Center of Excellence in Livestock Diseases and Human Health
2008 Annual Report

Nutrition & Metabolic Disorders

Degenerative Diseases

Atherosclerosis

Laminitis

Mastitis

Colorectal Cancer

Food Animal & Population Health

The University of Tennessee
Institute of Agriculture
College of Veterinary Medicine
Welcoming Remarks

We are pleased to present the 2008 annual report for the Center of Excellence in Livestock Diseases and Human Health. Along with benchmark data for fiscal years 2004-2008, this report includes highlights of faculty research projects funded by the center in fiscal year 2008.

During 2008, the center supported the research efforts of 20 different faculty who were engaged in scientific investigations that ultimately will benefit the citizens of Tennessee, the nation, and the world, as well as affect the economy at both the state and national levels. Center faculty have made significant advancements in cancer biology, molecular pathophysiology, host defense, and disease transmission. Center faculty have also made significant advancements in the prevention and treatment of infectious and non-infectious livestock diseases that affect agricultural productivity.

Productivity among center faculty has been outstanding during 2008. External funding decreased slightly from $20,412,786 in 2007 to $19,306,048, in part because of the decrease in federal funding (the National Institutes of Health are operating below their 2005 budget level). However, despite a 3.5% center decrease in federal funding, center faculty ambitiously sought and obtained $3,622,708 in industry and private/foundation funding to continue ongoing projects and begin new ones. Research expenditures continued to stabilize at $3,118,056 in 2008. The one-year return on the state’s investment in the center, as the ratio of research expenditures to the state’s appropriation, is 5.5:1.

Center faculty continue to garner national and international recognition for their research and scholarship. During calendar year 2008, center faculty published 60 peer-reviewed articles and gave 44 invited presentations at regional, national, and international meetings.

We are proud of the progress made by center faculty, and we hope you enjoy this summary presentation of center activities and accomplishments.

Leon Potgieter, Interim Dean

Robert N. Moore, Director

L-R: Moore, Misty Bailey (ed), Potgieter

Photo: Phil Snow
Center of Excellence in Livestock Diseases and Human Health
2008 ANNUAL REPORT

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In accordance with the requirements of Title VI of the Civil Rights Act of 1964,
Title IX of the Education Amendments of 1972, Section 504 of the Rehabilitation
Act of 1973, and the Americans with Disabilities Act of 1990, The University of
Tennessee affirmatively states that it does not discriminate on the basis of race,
sex, or disability in its education programs and activities, and this policy extends
to employment by the University. • Inquiries and charges of violation of Title
VI (race, color, national origin), Title IX (sex), Section 504 (disability), ADA
(disability), Age Discrimination in Employment Act (age), sexual orientation, or
veteran status should be directed to the Office of Equity and Diversity (OED), 1840
Melrose Avenue, Knoxville, TN 37996. • Publication No. E180103-00-001-09
# Comparative Summary of Accomplishments

<table>
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<th>Benchmark</th>
<th>2008 (20 faculty in center)</th>
<th>2007 (18 faculty in center)</th>
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<tr>
<td>Return on investment</td>
<td>5.5:1</td>
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* Based on calendar year through publication date of this report.
† Based on fiscal year.
DISSEMINATION of RESEARCH

The UTCVM distributes two publications to the public—the magazine *Veterinary Vision* and the newsletter *Volunteer Vet*—and one in-house newsletter, *Discovery*.

The quarterly, in-house newsletter *Discovery* keeps UTCVM researchers informed about each other’s work and research-related policies and resources. [www.vet.utk.edu/research/newsletters/](http://www.vet.utk.edu/research/newsletters/)

The annual magazine *Veterinary Vision* carries features concerning ongoing research activities and the results of concluded research studies. It is written for a general audience.

The quarterly newsletter *Volunteer Vet* features research activities and results and is distributed to donors and employees.
Comparative & Experimental Medicine Research Symposium

The COE was a major sponsor of the 2nd Annual Comparative & Experimental Medicine Research Symposium, which brought together researchers from 16 different departments across three UT-Knoxville campuses for a day-long event opening with influenza virus expert Robert G. Webster, PhD, FRS, and culminating with an awards banquet.

Thirty-nine researchers from the Institute of Agriculture presented talks at the symposium, including heavy participation by members of the Department of Animal Science. These 39 representatives were among 60 new scientists to present, and at the end of the day, the institute was able to boast 12 winners of travel awards.

The symposium was designed to allow sharing of research results, promote collaboration, and provide new investigators meeting-format experience with 10-minute presentations.

http://www.vet.utk.edu/research/symposium/

Sharing Ideas

Robert Webster, St. Jude Prof., explains his avian influenza research. Maria Prado accepts an award from Karla Matteson. Jae-Hoon Bahn answers questions about his research poster.
Center investigators traveled to seven countries and 15 states in 2008 disseminating their research findings. The map below shows their extensive travels.
INTRODUCTION

The center was created in 1984 to promote interdisciplinary activities designed to improve the quality of human life through better animal health; expand livestock disease research capabilities in the College of Veterinary Medicine (UTCVM) and the Institute of Agriculture; identify and characterize animal diseases that are similar to human diseases; and develop new strategies for the diagnosis, treatment, and prevention of disease.

Since 1984, the center has developed successful programs that affect the understanding, treatment, and prevention of livestock and human diseases. These programs predominately focus on molecular and cellular approaches to research in infectious diseases, toxicology, host defense, molecular genetics, and carcinogenesis.

The center has developed investigative strengths along innovative, sophisticated, and contemporary lines in two general areas:

1) Animal Models and Comparative Medicine
2) Mechanisms of Disease, Pathogenesis, and Immunity

These areas are each highly interrelated, and the center plays a critical role in developing these focused areas of strength in both the UTCVM and the Institute of Agriculture.

PERSONNEL

Dr. Robert N. Moore, Professor and Associate Dean for Research and Graduate Studies, continues as director of the center. In January 2008, Dr. Leon Potgieter began as interim dean after Dr. Michael Blackwell retired. Dr. James Thompson will join the college as dean on October 1.

COLLABORATIONS

Several center faculty are pursuing collaborative research between laboratories in basic and clinical science. Dr. Robert Hwa-Chain Wang and Dr. Jeffrey Phillips are co-investigators in Phillips’ canine cancer project. When Dr. Phillips receives a canine cancer patient, he sends a sample of the tumor tissue to Dr. Wang, who, in turn, determines the best chemotherapy treatment by testing the tissue’s reaction to different forms of treatment.

While Dr. Mei-Zhen Cui looks at lysophosphatidic acid in relation to its causative effects on heart disease, Dr. Xuemin Xu is now studying the effect of lysophosphatidic acid on Alzheimer’s disease by using Dr. Cui’s expertise to his advantage.
ACCOMPLISHMENTS

Center faculty continue to make excellent progress in ongoing projects, gaining national and international recognition for their expertise and accomplishments. Details of current faculty research are provided in the Faculty Reports section (p. 12–31). Despite a nationwide decrease in new and existing federal funding, center accomplishments for 2008 were excellent in terms of benchmarks and extramural funding base. Center researchers are compensating for the lack of federal funds by seeking and receiving more awards from foundations, industry, and other private entities. Figure 1 shows the percentage breakdown of external funding by source.

The 20 center faculty averaged 3.8 peer-reviewed publications (76 total) and 1.55 invited presentations (31 total) at prestigious national and international meetings. See Publications and Presentations (p. 32–49) for details.

The return on the state’s investment in the center was 5.5:1, calculated as ratio of expenditures from extramural funding to center appropriation. Extramural funding totaled $19,306,048 this year. The total funding includes new, multi-year awards for Drs. Brian, Kania, Kirk, Phillips, Prado, Rouse, Schuller, and Wang, totaling $4,448,849; and new, one-year awards for Drs. Andrews, Dhar, Frank, Kania, Kirk, Oliver, Phillips, and Sangster, totaling $294,298. Research expenditures continued to stabilize at $3,118,056. See “Research Funded Externally” and “Research Expenditures” on p. 3 for the fiscal year 2008 data summary.
## Research Funded Externally FY 2008

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* Represents total, all-years funding for active grants and contracts

## Research Expenditures FY 2008

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Allocation of Funding

The Center of Excellence in Livestock Diseases and Human Health supports investigators and promotes research through a variety of mechanisms. Although it is not a primary source of research funding, the center facilitates established investigators’ efforts to maintain and expand their research programs and promotes new investigators’ potential to develop competitive research programs.

Center faculty consist of senior members who have research interests in line with center objectives and a strong history of securing external funding using center funds. Junior members are those who have received seed money or bridge funding, or new faculty who have received start-up funds. Junior members are expected to secure external funding within two years; members who fail to secure such funding will be placed on probation for one year. If, at the end of the probationary period, external funding has not been secured, the member will be dismissed from the center.

Start-Up Funds

The center provided start-up funds for two faculty to secure additional external funding. Drs. Michael Fry and Juergen Schumacher were awarded a total of $13,000.

Dr. Fry’s research involves developing a procedure for measuring canine and human iron metabolism via the protein hepcidin. Dr. Schumacher studies the pharmacokinetics of oral and intravenousitraconazole (an anti-fungal) and its hepatotoxic effects in the green iguana.

Infrastructure

$56,841 helped fund service contracts and equipment

The center promotes the research infrastructure of both the UTCVM and the Institute of Agriculture through the purchase and maintenance of essential research equipment. The Research and Graduate Programs Advisory Committee reviews equipment requests based on three criteria: justification of need, current availability of equipment, and number of investigators who may benefit. During fiscal year 2008, the committee authorized $25,538 toward the purchase of four pieces of equipment. An ultra-low temperature freezer was purchased as a necessary replacement for Dr. Xuemin Xu’s laboratory personnel to store biological material. The analgesia and anesthesia faculty benefited from Dr. Christine Egger’s request for the purchase of an analgesiometer to assess pain levels. Dr.
Barry Rouse requested a special ergonomic chair for use in the animal procedures room. For Dr. Jeffrey Phillips, a MyiQ Single-Color Real-Time PCR Detection System was purchased to detect fluorescent green dyes used to examine stained portions of tissues. This system will prove useful across the UTCVM.

In support of the UTCVM’s research enterprise, the center funded service contracts for three pieces of equipment purchased previously with COE funds. Service for fume hoods, a flow cytometry system, and an ultracentrifuge totaled $31,303. This equipment benefits nearly every investigator in the college, including clinicians.

SEMINARS AND SPONSORED LECTURES

Topics in Laboratory Animal Pathology Graduate Course
The COE provided sponsorship for this course, which emphasized responsible care of laboratory animals and appropriate interpretation of data gained from the use of the animals. The following guest lectures were incorporated into the course:

Krista LaPerle, “Genetically Engineered Mice Phenotyping 101”
Director, Tri-Institutional RADL & Genetically Engineered Mice Core, Memorial Sloan-Kettering Cancer Center

Mac Law, “Fish as Laboratory Animals”
Associate Professor of Pathology, North Carolina State University

Richard Peterson, “Laboratory Rodents in Preclinical Drug Development”
Molecular and Ultrastructural Pathology Group, GlaxoSmithKline

Wayne Buck, “Pathology of Nonhuman/Old World Primates”
Department of Cellular and Molecular Toxicology, Abbott Laboratories

In addition, the COE helped offset expenses for two special lectures for faculty, staff, and graduate students on UT Knoxville campuses:

Lawrence J. Marnett, “COX-2 Inhibitors and Cancer—Where to Go Next”
Director, Vanderbilt Institute of Chemical Biology, Vanderbilt University Medical Center

Robert G. Webster, “H5N1 Influenza: Has the Risk Been Overblown?”
Professor & Rose Marie Thomas Chair, Division of Virology, Department of Infectious Diseases, St. Jude Children’s Research Hospital
**DISSEMINATION OF RESEARCH**

The center contributed $1,194 for a COE researcher to present at two national-level, scientific meetings. Travel awards totaling $1,338 for five students in the Comparative and Experimental Medicine graduate program allowed them to disseminate their research at five different national meetings. For scientific, peer-reviewed journal articles, the center gave one faculty member $1,705 to offset publication charges. A complete list of faculty publications and presentations for the 2008 calendar year can be found in the Publications and Presentations section (p. 32-49). Faculty are encouraged to share their research by speaking to professional groups, community groups, and civic groups. In addition, the UTCVM issues press releases to state, regional, and national media, resulting in numerous television and print features, many of which relate directly to research conducted through the center. The three UTCVM news publications are available on the UTCVM Web site (http://www.vet.utk.edu/), which also provides an overview of the types of research conducted by UTCVM and COE faculty.

**CENTER OF EXCELLENCE SUMMER STUDENT RESEARCH PROGRAM**

In an effort to foster interest in careers in biomedical research, the center helped provide opportunities for 18 veterinary students to perform research within the UTCVM during the summer.

In addition to laboratory and field research, students attended a week of professional development seminars, during which guest speakers addressed topics such as career opportunities in research, compliance issues in lab animal care, scientific writing, and the grant proposal process. They also participated in the Comparative & Experimental Medicine Research Symposium, either as presenters or as assistants.

Near the end of the 10-week program, the students presented their research findings to their colleagues and to UTCVM faculty as well as prepared a scientific abstract.

Two students who participated in last year’s COE summer program now have published scientific articles as a result of their participation in the program. Deborah Spector and Thomas Chen are first authors on two separate papers on canine blastomycosis (*Journal of Veterinary Internal Medicine*. 2008;22:839-843 and *Medical Mycology*. In press).

To maximize student participation, the program is open to both center and non-center faculty. During fiscal year 2008, seven COE faculty participated in the program. The center will continue to encourage participation of center faculty.

The students involved in the summer research program and a brief description of their activities follow:
**Rosalie Atkins**, a 3rd-year student from Santa Rosa, CA, earned a BS in biology from the University of Hawaii at Manoa in Honolulu. Dr. Sharon Patton served as her mentor in detecting the prevalence of *Giardia lamblia*, a parasitic infection, in the Knoxville area. After graduating, Rosalie says she would like a career in clinical pathology and/or ophthalmology.

Second-year student **Kate Carpenter** worked with Dr. Robert Donnell to detect malignant catarrhal fever in Tennessee goat herds. A native of Spencer, TN, Kate earned her BS from UT in animal science and wildlife and fisheries science, minoring in forestry. She plans to pursue large animal medicine.

Dr. Gal Kelmer mentored COE student **Cristina Catasus** in indwelling intravenous regional limb profusions in horses. Originally from Gainesville, FL, Cristina received a BS in biology with minors in chemistry and business administration from Jacksonville University. This 2nd-year student is interested in equine medicine as a career.

**Nathan Chumbler** is a 3rd-year student from Smyrna, TN, who studied animal science at Tennessee Tech. This summer, he worked with Dr. Nicholas Frank evaluating the effectiveness of using an oral drug in diagnosing pituitary pars intermedia dysfunction and Cushing’s disease in horses. Nathan would like to serve as a US Army veterinarian after graduation.

**Thierry Clermont** is a 3rd-year student from Montreal, Quebec, Canada. She took a BS from the University of Pittsburgh, where she majored in ecology & evolution and psychology, with a minor in chemistry. Dr. Casey LeBlanc and Dr. Amy LeBlanc served as mentors to Thierry in studying a possible link between radiotherapy and myelosuppression in dogs, as well as studying neutrophil function in dogs undergoing chemotherapy.

Dr. Stephen Kania served as **Martha Cline’s** mentor on a project involving malignant catarrhal fever (MCF) specific to sheep and wildebeest. The obvious lack of wildebeest in the area led Martha to South Africa this summer. The blood samples she obtained were used to create a test to detect antibody response to the virus in hopes of eventually creating a vaccine to prevent MCF. A recipient of a BS in biology from Lipscomb University in Nashville (minors in chemistry and philosophy), Martha hopes to remain in research for a while after graduating.

Working with Dr. Claudia Kirk was **Rebecca Costello**, a 3rd-year student from Warminster, PA. Rebecca earned a BS in animal science from the University of Maryland and has career interests in zoo medicine, nutrition, and dermatology. This summer, she assisted in a dose-response study on garlic toxicity in dogs.

Third-year student **Erica Eads** earned a BS in animal science from the University of Minnesota, but she is originally from Mt. Prospect, IL. Erica’s passion for wildlife medicine led her to study Asian elephants with Dr. Edward Ramsay this summer at the Elephant Sanctuary in Hohenwald. They focused on improving diagnostics for tuberculosis and elephant response to treatment.
Working with Dr. Claudia Kirk was 3rd-year student Katie Ellis. Together with Dr. Angela Lusby, they studied the effect of food bowl and scoop size on food portions offered to dogs by their owners by doing owner interviews. Katie attended UT Knoxville, where she earned a BS in animal science.

Second-year student Joci Forkner earned a BS in biochemistry with a minor in chemistry in her hometown of Blacksburg, VA, at Virginia Tech. Her interests in ophthalmology led her to Dr. Barry Rouse’s lab for the summer, where she studied what inflammatory cell types enter the cornea at various times after infection with herpes simplex virus-1 and how those cells are involved in controlling infection and mediating tissue damage in stromal keratitis.

Catherine Gibson is a 2nd-year student from Powell, TN, who earned a BS in animal science (minor in chemistry) from UT at Martin. Dr. Agricola Odoi has helped Catherine develop her interest in the “one health” initiative, and she wants to carry that interest to developing countries, where she would like to teach improved methods for animal care. This summer, she did a spatial analysis of methicillin-resistant streptococcal infections in Knox County dogs.

Dr. Stephen Kania and Dr. David Bemis served as mentors for Selena Hannah, a 2nd-year student from Fayetteville, TN. She assisted mainly with Dr. Kania’s COE project examining Staphylococcus pseudintermedius resistance to antibiotics. Selena earned a BS in animal science from UT Knoxville and looks to pursue small animal medicine, particularly dermatology.

Third-year student Meredith Hobbs studied pre-veterinary science at Auburn University in Alabama and is now interested in a career in mixed-animal practice. With her summer mentor, Dr. Christine Egger, Meredith studied the effects of ketamine, sevoflurane, and nitrous oxide on anesthesia and pain management.

Sarah (Meg) Lawson assisted Dr. Silke Hecht in reviewing medical records of cats and dogs that had undergone renal scintigraphy. Their work led to a scientific article and a conference presentation. Meg is a native of Owensboro, KY, but she earned an AB in political science with minors in biological anthropology and anatomy from Duke University in North Carolina. After graduating, this 3rd-year student hopes to practice small animal and exotic medicine, focusing on anesthesiology and pain management.

Holding a BS in ecology from the University of Georgia is Iris Mixon, a 2nd-year student from Johnson City, TN. Her interest in small ruminant care led her to Dr. Jerry Roberson this summer. Together, they worked on finding a successful drug therapy for mastitis in goats.

Dr. Linda Frank and Dr. Stephen Kania mentored Rebekah Mullins in characterizing methicillin-resistant Staphylococcus species in client-owned dogs. Rebekah is a 2nd-year student from Kingsport, TN, and attended the nearby East Tennessee State University, taking a degree in biology.

Bonnie Price is a 2nd-year student who earned a BS in biochemistry, cellular, and molecular biology and a BA in anthropology from UT Knoxville. This summer, Bonnie worked with Dr. David Rotstein reviewing neonatal mortality in right whales. She also drafted a case report about systemic mycosis in a bottlenose dolphin and participated in marine mammal and other
Second-year student Kathryn Purple is from Germantown, TN, but she attended the University of Illinois Urbana-Champaign, where she took a BS in natural resources and environmental sciences. Dr. Sharon Patton and Dr. Linden Craig served as her mentors in performing parasite surveys in common wildlife species in the Knoxville area with a focus on zoonotic and domestic animal implications. Kathryn’s career interests lie with pathology.

Working with Dr. Madhu Dhar was Sara Roshwalb, a 3rd-year student from Silver Spring, MD. Sara earned a BS in biology with a minor in Jewish studies from the University of Maryland. This summer, she collected adipose tissue samples from client-owned dogs presented for surgery in order to study gene expression within the tissues. Sara would like to be able to combine her interests of ophthalmology, zoo medicine, and molecular biology in a future career.

Third-year student Linda West has a BA in music from the University of Virginia, but she also studied biology at the University of Iowa near her hometown of Des Moines. Dr. Mark Bohling served as Linda’s mentor as she mapped direct cutaneous arteries in chickens for Dr. Bohling’s future research. She is interested in avian and small animal medicine.

Dr. Thomas Doherty mentored Rebekah Willis this summer on the effects of hyperbaric oxygen therapy on horses with endotoxemia. Rebekah majored in animal science at North Carolina State University and minored in genetics and nutrition for her BS. This 3rd-year student from Morganton, NC, has an interest in radiology and small/mixed animal practice.

Benjamin Young is originally from Knoxville, TN, but his BA was earned in Annapolis, MD, at St. John’s College, where he majored in philosophy and minored in the history of mathematics. Now, as a 3rd-year veterinary student, Ben says he is “drawn to research and teaching.” Dr. Joseph Bartges benefited from Ben’s assistance in studying the formation of urinary tract stones in dogs.
Five-Year Benchmark Data

Productivity among center faculty has been outstanding during the last 5-year period. From 2004-2008, center faculty published 399 articles in peer-reviewed journals and gave 218 invited presentations at national and international meetings.

Total research funding was down from $20.4 million in 2007 to $19.3 million in 2008, reflecting decreased availability of new funding from the National Institutes of Health (NIH) and an across-the-board decrease in already-awarded grants. However, over the last 5 years, COE faculty have held steady in obtaining federal funding, despite a 2% decrease in overall NIH appropriations, when adjusted for inflation. In addition, the $19.3 million in 2008 represents a $1.1 million increase over total funding in 2004. Funding from foundations and other private sources increased dramatically from approximately $286,000 in 2004 to $1.6 million in 2008. Research expenditures have begun to stabilize.

The 5-year average return on the state’s investment in the center is 6.8:1, the ratio of research expenditures to the state’s appropriation. For comparison, benchmark data from 2004-2008 are summarized in Figs. 2-4.

Benchmark Summary (2004-2008)

- Average refereed articles per faculty member = 4.3
- External funding increased = 5.8%
- Average return on investment = 6.8:1
FUTURE PLANS

The center will continue to concentrate on developing newly recruited investigators while promoting initiatives to enhance its research capacity and direction. This year (FY09), the center will expend approximately $420,240 to fund 15 projects in the UTCVM, and the Department of Animal Science and will continue to support core facilities for flow cytometry/cell sorting, tissue culture, and microscopy.

To help recruit and retain top quality veterinary and graduate students, the center will continue to increase its involvement in research training to provide expanded opportunities for summer internships, matching travel grants, and stipend upgrades. The center will continue to offer invited speaker courses to increase national and international exposure of the center’s faculty, students, and programs, and at the same time enhance the potential for developing external collaborations for our faculty and postdoctoral opportunities for our students. As part of this effort, during FY09, the center will sponsor invited speakers for a general graduate-level seminar for the Comparative & Experimental Medicine (CEM) graduate program and an intercollegiate graduate course in microbial pathogenesis. In addition, the center will again provide support for the highly successful CEM Research Symposium. The 2009 symposium promises to be even more successful than the 2008 symposium, where more than 60 new investigators from 16 different UT programs and departments presented original research findings related to animal and human health.

Concurrent with the enhanced funding of center faculty, the UTCVM has seen dramatic growth in extramural support over the past 8 years. Much of the increase was accomplished during the college’s preceding 5-year strategic plan. That plan created a supportive infrastructure for research, helping to drive a doubling in annual college research expenditures (Fig. 5). The expansion was limited only by the depressed US economy and the reduction in federal funds available over the past 3 years. The center played a key role in the preceding strategic plan, and the current plan (2007-2011) further promotes research, including the development of the four emphasis areas highlighted on this year’s report cover and a strategy to enhance the national prominence of UTCVM research. The center will continue to play an active and critical role in promoting the strategic plan of the college.

The center has a long history of promoting translational research and will continue to promote and pursue collaborative projects with other units to enhance research that supports its objectives. Ongoing collaborations include established efforts with UT AgResearch, the Food Safety Center of Excellence, the Center for Environmental Biotechnology, and the Department of Nutrition.

![Graph](image.png)

Fig. 5. UTCVM restricted account expenditures by FY
Nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen and aspirin, are well known for treating inflammatory diseases like arthritis. These NSAIDs work by inhibiting cyclooxygenase (COX), an enzyme that causes inflammation and pain. Less known, and the focus of Dr. Baek’s studies, is the effect NSAIDs have on the development of human colorectal and other cancers.

Dr. Baek’s research team has preliminary evidence that NSAIDs work to prevent cancer not by inhibiting COX, but by inducing the expression of genes in the body that may cause cancer cell death. The effect of one of these genes (NAG-1 [nonsteroidal anti-inflammatory drug activated gene]) on cancer cell death and how the gene responds to NSAIDs to initiate cell death comprise Dr. Baek’s main research focus. Specifically, his laboratory is investigating the NSAID sulindac sulfide and its ability to induce gene expression.

This year, Dr. Baek expanded his studies to include two other potential target genes, both that were expressed even more than NAG-1 when exposed to NSAID treatment. These preliminary results suggest that other genes are also involved in sulindac sulfide’s anti-cancer effects. The results of Dr. Baek’s research may lead to the development of a new family of anti-cancer drugs.
THE ROLE OF
LYSOPHOSPHATIDIC ACID
IN ATHEROSCLEROSIS

Dr. Cui’s research team is investigating the causes of atherosclerosis, or the build-up of plaque in arteries that can reduce blood flow or cause arteries to rupture, sometimes resulting in a heart attack or stroke. The disease is estimated to affect one in three Americans in 2008, costing $448.5 billion. In 2005, Tennessee ranked third in the nation for deaths due to heart disease.

Although the role of lysophosphatidic acid (LPA) in atherosclerosis is unclear, it is one known substance that composes the plaques that accumulate on the inner-most layer of the artery wall. Dr. Cui’s laboratory has been focusing on how LPA contributes to the proliferation and migration of the smooth muscle cells that make up the middle layer of the artery wall.

Once these smooth muscle cells multiply and migrate to the inner-most layer of the artery wall, they join with fat-laden white blood cells to form foam cells. All these events lead to the ultimate formation of arterial plaques.

During the past year, Dr. Cui has studied LPA’s effect on smooth muscle cells using in vivo techniques in a mouse model. She has found that pertussis toxin, a cause of Whooping cough, seems to have therapeutic effects on aortic smooth cell migration and proliferation. Therefore, her research may lead to the identification of new therapeutic targets to prevent and cure vascular diseases.

MEI-ZHEN CUI
Associate Professor
Pathobiology Department
PhD, Tokyo Institute of Technology, Japan
2 refereed publications in 2008
In addition to center funds, Dr. Cui’s research is supported by the National Institutes of Health.
Approximately 30% of adults in Tennessee are now considered obese. By comparison, in 1985, this number was less than 10%. Most Tennesseans recognize obesity as a contributor to insulin resistance, which coincides with diabetes. However, precisely how these two metabolic disorders are related is still not clear.

Dr. Dhar seeks to understand the association between obesity and diabetes, and this past year, she focused on determining how amino-phospholipid translocases (APLTs) regulate fat and sugar metabolism. Cells rely on APLTs for maintenance and regulation, and Dr. Dhar suspects that a particular APLT called ATP10C controls the flow of molecules in and out of the cells. Therefore, any alteration in ATP10C could lead to serious changes in the cell’s function.

She has developed a mouse model by which to study the effects of Atp10C in obesity and type II diabetes. Dr. Dhar is shown above overlooking two different mouse diets. The food pellets on the left are high in fat, while the ones on the right are the more healthy choice.

The long-term goal of her investigation is to answer part of the age-old question of nature versus nurture by determining how an inherited predisposition for obesity and a high-fat diet contribute to the development of diabetes.
Clarifying Methicillin Resistance in Staphylococci

Physicians often warn their human patients about the possibility of creating drug-resistant strains of bacteria by failing to complete full treatment of an infection with antibiotics. However, mutant strains of bacteria evolve in both humans and animals, and some forms of bacteria are shared between the two.

Both humans and animals are susceptible to staphylococci, but each is susceptible to different strains. The focus of Dr. Kania’s research is to develop a genetic fingerprinting method to determine the relatedness of staphylococci infections between humans and animals, specifically between humans and dogs, to then examine relationships among methicillin-resistant staphylococci.

Methicillin was first used to treat a penicillin-resistant form of staphylococci infection (S. aureus), but just two years later, scientists began to see methicillin-resistant forms. Dr. Kania and his research group want to answer whether this resistance is being transferred between humans and animals. In other words, could Fido the family pet become resistant to methicillin while giving his owner some slobbering face love?

This work could help identify the most effective treatments for staphylococci infections and influence decisions regarding the need for treatment in certain cases.
Determing the Role of Potassium Channels in Cancer

The main cancer-causing suspect in tobacco is a chemical compound known as NNK, which acts by altering normal cell structure. NNK also stimulates the activity of β-adrenergic receptors, which are important because they regulate the growth of cancer cells. With some types of cancer, proteins known as potassium channels are under the control of β-adrenergic receptors. Dr. Plummer’s research group hypothesizes that these potassium channels mediate the effects of NNK.

The American Cancer Society estimates that in 2008, there will be 170,000 tobacco-related cancer deaths in the United States; therefore, the importance of developing ways to prevent and treat cancers that express potassium channels is obvious. Researchers agree that potassium channels play a big role in small cell lung cancer, but their potential role in breast cancer has been under-explored. Dr. Plummer is examining both types of cancer.

Perhaps by controlling the activity of potassium channels, the proliferation of cancer cells could also be controlled. Knowledge from this study could then be used to develop new cancer prevention and therapeutic strategies targeting potassium channels and β-adrenergic receptors.
REGULATORY MECHANISMS IN LUNG CANCER

East Tennessee has one of the highest lung cancer death rates in the country. In an attempt to help combat that problem, Dr. Schuller is focusing on the effects of nitrosamines on the lungs.

Nitrosamines are cancer-causing substances found in nicotine, food, beverages, cosmetics, and drugs. The tobacco-specific nitrosamine NNK reacts with nicotinic acetylcholine receptors (nAChRs) on cells, resulting in hyperstimulation of these receptors, a reaction that causes toxic effects.

In her laboratory, Dr. Schuller has determined that many of nicotine’s biological effects may be caused by the interaction of nitrosamines (like NNK) with nAChRs. Likewise, other factors in the human environment, such as diet and use of certain cosmetics and medicines, may also heighten the sensitivity of nAChRs, thus increasing the possibility of lung cancer.

Still, a host of factors in the human environment affects the sensitivity of these receptors, making it important to develop tools to identify hyperstimulation in individual patients. Dr. Schuller’s research can be used to help design lung cancer prevention and treatment strategies based on that hyperstimulation.
Cell Death Selectivity in Cancer Prevention

The American Cancer Society estimates that in 2008, there will be 184,450 new cases of breast cancer diagnosed in the United States. Environmental factors are estimated to account for 75%-80% of these new cases.

Although many of these cases could be prevented by modifying environmental factors such as tobacco use, inactivity, and poor nutrition, it is difficult to control other environmental factors such as pollution in the air, water, or soil. In those cases, an alternative method of prevention is key. That is precisely where Dr. Wang’s research is focused: finding an alternative method for prevention.

To be successful, a cancer treatment should, of course, kill cancer cells by targeting specific molecules or pathways. However, some treatments cannot distinguish between cancerous and non-cancerous cells, causing unwanted side-effects. Dr. Wang’s laboratory team has confirmed that histone deacetylase inhibitors (HDACIs) and dietary components called polyphenols can induce selective death of the cells that matter—cancer cells—while leaving normal cells to thrive.

His studies involve determining which pathways are targeted by these anti-cancer agents in order to suppress these pathways and ultimately prevent further development of cancer.
A Potential Link Between Smoking and Alzheimer’s

We recognize that cigarette smoking can increase our risk for cancer and cause lung diseases, but does smoking contribute to other diseases as well? Dr. Xu’s research team is investigating this question as it relates to Alzheimer’s disease.

Scientists believe that the main cause of Alzheimer’s disease is the accumulation of β-amyloid peptide (Aβ). Dr. Xu’s group confirmed that oxidized low-density lipoprotein (oxLDL) may increase Aβ production. Smoking has been shown to increase oxLDL, also known as “bad cholesterol,” but the way oxLDL causes Aβ to accumulate is unknown and the focus of Dr. Xu’s research.

During the past year, his group has worked to determine whether and how oxLDL affects the parent protein of Aβ. Aβ is formed when a long protein is cleaved at three different sites, and knowing which (and how many) of these sites may be a target of oxLDL could help clinical scientists develop treatments that target the appropriate biological pathway.

Results from these studies could also provide a link between heart disease and Alzheimer’s disease.
Determining how Horses Get Ulcers

Gastric ulcers in horses result in abdominal pain, weight loss, and poor performance, causing economic loss to the industry, particularly in race horses. According to the latest USDA survey, Tennessee ranks second in the United States in equine ownership, a total value of approximately $565 million.

The non-glandular squamous region, covering a third of a horse’s stomach, contains tender tissue with minimal protection against acid injury. Thus, ulcers in this region of the stomach appear to be more susceptible to the volatile fatty acids (VFAs) that damage stomach cells.

The focus of Dr. Andrews’ research is to determine how VFAs cause that damage. During the past year, his research team used an Ussing Chamber system, seen above, to examine the reaction of tissue to VFAs. The system mimics the natural stomach environment, allowing Dr. Andrews to study whether VFAs affect the salt transporter in the stomach lining.

He hypothesizes that damage to the salt transporter alters its function, ultimately resulting in gastric ulcers. This information builds a foundation for future clinical studies to develop prevention and treatment plans aimed at stabilizing the salt transporter, which will ultimately reduce horse suffering and economic loss.

Mechanisms of Disease, Pathogenesis, and Immunity
PREVENTING REPLICATION OF BOVINE CORONAVIRUS

Bovine coronavirus (BCV) has a high incidence rate among cattle, especially dairy cows, in which it can cause decreased milk production and weight loss. In adult cows, the disease is marked by intestinal problems, while calves usually experience respiratory disease.

Dr. Brian’s research team is examining the elements required for the replication of BCV. The replication method for any given virus family is unique; therefore, specifying the replication pattern provides potential for designing inhibitory drugs.

Dr. Brian has determined that the 2’-O-methyl transferase protein in BCV binds to a specific replication element. His research on this protein and its contribution to BCV replication will be the focus of continuing studies. This past year, his research group has been mapping interaction sites of the protein and testing how changes in the chemical structure of BCV affect virus replication.

The viral group to which BCV belongs also includes the human-type severe acute respiratory syndrome (SARS). Therefore, research on BCV could lead to breakthroughs in SARS treatment.

MECHANISMS OF DISEASE, PATHOGENESIS, AND IMMUNITY
MALIGNANT CATARRHAL FEVER PREVALENCE

A viral infection affecting wildlife in Tennessee may be more widespread than first thought. This virus, malignant catarrhal fever (MCF), poses a potential endemic threat to the animal agriculture industry and affects four known species: cattle, sheep, goats, and deer.

The little-understood MCF virus is characterized by fever and high mortality rates. Transmission is thought to occur via inhalation or ingestion of infectious secretions.

Because no vaccine exists for the disease, segregation of disease hosts from the herd is currently the only method of control. But a lack of coherent surveillance prevents proper control measures.

Dr. Donnell seeks to determine the distribution and prevalence of MCF throughout the state. After collecting samples during 2006 and 2007, his research team spent this past year testing the samples for the presence of MCF. Preliminary data indicate that goats were found to have a higher prevalence rate than cattle or sheep.

Above, Dr. Donnell is seen with COE summer student Kate Carpenter collecting a blood sample for testing. He is continuing to educate producers, managers, and policymakers within Tennessee about the disease risks.
Managing Pain Via a Controlled-Release Drug

Pain from a cut on a human finger or animal paw is recognized by the brain by traveling, via pain receptors, through the spinal cord. Dr. Egger is demonstrating this pain pathway on the skeleton at right. With the moderate to severe pain that often accompanies chronic illness, pain management is particularly important.

However, some traditional pain relievers for dogs have problems associated with their use. For example, some pain-relieving patches can be expensive and may irritate the dog’s skin. In addition, if one becomes loose, it loses its effect. If it falls off completely, it may end up in the hands of a child and cause a whole other set of problems.

Injectable buprenorphine is inexpensive and safer to use, but multiple repeated injections cause anxiety for the animal. Dr. Egger has been working with investigators at the UT College of Pharmacy on a longer-lasting formulation that will maintain its therapeutic value for 5 to 7 days, thus eliminating the stress of possible daily injections.

If this long-acting formulation is successful in treating pain in dogs, it could be optimized for other animal species and humans.
Laminitis, a condition that causes the hoof to separate from the bone, can result in permanent lameness, forced retirement, or euthanasia of horses. The latest USDA report on laminitis frequency indicates that 13% of U.S. horse owners reported at least one of their horses had developed laminitis in 1998.

Two important risk factors for laminitis are carbohydrate overload and endotoxemia (the presence of toxic bacteria in the blood). Dr. Frank hypothesizes that these two conditions contribute to the development of laminitis by inducing insulin resistance.

Although researchers are still not sure how insulin resistance contributes to laminitis, they suspect that it may 1) hamper the amount of glucose getting to hoof cells, essentially starving them, 2) reduce blood flow to the hoof, and/or 3) cause adipose tissues to exceed their capacity for fat storage, leading to inflammation and lowering a horse’s threshold for laminitis.

Dr. Frank’s investigative team wants to know how carbohydrate overload and endotoxemia affect insulin resistance in aiming for the long-term goal of finding solutions for managing laminitis. His research could have a huge economic impact on the Tennessee horse industry, which was worth about $565 million in 2004.
DEVELOPING A SCREENING METHOD FOR CANINE AMYLOIDOSIS

When abnormal proteins deposit within the body, a condition called amyloidosis occurs. Amyloidosis is seen in multiple myeloma (a form of cancer), Alzheimer’s disease, and type II diabetes in humans.

In Chinese Shar-Pei dogs, a hereditary form of amyloidosis, Shar-Pei Fever, can cause renal failure via protein deposits in the kidneys.

Although some methods exist to screen for amyloidosis in humans, veterinary medicine does not have an adequate screening test for renal amyloidosis. Currently, the only way to diagnose the disease is to wait on the clinical signs, but by then, the disease is in its late and irreversible stages.

Dr. Kirk’s goal in this study is to develop a PET/CT screening method to allow for early detection of the disease. This test would enhance the ability of breeders to identify affected animals and thus facilitate breeding away from this trait.

In addition, validating a canine model may have far reaching implications for the treatment of other amyloid-associated disorders in humans.
CURING MASTITIS BY MANIPULATING THE CAUSE

Mastitis is an inflammatory condition in cows that can last for months or even years, negatively affecting milk production by causing abnormal milk or lowering production quantity. A specific type of mastitis—Streptococcus uberis mastitis—has been the focus of Dr. Oliver’s research for the last decade.

His research resulted in the discovery of a novel bacterial protein, the Strep. uberis Adhesion Molecule (SUAM), which is a factor in the development of Strep. uberis mastitis. Collectively, experiments from his laboratory have proven that SUAM facilitates the adhesion of Strep. uberis to mammary cells.

This year, Dr. Oliver focused on the role of Strep. uberis adhesion to and entry into specific bovine mammary cells. He believes that both adherence and internalization are important in the early stages of intramammary infection. The long-term goal of this study is to develop a genetic system for Strep. uberis chromosomal manipulation in order to control this bacterial infection.

His research could positively affect Tennessee’s dairy industry by giving dairy owners treatment options and ensuring continued high quality of Tennessee’s milk.
Osteosarcoma is the most common cancerous bone tumor in dogs and is characterized by aggressive behavior and the ease with which it spreads to other parts of the body. Large and giant breed dogs have been shown to have an increased incidence of the disease, and in the Scottish Deerhound, the incidence rate is 10%.

Dr. Phillips’ research group has discovered that a dominant gene is responsible for osteosarcoma in the Deerhound. Now, his mission is to determine the genetic mutation associated with osteosarcoma development to eventually develop a screening test for the presence of this genetic trait.

At right, Dr. Phillips is seen with a cancer patient receiving chemotherapy. Another benefit to elucidating the genetic changes behind osteosarcoma is that these changes can then be used as targets to design specialized osteosarcoma treatment.

Osteosarcoma has the same aggressive behavior in humans as in human’s best friend, the dog. Therefore, these naturally-occurring tumors in dogs seem to be good translational models for the human form of this cancer. Information from these studies could be used to treat human osteosarcoma as well.
Developing Therapeutic Targets to Control Mastitis and Bovine Respiratory Disease

Dr. Pighetti, like Dr. Oliver (p. 26), is studying ways to remedy mastitis and its effects on the dairy industry. Mastitis results when an invading organism penetrates the cow’s body. In an attempt to rid itself of the invader, the body responds with inflammation very similar to that seen with bovine respiratory disease.

These similarities led Dr. Pighetti to hypothesize that preventive strategies developed for one disease might also be effective for the other. In both conditions, neutrophils, a type of white blood cell, migrate to the site of infection as a normal bodily response. Dr. Pighetti’s research focuses on understanding neutrophil activity in disease susceptibility and severity.

This past year, her group has worked to identify potential regulators of neutrophil migration and survival and to identify neutrophil-related gene markers for bovine respiratory disease susceptibility. Once these markers are identified, they can be targeted for the development of novel therapeutics designed to alter neutrophil activity.

Food safety would be enhanced by improving overall milk quality and reducing the use of antimicrobials.

Mechanisms of Disease, Pathogenesis, and Immunity
Selective Resistance to Bovine Respiratory Disease

Bovine respiratory disease (BRD) is perhaps the most economically important disease affecting feedlot cattle, costing the North American beef cattle industry $1 billion each year. *Mannheimia haemolytica* is the number one bacterium isolated from cases of BRD, which causes an often fatal form of pneumonia specific to cattle. The disease’s progression is still poorly understood and is the focus of Dr. Prado’s research.

Following successful invasion and colonization in the bovine lung, *M. haemolytica* secretes leukotoxin, and a massive influx of neutrophils takes place. Although neutrophils are one of the body’s defense mechanisms, coming to the rescue when something out of the ordinary is detected, they cause extensive lung tissue damage in cattle with *M. haemolytica* pneumonia.

Dr. Prado’s group has found that in some cattle, certain gene receptors that interact with *M. haemolytica* leukotoxins morph to increase resistance to BRD. Associating gene markers with resistance to *M. haemolytica* pneumonia might be an alternative for controlling the incidence of BRD in cattle.

**Maria Prado**

Research Assistant Professor
Animal Science & Large Animal Clinical Sciences Departments
DVM, University of Zulia
PhD, Oklahoma State University

In addition to center funds, Dr. Prado’s research is supported by USDA.
Numerous reports have documented that increasing age is associated with a decline in the ability of the immune system to respond to emerging infectious agents or vaccines to prevent them. With increasing age, we see enhanced morbidity and mortality to several infections, including herpes simplex virus, influenza, and hepatitis.

This decline in immune response could be the result of multiple defects, ranging from functional exhaustion to the loss of specific virus-fighting cell types. Specifically, T and B cells seem to be impaired with increasing age, but a detailed mechanistic understanding of age-related immunological defects remains unavailable.

As types of white blood cells that work to destroy virus-infected cells, T and B cells are important in the body’s ability to ward off viral infection. Dr. Rouse’s investigative team hypothesizes that neutralizing the activity of a specific regulatory cell, CD4+Foxp3+, will increase the immune response of T and B cells to herpes simplex virus-1 (HSV-1) infection.

Long-term, these studies can be expected to aid the development of effective viral vaccines in elderly individuals, prolonging life and improving its quality.
Memory Cell Protection from the Influenza Virus

It is common knowledge that once a person has had chicken pox, that person will never get chicken pox again. The reasons chicken pox is a one-time infection are memory B and T cells, which play a key role in long-term resistance to previously-encountered infection. These memory cells disperse throughout the body, creating long-lasting cell populations.

Dr. Sangster, seen at right with graduate student Hye Mee Joo, is interested in how memory B cells ($B_{\text{Mem}}$) protect us from specific forms of the influenza virus. He found recently that a relatively high amount of virus-specific $B_{\text{Mem}}$ cells are established and maintained in the lung after influenza infection, thereby providing resistance to future respiratory infections.

Future studies in this area may have important implications for influenza vaccine development, which has become even more in demand in the last two decades with the increasing aging population. In 2005, 62,000 people were hospitalized because of influenza, and 58% of these people were over the age of 65. The development of better vaccines would lower the physical and financial strain of influenza on all populations, but particularly the elderly.

Mark Sangster
Assistant Professor
Microbiology Department
PhD, University of Western Australia
1 refereed publications in 2008
In addition to center funds, Dr. Sangster’s research is supported by the National Institutes of Health, the University of Rochester, and POM Wonderful.
FRANK ANDREWS (p. 20)


Andrews FM. Colic in the horse, when to refer. Invited presentation at: University of Pennsylvania Annual Conference; March 7, 2008; Philadelphia, PA.

Andrews FM. Gastric ulcers in horses. Invited presentation at: University of Pennsylvania Annual Conference; March 7, 2008; Philadelphia, PA.

Andrews FM. Pituitary adenoma in horses. Invited presentation at: University of Pennsylvania Annual Conference; March 7, 2008; Philadelphia, PA.

Andrews FM. Metabolic syndrome in horses. Invited presentation at: University of Pennsylvania Annual Conference; March 7, 2008; Philadelphia, PA.

Andrews FM. Gastric ulcer disease in horses. Invited presentation at: Kentucky Equine Research Annual Nutrition Conference; April 2008; Lexington, KY.

Andrews FM. Pathogenesis of endocrine diseases in horses. Invited presentation at: Kentucky Equine Research Annual Nutrition Conference; April 2008; Lexington, KY.

Seung Joon Baek (p. 12)


Lee SH, Bahn JH, Choi CK, Whitlock NC, English AE, Safe S, Baek SJ. Tolfenamic acid induces apoptosis

**Baek SJ.** Pro-apoptotic protein NAG-1 suppresses obesity and inflammation. Invited presentation at: University of Massachusetts Molecular and Cellular Biology Program; March 25, 2008; Amherst, MA.


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MADHU DHAR (p. 14)


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Dhar M. RNAi technology reveals a novel target for obesity and diabetes. Invited presentation at: Beyond Genome Conference: Tools to Therapies; June 2008; San Francisco, CA.

Dhar M. P-type ATPases in obesity and diabetes. Invited presentation at: Metabolex Inc; June 10, 2008; Hayward, CA.

Dhar M. Role of a novel P-type ATPase in obesity and diabetes. Invited presentation at: University of Tennessee, College of Veterinary Medicine, Research Roundtable; March 27, 2008; Knoxville, TN.

**ROBERT DONNELL** (p. 22)


**CHRISTINE EGGER** (p. 23)


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Seddighi R, Egger C, Doherty T. The effect of tramadol on the sevoflurane minimum alveolar concentration
in dogs. *Veterinary Anaesthesia and Analgesia*. Accepted for publication.

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**Seddighi R, Egger C, Doherty C, Greer A, Rohrbach B, Cox S.** The efficacy of midazolam in isoflurane anesthetized dogs. Oral presentation (Seddighi) at: Annual Meeting of the American College of Veterinary Anesthesiologists; September, 2008; Phoenix, AZ.

**Jiminez-Martin T, Fernandez E, Seddighi R, Cox S, Egger C.** Pharmacokinetics and pharmacodynamics of tramadol in anesthetized dogs. Oral presentation (Jiminez-Martin) at: Annual Meeting of the American College of Veterinary Anesthesiologists; September, 2008; Phoenix, AZ.

**Wilson J, Doherty T, Egger C, Greer A, Rohrbach BW.** Determination of MAC and MAC derivatives in isoflurane and sevoflurane anesthetized dogs. Oral presentation (Wilson) at: Annual Meeting of the American College of Veterinary Anesthesiologists; September, 2008; Phoenix, AZ.

**Egger C.** Simple ways to monitor patients under anesthesia. Oral presentation at: North American Veterinary Conference; January 2008; Orlando, FL.


**Egger C.** Local, regional, and epidural analgesia. Oral presentation at: North American Veterinary Conference; January 2008; Orlando, FL.

**Egger C.** Anesthetic protocols for challenging feline cases. Oral presentation at: North American Veterinary Conference; January 2008; Orlando, FL.

**Egger C.** Clinical brief: Fentanyl patches – useful or not, and what are the alternatives? Oral presentation at: North American Veterinary Conference; January 2008; Orlando, FL.

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**NICHOLAS FRANK** (p. 24)


Geor R, Frank N. Metabolic syndrome – from human organ disease to laminar failure in equids. *Veterinary Immunology and Immunopathology*. Accepted.


Carter R, McCutcheon J, Burns T, Belknap J, Frank N, Geor R. Increased adiposity in horses is associated with decreased insulin sensitivity but unchanged inflammatory cytokine expression in subcutaneous adipose tissue. Oral presentation (Carter) at: American College of Veterinary Internal Medicine 26th Annual Forum; June 2008; San Antonio, TX.


Frank N. Equine metabolic syndrome. Invited oral presentation at: Department of Veterinary Science Equine Diagnostic and Research Seminar, Gluck Equine Research Center; June 2008; Lexington, KY.


Tóth F, Frank N, Geor RJ, et al. Effects of pretreatment with dexamethasone or levothyroxine sodium on
endotoxin-induced insulin resistance in horses. Poster presented at: American College of Veterinary Internal Medicine 26th Annual Forum; June 2008; San Antonio, TX.


**STEPHEN KANIA (p. 15)**


**Kania SA**, Lewis SL, New, Jr. JC. Collection of potential vectors and reservoir hosts of zoonotic diseases. Presentation at: Great Smoky Mountains National Park Science Colloquium; April 14, 2008; Gatlinburg, TN.


**Kania SA**, Lewis SL, New, Jr. JC. Detection of Hantavirus in the Great Smoky Mountains National Park. Presidential Symposium, Annual Meeting of the Association of Southeastern Biologists; April 16, 2008; Spartanburg, SC.

**CLAUDIA KIRK (p. 25)**


Smith JR, Cox SK, Lauten SD, Hill RC, Bartges JW, Kirk CA. Antioxidant status and biomarkers of oxidative stress in dogs with diabetes mellitus. Oral presentation (Smith) at: American College of Veterinary Internal Medicine 26th Annual Forum; June 2008; San Antonio, TX. Abstract 139.


Kirk CA. Pass the salt: diagnosis and management of hypernatremia. Oral presentation at: American College of Veterinary Internal Medicine 26th Annual Forum; June 2008; San Antonio, TX.

**STEPHEN OLIVER** (p. 26)


Luther DA, Almeida RA, Oliver SP. Elucidation of the DNA sequence of Streptococcus uberis adhesion molecule gene (sua) and detection of sua in strains of Streptococcus uberis isolated from geographically diverse locations. Veterinary Microbiology. 2008;128:304-312.

Gillespie BE, Headrick SI, Boonyayatra S, Oliver SP. Prevalence of coagulase-negative Staphylococcus species from three dairy herds. Veterinary Microbiology. In press.

Andrew SM, Moyes KM, Borm AA, Fox LK, Leslie KE, Hogan JS, Oliver SP, Schukken YH, Owens WE, Norman C. Factors associated with the risk of antibiotic residues and intramammary pathogen presence in milk from heifers administered prepartum intramammary antibiotic therapy. Veterinary Microbiology. In press.

Sawant AA, Gillespie GE, Oliver SP. Antimicrobial susceptibility of coagulase-negative Staphylococcus species isolated from bovine intramammary infections. Veterinary Microbiology. In press.


Oliver SP. Developments and future outlook for preharvest food safety: centennial presentation. Invited oral presentation at: American Society of Animal Science Centennial Meeting; July 2008; Indianapolis, IN. Presentation 542.

Oliver SP. Public health and food safety issues associated with foodborne pathogens from the dairy farm environment. Invited lecture at: College of Animal Sciences, Zhejiang University; June 2008; Hangzhou, China.

Oliver SP. Streptococcus uberis: epidemiology and some factors involved in virulence of this important mastitis pathogen. Invited lecture at: College of Animal Sciences, Zhejiang University; June 2008; Hangzhou, China.


Oliver SP. Heifer mastitis: prevalence, risk factors and strategies of control. Invited lecture at: The XIII Congreso Internacional ANEMBE Annual Meeting; May 2008; Salamanca, Spain.

Oliver SP. Best management practices to improve milk quality. Keynote presentations at: Southwestern Pennsylvania Dairy Field Days; March 2008; Bedford, PA, and Greensburg, PA.


Maxwell ML, Gillespie BE, Oliver SP. Real-time polymerase chain reaction for simultaneous detection of


Oliver SP. Seminario de mastitis en Novillas. Oral presentation at: The XIII Congreso Internacional ANEMBE Annual Meeting; May 2008; Salamanca, Spain.

Almeida RA, Luther DA, Park HM, Prado ME, Oliver SP. Identification, isolation & characterization of *Streptococcus uberis* adhesion molecule. Poster presented at: 2nd Annual Comparative and Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN. Abstract 8.

Almeida RA, Patel DA, Prado ME, Luther DA, Oliver SP. Blocking effect of *Streptococcus uberis* adhesion molecule affinity purified antibodies on adherence to and internalization of *Streptococcus uberis* into bovine mammary epithelial cells. Poster presented at: 2nd Annual Comparative and Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN. Abstract 11.


Patel DA, Almeida RA, Prado ME, Oliver SP. Characterization of *Streptococcus uberis* transposon mutants deficient in mammary epithelial cell entry. Oral presentation (Patel) at: 2nd Annual Comparative and Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN. Abstract 12.

Stenske KA, Gillespie BE, Oliver SP, Bemis DA, Matteson KJ, Draughon FA, Bartges JW. Comparison of clonal relatedness of fecal *Escherichia coli* from dogs and their owners and epidemiological analysis of within household sharing of bacteria. Poster presented at: 2nd Annual Comparative and Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN. Abstract 2.

Almeida RA, Luther DA, Park HM, Prado ME, Oliver SP. Identification, isolation & characterization of *Streptococcus uberis* adhesion molecule. Oral presentation (Almeida) at: 2nd Annual Comparative and Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN.

Almeida RA, Patel DA, Prado ME, Luther DA, Oliver SP. Blocking effect of *Streptococcus uberis* adhesion molecule affinity purified antibodies on adherence to and internalization of *Streptococcus uberis* into bovine mammary epithelial cells. Oral presentation (Almeida) at: 2nd Annual Comparative and Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN.

Prado ME, Ozen C, Almeida RA, Oliver SP. Expression of the recombinant form of a novel surface protein (SUAM) of *Streptococcus uberis*. Oral presentation (Prado) at: 2nd Annual Comparative and
Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN.

Prado ME, Luther DA, Oliff KE, Lewis MJ, Headrick SI, Almeida RA, Oliver SP. Vaccination with Streptococcus uberis adhesion molecule induces isotypic antibody responses in bovine serum and colostrum. Oral presentation (Prado) at: 2nd Annual Comparative and Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN.

Stenske KA, Gillespie BE, Oliver SP, Bemis DA, Matteson KJ, Draughon FA, Bartges JW. Comparison of clonal relatedness of fecal Escherichia coli from dogs and their owners and epidemiological analysis of within household sharing of bacteria. Oral presentation (Stenske) at: 2nd Annual Comparative and Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN.

Oliver SP. Heifer mastitis and strategies for control. Invited lecture for: Veterinarians and dairy consultants; March 5–6, 2008; Bedford, PA, and Greensburg, PA.


Maxwell ML, Gillespie GE, Oliver SP. Real-time polymerase chain reaction for simultaneous detection of mastitis pathogens directly from milk. Poster presented at: Annual Meeting of the National Mastitis Council; January 2008; New Orleans, LA.


Jeffrey Phillips (p. 27)


Phillips JC. Cancer facts and fallacy in the Belgian Tervuren. Oral presentation at: American Belgian Tervuren Club National Specialty; May 2008; Chattanooga, TN.

Gina Pighetti (p. 28)

Howard Plummer (p. 16)


Hance MW, Plummer III HK. Effects of 17 beta estrodiol on G protein inwardly rectifying potassium channels (GIRK) in breast cancer. Oral presentation (Hance) at: 2nd Annual Comparative and Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN.

Maria Prado (p. 29)


Prado ME. Coccidiosis in goats: an update. Oral presentation at: Second Annual Goat Producers Conference; February 2008; Knoxville, TN.

Prado ME. Anaplasmosis in cattle. Oral presentation training at: TRICOR; February 2008; Knoxville, TN.


Prado ME, Luther DA, Oliff KE, Lewis MJ, Headrick SI, Almeida RA, Oliver SP. Vaccination with *Streptococcus ubeiris* adhesion molecule induces isotypic antibody responses in bovine serum and colostrum. Oral presentation at: 2nd Annual Comparative and Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN.

Prado ME, Ozen C, Almeida RA, Oliver SP. Expression of the recombinant form of a novel surface protein (SUAM) of *Streptococcus ubeiris*. Oral presentation at: 2nd Annual Comparative and Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN.


Prado ME, Ozen C, Almeida RA, Oliver SP. Expression of the recombinant form of a novel surface protein (SUAM) of *Streptococcus ubeiris*. Poster presented at: 2nd Annual Comparative and Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN. Poster 9.


Sarangi P, Woo SR, Rouse BT. Control of viral immunoinflammatory lesions by manipulating CD200/CD200 receptor interaction. Clinical Immunology. Accepted


Rouse BT. Invited oral presentation at: Center of Biomedical Research Excellence Infectious Disease Symposium; May 2008; Covington, L.A.
**MARK SANGSTER** (p. 31)


**Sangster M**. In vitro analysis of the anti-influenza virus activity of pomegranate juice. Invited oral presentation at: POM Wonderful 5th Annual Research Summit; June 2008; Los Angeles, CA.

**Sangster M**. Influenza-specific B cell responses in HLA-DR1 transgenic mice: potential influences on antibody isotype expression and response magnitude. Invited oral presentation at: University of Rochester; August 2008; Rochester, NY.

Richards K, Chaves F, Krafcik F, Nayak J, **Sangster M**, Sant A. The response and kinetics of the primary CD4 T cell response to a human isolate of influenza A in HLA-DR1 transgenic mice. Poster presented at: 2nd Annual National Institute of Allergy and Infectious Diseases Center of Excellence for Influenza Research and Surveillance Network Meeting; April 2008; Memphis, TN.

Joo HM, He Y, **Sangster MY**. Influenza virus-specific B cell memory induced by intramuscular vaccination with inactivated virus. Poster presented at: Immunobiology and Pathogenesis of Influenza Infection meeting; June 2008; Atlanta, GA.


Huan L, Joo HM, Webby R, Sant A, **Sangster M**. Unusual isotype skewing of the influenza-specific B cell response in HLA-DR1 transgenic mice. Poster presented at: Immunobiology and Pathogenesis of Influenza Infection meeting; June 2008; Atlanta, GA.

Sundararajan A, Joo HM, **Sangster M**. Comparative analysis of the B cell response to influenza A virus and murine gammaherpesvirus 68. Poster presented at: Immunobiology and Pathogenesis of Influenza Infection meeting; June 2008; Atlanta, GA.

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**HILDEGARD SCHULLER** (p. 17)


**Schuller HM**, Al-Wadei HAN, Majidi M. Gamma-aminobutyric acid, a potential tumor suppressor for small airway-derived lung adenocarcinoma. *Carcinogenesis*. Published online ahead of print.

Hwa-Chain Robert Wang (p. 18)


Rathore K, Choudhary S, Wang H-CR. Reactive oxygen species-dependent anticancer therapeutics. Oral presentation (Rathore) at: 2nd Annual Comparative and Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN.

Song X, Siriwardhana N, Wang H-CR. Precancerous cellular model for studying breast cancer associated with environmental carcinogenesis. Oral presentation (Song) at: 2nd Annual Comparative and Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN.


Helstowski C, Siriwardhana N, Wang H-CR. Elucidation of low-dose minima of green tea catechin mixture and grape seed proanthocyanadin extract as dietary prevention methods against the formation of precancerous MCF10A breast epithelial cells caused by tobacco and environmental carcinogens. Poster presented at: University of Tennessee/Oak Ridge National Laboratory Graduate School of Genome Science & Technology 2008 Retreat; March 14, 2008; Knoxville, TN. Poster 10.


Choudhary S, Wang H-CR. Histone deacetylase inhibitors for selective anticancer therapeutics. Oral presentation (Choudhary) at: 2nd Annual Comparative and Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN.

Siriwardhana N, Wang H-CR. Target endpoints for dietary prevention of breast cancer. Oral presentation (Siriwardhana) at: 2nd Annual Comparative and Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN.

Wang H-CR. Precancerous carcinogenesis of human breast epithelial cells by chronic exposure to benzo[a]pyrene. Invited oral presentation at: China Agricultural University College of Veterinary Medicine; May 31, 2008; Beijing, China.

Wang H-CR. Manuscript preparation for scientific reports. Invited oral presentation at: China Agricultural University College of Veterinary Medicine; May 31, 2008; Beijing, China.

Wang H-CR. International Multi-Task Cooperative and Exchange Program in China. Invited oral presentation at: Summer Meeting of the Association of American Veterinary Medicine Colleges, International Affairs Committee; July 19, 2008; New Orleans, LA.

**Xuemin Xu** (p. 19)


Mao G, Dong Y, Tan J, Cui M-Z, Xu X. Both the N-terminal fragment and the protein-protein interaction domain (pdz domain) are required for the pro-apoptotic activity of presenilin-associated protein PSAP. *Biochimica et Biophysica Acta*. 2008;1780: 696–708.

Mao G, Tan J, Sisodia SS, Cui M-Z, Xu X. The role of the GXXXG motif in the interaction of APP with γ-secretase and formation of Aβ. Oral presentation (Mao) at: 2nd Annual Comparative and Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN.

Tan J, Mao G, Cui M-Z, Lamb BT, Sy M-S, Xu X. Effects of γ-secretase cleavage region mutations on APP processing and Aβ formation. Oral presentation (Tan) at: 2nd Annual Comparative and Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN.

Hao F, Wu D, McEntee M, Xu X, Cui M-Z. Lysophosphatidic acid in inflammation and atherosclerosis. Oral presentation (Hao) at: 2nd Annual Comparative and Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN.


Comparative and Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN. Poster 60.

Lu X, Cui M-Z, Xu X. Calpains affect the degradation of amyloid beta (Aβ) protein. Oral presentation (Lu) at: 2nd Annual Comparative and Experimental Medicine Research Symposium; June 17, 2008; Knoxville, TN.

* Publications and presentations listed are for the 2008 calendar year to the publication date of this report. Some items may be duplicated between individual investigators.
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<td>Validation of the use of the SmartPill Capsule for measurement of transit time,</td>
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<td>$23,008</td>
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<td>pH, temperature, and liminal pressure in the gastrointestinal tract of horses and dogs</td>
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<td>The efficacy of Seabuckthorn liquid supplement in prevention of gastric ulcers in horses</td>
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<td>Effect of volatile fatty acids on bioelectric properties of the equine stomach</td>
<td>Comparative Gastroenterology Society</td>
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<td>$6,000</td>
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<td>Baek, Seung Joon</td>
<td>PPAR-gamma ligands in colorectal cancer</td>
<td>National Institutes of Health</td>
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<td>National Institutes of Health</td>
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<td>Gene alterations by NSAIDs</td>
<td>American Cancer Society</td>
<td>07/01/06-06/30/09</td>
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<td>$158,911</td>
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<td>Development of noninvasive bioluminescence imaging for cancer diagnosis and therapeutic testing</td>
<td>National Institutes of Health</td>
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<td>Brian, David</td>
<td>Coronavirus RNA Replication</td>
<td>National Institutes of Health</td>
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<td>$1,778,750</td>
<td>$28,259†</td>
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<td>Mechanisms of coronavirus RNA amplification</td>
<td>National Institutes of Health</td>
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<td>$1,735,219</td>
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<td>Cui, Mei-Zhen</td>
<td>Lyposphosphatidic acid and tissue factor in atherosclerosis</td>
<td>National Institutes of Health</td>
<td>07/01/04-04/30/08</td>
<td>$983,316</td>
<td>$170,110</td>
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<td>Dhar, Madhu</td>
<td>Characterization of P-type ATPase, an integral membrane</td>
<td>American Kennel Club Canine Health Foundation</td>
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<td>$12,960</td>
<td>$1,608</td>
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<td>Levothyroxine as a treatment for insulin resistance</td>
<td>Lloyd</td>
<td>04/01/07-03/31/09</td>
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<td>Effects of SmartControl IR on insulin sensitivity in obese insulin resistant horses</td>
<td>SmartPak Equine</td>
<td>06/01/07-05/31/10</td>
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<td>American Quarter Horse Association</td>
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<td>Improved diagnosis and monitoring of equine endocrine disorders</td>
<td>American College of Veterinary Internal Medicine</td>
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<td>Molecular pathways that mediate genetic susceptibility to low dose ionizing radiation</td>
<td>UT-Battelle-Oak Ridge National Laboratory</td>
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<td>Reverse transcription free microarray analysis</td>
<td>Sci-Tec</td>
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<td>Bioluminescent assay for gene expression analysis</td>
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<td>Immune response to viral interleukin 10 in gamma herpesvirus-infected black wildebeest</td>
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<td>Kania, Stephen</td>
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<td>East Tennessee Clinical Research</td>
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<td>RNA interference of the glycoprotein-D and DNA polymerase genes of feline herpesvirus by synthetic siRNAs</td>
<td>Winn Feline Foundation</td>
<td>01/01/06-12/31/07</td>
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<td>RNA interference of feline herpesvirus by synthetic siRNAs in cornal epithelial cells</td>
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<td>Evaluation of neutrophil function in treated tumor-bearing dogs</td>
<td>American Kennel Club Canine Health Foundation</td>
<td>10/01/06-09/30/07</td>
<td>$12,906</td>
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<td>Nutrition resident support</td>
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<td>Influence of gender and sexual alteration status on feline adiponectin</td>
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<td>Characterize the hormone adiponectin in felids by determining cDNA sequence, mRNA expression, and molecular weight composition</td>
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<td>The impact of visual cues associated with food bowl and scoop size on food portions offered to dogs by their owners</td>
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<td>Activity product ratios and calcium oxalate urolith risk in cats with chronic renal disease</td>
<td>Morris Animal Foundation</td>
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<td>$27,099</td>
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<td>Antioxidant status and oxidative stress in dogs with diabetes mellitus</td>
<td>Waltham Foundation</td>
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<td>Oliver, Stephen</td>
<td>Role of <em>Streptococcus uberis</em> adhesion molecule (SUAM) in the pathogenesis of bovine mastitis</td>
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<td>Efficacy of a drug for lactating dairy cows with severe clinical mastitis</td>
<td>Pfizer Animal Health</td>
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<td>Development of a chronic <em>E. Coli</em> experimental intramammary infection model</td>
<td>Epitopix</td>
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<td>Dosing and duration of an intramammary treatment of experimentally-induced <em>Streptococcus uberis</em> mastitis in lactating dairy cattle</td>
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<td>Efficacy and safety of Draxxin in the treatment of clinical mastitis associated with <em>Streptococcus uberis</em> in lactating dairy cattle</td>
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<td>Project Period</td>
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<td>Phillips, Jeffrey</td>
<td>Population pharmacokinetics of carboplatin in dogs</td>
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<td>Evaluation of tryosinase antigen expression in canine and equine melanoma</td>
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<td>12/06/07-12/05/08</td>
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<td>GIRK channels, beta-adrenergic signaling and breast cancer</td>
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<td>Prado, Maria</td>
<td>Molecular mechanisms associated with <em>Streptococcus uberis</em> mastitis in dairy cows</td>
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<td>University of Rochester</td>
<td>03/30/07-03/29/09</td>
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<td>Schuller, Hildegard</td>
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<td>Wang, Hwa-Chain</td>
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<td>National Science Foundation</td>
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<td>The role of the new zeta-cleavage in Abeta formation</td>
<td>National Institutes of Health</td>
<td>04/01/07-03/31/12</td>
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* Early termination due to transfer of investigator.
* New award.
* No-cost extension.
* Spent completely during previous fiscal year.
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<tr>
<th>Expenditures</th>
<th>FY 2007-08 Actual</th>
<th>FY 2008-09 Proposed</th>
<th>FY 2009-10 Requested</th>
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<tr>
<td>Matching</td>
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<td>Total</td>
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<td>Salaries</td>
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<td>Faculty</td>
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<td>Other professional</td>
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<td>Total salaries</td>
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<td>Fringe benefits</td>
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<tr>
<td>Non-personnel</td>
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<tr>
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<td>Software</td>
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<td>Books &amp; journals</td>
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<td>Total Non-Personnel</td>
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<td>29,119</td>
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<td>Carryover from Previous Matching Funds</td>
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<td>Total Revenue</td>
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