a biologist, Dr. Michael Tamkun had a keen interest in venomous animals – more precisely, how venom from poisonous animals worked to kill prey. Many venoms, including the venoms of cobras, poison dart frogs, scorpions and sea snakes, act by interfering with ion channel activity, effectively shutting down cell function.

So it was from an early fascination with venomous animals that Dr. Tamkun grew interested in ion channel proteins. Now a Professor in the Department of Biomedical Sciences and a faculty participant with the Program in Molecular, Cellular and Integrative Neurosciences, Dr. Tamkun is studying ion channel proteins to develop a greater understanding of the role these ubiquitous proteins play in different tissue types.

"What my lab is interested in is how ion channel proteins move around in cells," said Dr. Tamkun. "These are the proteins that are the basis of electrical activity in the nervous system. For example, when a dentist uses lidocaine to numb a tooth, the lidocaine binds with ion channel proteins so they can't function enabling a dentist to do his work without the patient feeling any sensation of pain."

For dental patients, that's a good thing. But ion channel malfunctions are also at the root of a number of devastating diseases including cystic fibrosis and cardiac arrhythmias. Understanding the normal function of ion channel proteins, including how they get to where they are going and how the cell knows where to place them, will lead to a greater understanding of cell biology and perhaps help develop more effective treatments and cures for illnesses that have as a hallmark ion channel irregularities.

"We work mainly with a potassium channel known as Kv2.1, one of 50 members of this family type in the body," said Dr. Tamkun. "Why we have 50 different genes encoding this type of channel is another question, but it probably is because it gives the cells the capability to regulate electrical excitability in many different ways. What we are doing in our lab is studying how these channels move in living cells using a technique that tethers fluorescent proteins to the channel. Using a high-resolution fluorescence, confocal microscope, we can then localize and track the ion channel as it moves to and from the cell surface of living neurons and cardiac myocytes."

What the work of Dr. Tamkun and others has shown is that distinct ion channel proteins are expressed differently in different types of cells, and are always changing. In cardiac cells, for example, the number and location of channel proteins can change from one beat to the next. Researchers also are seeing that discreet domains exist that compartmentalize ion channels. This leads to additional questions about why domains exist, how channels get to specific domains, and how the cells keep channels within those domains.

"We know very little about this dynamic behavior," said Dr. Tamkun. "The technology simply hasn't been there to help us answer these questions, but new research methodologies and technological advances are moving us forward so that we may one day delve even deeper into these mysteries of the cell."

The cells being studied in Dr. Tamkun's laboratory present research challenges because they are always changing. The brain is always thinking and the heart is always beating so these systems are not static and are always changing the number of proteins from one beat to the next and from one action to the next. New tagging and recording technology is helping researchers see and follow proteins of interest, one day leading to breakthroughs in understanding of the most basic but complex functions of the cell. ■

Understanding the normal function of ion channel proteins, including how they get to where they are going and how the cell knows where to place them, will lead to a greater understanding of cell biology and perhaps help develop more effective treatments and cures for illnesses that have as a hallmark ion channel irregularities.

Programs of Research and Scholarly Excellence Set High Standards Within College

PRSE

Programs of Research and Scholarly Excellence

Fifteen years ago, Colorado State University established the Programs of Research and Scholarly Excellence to recognize programs that achieve great distinction and set high standards for excellence. These programs, which are selected after an extensive nomination and review process, serve as models for research and academic programs throughout the University. Today, the College of Veterinary Medicine and Biomedical Sciences houses four PRSEs and provides the majority of the faculty affiliates to a fifth, the Program in Molecular, Cellular and Integrative Neurosciences.

"The Programs of Research and Scholarly Excellence reflect the high quality of our College's faculty and staff, and the diverse nature of our research, academic and outreach programs," said Dr. Lance Perryman, Dean of the College. "Designation as a Program of Research and Scholarly Excellence is truly an honor, and we are very proud at how well the College is represented within this elite group of University programs."

Programs of Research and Scholarly Excellence at the College are:

1. Animal Reproduction and Biotechnology Laboratory (ARBL)
2. Infectious Diseases Program
3. Musculoskeletal Research Program
4. Radiological Health Sciences and Cancer Research
5. Program in Molecular, Cellular and Integrative Neurosciences (The director of this program, Dr. Jim Bamburg, is in the College of Natural Sciences, though many affiliate faculty members are in the College of Veterinary Medicine and Biomedical Sciences' Department of Biomedical Sciences.)

1

Animal Reproduction and Biotechnology Laboratory (ARBL)

The Animal Reproduction and Biotechnology Laboratory brings together scientists with a common interest in the reproductive physiology of cattle and horses. Research programs include hypothalamic and pituitary function, ovarian function, gamete biology and andrology, placental and fetal physiology, reproductive technology, and diseases and toxicology. Outreach and service programs include the Reproductive Endocrinology Laboratory, Transgenic Core Facility, Equine Reproductive Services and Equine Continuing Education. ARBL facilities are located mainly on the Foothills Research Campus.

Firecracker, the first test-tube horse by sperm injection.

2

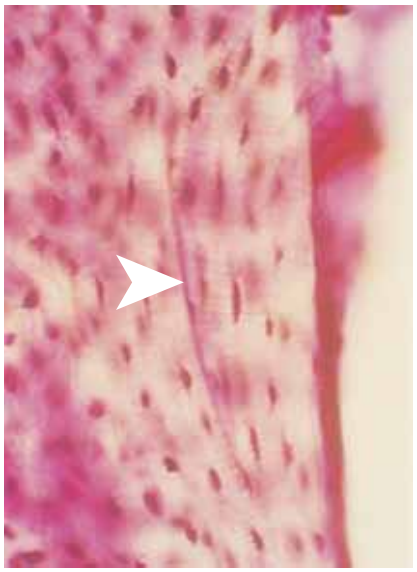
Infectious Diseases Program

The Infectious Diseases Program is home to many of the College's biomedical researchers, mainly within the Department of Microbiology, Immunology and Pathology. The Infectious Diseases Program concentrates on better means to diagnose, treat and prevent through vaccination four categories of infections caused by retroviruses (AIDS and other diseases), mycobacterial infections (including tuberculosis and leprosy), vector-borne diseases (including West Nile fever and encephalitis) and blood parasites (the major cause of disease in the world, including malaria). The Infectious Diseases Program recently was selected by the National Institute of Allergy and Infectious Diseases to establish a Regional Center of Excellence for Biodefense and Emerging Infectious Diseases.

Sandflies, Phlebotomus spp.*, act as vectors for various diseases including leishmaniasis.*

3
Musculoskeletal Research Program

The interdisciplinary Musculoskeletal Research Program is comprised of three units: the Orthopaedic Research Center focuses on articular cartilage healing, microdamage in subchondral bone, development of fluid markers, and development of molecular biology techniques to evaluate early changes in cartilage healing and to document early molecular events in arthritis; the Orthopaedic Bioengineering Laboratory advances treatment and prevention of muscular, neuromuscular and skeletal injury and disease; and the Comparative Ruminant Orthopaedic Laboratory which has developed during the last 15 years and involves collaboration with a number of researchers who use sheep as a model for researching important orthopaedic problems, including osteoporosis. Most facilities are located at the South Campus.



Microcrack in subchondral bone.

4
Radiological Health Sciences and Cancer Research

The Radiological Health Sciences and Cancer Research PRSE provides education, research and service related to carcinogenesis, radioecology, radiation protection, cancer diagnosis and experimental therapeutics. This multi-departmental and multi-college program collaborates on many projects with researchers 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.

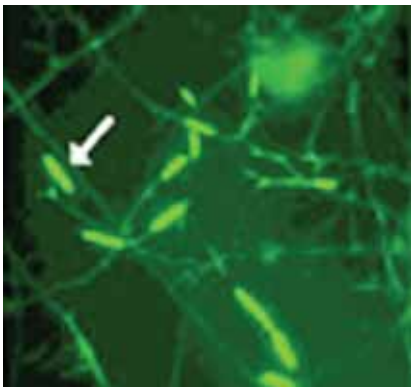
Researchers at Colorado State have pioneered radiation protocols for animal cancer treatment that have been developed during the last 30 years at the most proven radiation therapy program for animals in the world. This PRSE not only examines the benefits of radiation in cancer therapy, but looks at the risks radiation poses to healthy cells. Some current studies include: radiation-induced genomic instability, genetic control of radiosensitivity, tumor cell kinetics and the effects of radiation and heat on the survival and cell cycle of mammalian cells in culture.

Colorado State University has the nation's longest running radiation treatment program for animals with cancer.

5
Program in Molecular, Cellular and Integrative Neurosciences

This interdisciplinary graduate research and education program was established in 1986 and has an international reputation that garners strong extramural support. Faculty research interests are focused on neuronal differentiation, degeneration and regeneration, ion channels and membrane physiology, synaptic mechanisms, neuronal circuitry and chronobiology, sensory biology, artificial neural networks, cognitive neuroscience and neurovirology.

The Program in Molecular, Cellular and Integrative Neurosciences has 25 neuroscience faculty affiliates in four colleges and eight departments including Biomedical Sciences, Biology, Biochemistry and Molecular Biology, Psychology, Occupational Therapy, Computer Science, and the Department of Environmental and Radiological Health Sciences, as well as the Department of Music, Theatre and Dance. The diversity of its faculty members allows for research not only into the neuron, but also cognitive function. ■



Immunofluorescence in rat hippocampal neurons. Photo from the laboratory of Dr. James Bamburg.

VMBS Hosts 67th Annual Conference for Veterinarians

Veterinarians from Colorado and around the nation will be coming to Colorado State University January 7-9, 2006, for the 67th Annual Conference for Veterinarians hosted by the College of Veterinary Medicine and Biomedical Sciences.

The conference features a comprehensive continuing education program, displays, guest speakers, networking time and more. Dr. Temple Grandin, an Associate Professor in the Department of Animal Sciences at CSU is the keynote speaker for the event. Other guest speakers include: Dr. Joseph Bartges of the University of Tennessee, College of Veterinary Medicine, small animal guest speaker; Dr. John Maas, University of California-Davis, School of Veterinary Medicine, large animal guest speaker; and Drs. Paul Lunn and Pat McCue, both of CSU's College of Veterinary Medicine and Biomedical Sciences, equine guest speakers.

Dr. Temple Grandin is a designer of livestock handling facilities and an internationally known expert on animal handling and welfare. Facilities she has designed are located in the United States, Canada, Europe, Mexico, Australia, New Zealand, and other countries. She also has developed an objective scoring system for assessing handling of cattle and pigs at meat plants. Dr. Grandin teaches courses on livestock behavior and facility design at Colorado State University and consults with the livestock industry on facility design, livestock handling and animal welfare. She has appeared on numerous television shows and in many publications. She has authored more than 300 articles in both scientific journals and livestock periodicals on animal handling, welfare, and facility design, and written four books.

To learn more about the 67th Annual Conference for Veterinarians, go to www.cvmbs.colostate.edu/clinsci/ce. The cost of the conference is $285 for registrations received on or before Dec. 15, and $325 after Dec. 15. For additional information, or to request a brochure or registration packet, contact Lori Williams at (970) 297-1273, or 1-800-457-9715. ■

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