Welcoming Remarks

We are pleased to present the 2011 annual report for the Center of Excellence in Livestock Diseases and Human Health. Along with benchmark data for fiscal years 2007–2011, this report includes highlights of faculty research projects funded by the center in fiscal year 2011.

The center continues to adapt to the changing extramural funding environment. With the precipitous increase in competition for decreasing federal research funds, the center has concentrated on maintaining competitiveness of active research programs and promoting the start-up of new College of Veterinary Medicine (UTCVM) investigators. In addition, the center is investing in initiatives that promote translational research, the coordinated movement of bench-level research to the clinic. Thus, the areas of active research in the UTCVM impacted by the center have increased.

During 2011, the center supported the efforts of 15 faculty. These faculty have made significant advancements in cancer biology, molecular pathophysiology, host defense, and disease transmission. Center faculty also made significant advancements in the prevention and treatment of infectious and non-infectious livestock diseases that affect agricultural productivity. Research funding grew, and the return on investment, as the ratio of research expenditures to the state appropriation for the center, was an improved 7:1.

Center faculty continue to garner national and international recognition for their research and scholarship. During calendar year 2010, center faculty published 59 peer-reviewed articles and gave 54 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.

Jim Thompson, Dean

Michael McEntee, Interim Director

Misty R. Bailey, Editor

L-R: McEntee, Bailey, Thompson

Center of Excellence in Livestock Diseases and Human Health

2011 Annual Report

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This report is produced by the University of Tennessee, College of Veterinary Medicine, Office of the Associate Dean for Research.

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Publication No. E180103-00-001-12

THE UNIVERSITY of TENNESSEE
INSTITUTE of AGRICULTURE
COLLEGE of VETERINARY MEDICINE

Comparative Summary of Accomplishments

Benchmark	2011 *(15 faculty)*	2010 *(15 faculty)*
Publications*		
Peer-reviewed articles	59	47
Books or book chapters	3	6
Abstracts or posters	69	69
Presentations*		
International	23	18
National	22	31
State or local	9	10
Research monies†		
External funding	$5,401,346	$5,039,087
Research expenditures	$3,916,121	$3,597,130
Return on investment	7:1	6.1:1

*Based on 2010 calendar year
†Based on 2011 fiscal year

Center of Excellence faculty share their research with a worldwide audience through scientific conferences. The map showcases where their research was presented in 2010.

Comparative & Experimental Medicine and Public Health Research Symposium

The Center of Excellence was a major sponsor of the Comparative & Experimental Medicine and Public Health Research Symposium, which brought together researchers from 22 different departments for a 2-day-long event that included special seminars on veterinary research, prevention and treatment of obesity, interdisciplinary model approaches to public health, and post-doctoral opportunities. Featured was Dr. Franziska Grieder of the National Center for Research Resources at the National Institutes of Health; she discussed translational research, the role of veterinarians in science and global health, and resources available through NIH. The symposium culminated with an awards banquet and guest speaker Dr. William Bass, known worldwide for his Anthropological Research Facility known as the "Body Farm."

Forty-eight researchers from the Institute of Agriculture presented talks at the symposium, including heavy participation by members of the Animal Science and Pathobiology departments. These 48 representatives were among 82 new scientists to present, and at the end of the 2 days, the institute was able to boast six winners of travel awards. The center sponsored four of the 2010 award winners to present at scientific meetings during fiscal year 2011, including one international and four national conferences.

The symposium was designed to allow sharing of research results, promote collaboration, and provide new investigators meeting-format experience via 10-minute presentations, with 5 minutes for questions from the audience.

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

Graduate student Leon Richardson presents his colorectal cancer research.

Keynote speaker Dr. Franziska Grieder talks about veterinary research.

Dr. Liesl Breickner, PhD student, discusses her equine stem cell research.

Dean Thompson welcomes awards banquet attendees.

Dr. William Bass discusses pets' role in a death investigation.

Doctoral candidate Dr. Shalini Sharma accepts an award at the banquet.

Photos by Landon Mathers

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 two areas are 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. These areas also encompass the "One Health" concept, wherein the interrelated disciplines of animal, human, and environmental health are combined for the betterment of all three.

Personnel

Dr. Michael McEntee began serving as interim director of the center in February 2011, replacing Dr. Leon Potgieter, who retired. Ms. Misty Bailey produces the annual report, and Ms. Kim Rutherford oversees submissions of faculty proposals for funds.

Collaborations

Alliance for Regenerative Medicine

The newly-formed Alliance for Regenerative Medicine involves collaborations with multiple investigators in both clinical departments, as well as with other programs at the University of Tennessee. In the Large Animal Clinical Sciences (LACS) Department, Drs. Steve Adair, Madhu Dhar, Dennis Geiser, and James Schumacher and Ms. Nancy Neilsen are collaborating with Dr. Christopher Stephens from the Graduate School of Medicine and with Small Animal Clinical Sci-

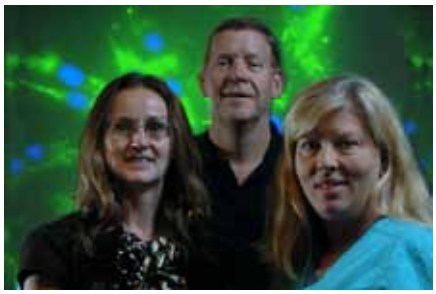
ences (SACS) faculty Drs. Maria Cekanova and Darryl Millis and Ms. Gina Galyon.

In the LACS Department, researchers are investigating the potential roles of equine progenitor cells in regenerative therapy. The project began in 2009 with funding obtained through the center. Since then, the results have been instrumental in initiating both basic and clinical experiments pertinent to equine regenerative medicine. The LACS group established and validated protocols to isolate progenitor stem cells from fat tissue and peripheral blood in horses. Continuing with this initiative, they also optimized protocols to make these cells differentiate into three other types of cells: osteocytes (bone), adipocytes (fat), and chondrocytes (cartilage). The next goal of the LACS research team is to understand the variation in these cells with regard to proliferation rate, differentiation capacity, and expression of markers used for identification. In order to use these cell-based therapies effectively, it is imperative to understand this variation and identify biomarkers that can be genetically modified to encourage the cells to perform a certain way. With these results, researchers are able to encourage regeneration of cells and tissues to restore normal function. Already, veterinarians are using these results to treat client cases of bone and tendon damage and laminitis. Effective treatment in horses can then be translated for use in human patients.

L-R: Drs. Madhu Dhar, James Schumacher, and Steve Adair, and Ms. Nancy Neilsen

Dr. Dennis Geiser leads a horse into the hyperbaric oxygen chamber for therapy to encourage stem cell circulation.

The SACS Department has already moved toward a pre-clinical trial of canine mesenchymal stem cells in dogs with knee injuries. After harvesting stem cells from bone marrow, they are then growing the cells in tissue culture outside the body. Later, they deliver these cells to the injured knee and evaluate gait and range of motion, as well as the biochemical changes going on in the joint. These analyses will serve as a basis for future clinical treatment in dogs with cranial cruciate ligament disease and osteoarthritis, as well as provide comparative information for treatment of people with corresponding anterior cruciate ligament (ACL) injury.



L-R: Drs. Maria Cekanova and Darryl Millis, and Ms. Gina Galyon

The Alliance for Regenerative Medicine's collaboration with the Graduate School of Medicine is aimed at generating and using custom biomaterial that will play an important role in tissue engineering.

Accomplishments

External Funding: $5,401,346

New Grants: $1,946,821

Despite the persisting, sluggish funding environment, 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 (pp. 19 – 32) and are excellent in terms of benchmarks for fiscal year 2011. Center faculty have successfully adapted to the increased competition for federal funds and are also aggressively seeking more awards from foundations and other private and industry sources. Figure 1 shows the percentage breakdown of external funding by source.

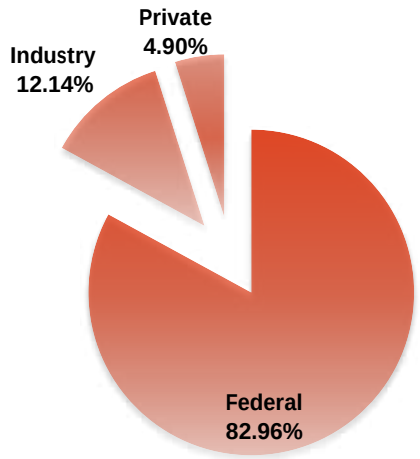


Fig. 1. *FY 11 external funding by type. Total = $5,401,346.*

During this reporting year, the 15 center faculty each averaged four peer-reviewed publications (59 total) and three presentations at prestigious national and international meetings (45 total). Particularly noteworthy are articles by Drs. David Brian and Barry Rouse in *Proceedings of the National Academy of Sciences USA* (Brian), *Nature Reviews Immunology*, and *PLoS Pathogens* (Rouse). The National Academy of Science is one of the (if not *the*) premier scientific organizations in the world and accepts only the highest quality research with the broadest impact for publication. *PLos Pathogens* has rapidly gained prominence among those publishing on infectious disease pathogenesis. Additionally, scientists asked to present their work in *Nature Reviews* are selected because of the seminal importance of their work and its international recognition within a particular discipline. Dr. Rouse's article in *Immunology* has already been cited 12 times by other scientists, and the journal itself has a 2010 impact factor of 35.196, which indicates that each article published in that journal in 2008 and 2009 had, on average, 35 citations in 2010. See Publications and Presentations (pp. 33 – 45) for more details.

The return on the state's investment in the center was 7:1, calculated as ratio of expenditures from extramural funding to center appropriation. Extramural funding totaled $5,401,346 this year, while expenditures for the year were $3,916,121. The funding includes new, multi-year awards for Drs. Cui, Oliver, Rouse, and Xu, expected to bring nearly $4.5 million over the course of the projects and new, one-year awards for Drs. Frank, Kania, and Oliver totaling $549,546. Research expenditures continued to increase at $3,916,121. See "Research Funded Externally" and "Research Expenditures" on p. 9 for the fiscal year 2011 data summary.

Success stories – The ***mastitis research laboratory***, under the direction of ***Dr. Stephen Oliver***, has been a part of the center since its inception in 1984 and has been continually successful during that time. Dr. Oliver has used his center funds primarily to launch new and innovative research projects in order to establish the preliminary data needed to apply for and receive larger

grant awards, such as those from the U.S. Department of Agriculture.

In reflecting on his continued support from the center, Dr. Oliver recently said, "Center funding is as valuable to new faculty as it is to those who have been around the block a few times. It has allowed us to do things we would never have been able to do otherwise, and the return on investment for us has been huge."

A huge return on investment may be an understatement, coming from Dr. Oliver. Just last year, all four of the grants he submitted were funded. A 100% success rate is practially unheard of, and Dr. Oliver estimates he leveraged his allotment of center funds approximately 20-fold. However, he notes that even if grants do not get funded initially, the critical feedback received is still beneficial to further the preliminary results achieved through center support.

Just over a year ago, in June 2010, Dr. Oliver was appointed as assistant dean for research and assistant director of AgResearch at the University of Tennessee Institute of Agriculture. Dr. Oliver's new role in the institute has allowed Dr. Raul Almeida, research assistant professor and expert in microbial pathogenesis, to manage the day-to-day operations of the mastitis laboratory and the 10–15 staff members that rotate through. Dr. Almeida is revitalizing the Tennessee Quality Milk Initiative to continue educating Tennessee dairy producers on science-based methods to improve the quality of their milk product.

"Center funding has allowed us to do things we would never have been able to do otherwise." – Dr. Stephen Oliver

Dr. Oliver, though, still serves as editor for the peer-reviewed journal *Foodborne Pathogens and Disease*, which he helped establish in 2004. The journal began as a quarterly publication, moved to six times yearly by 2008, and is now published monthly. Over 700 articles and 6,000 pages have been published to date.

Dr. Oliver's mastitis research laboratory is the epitome of what center support can allow scientists to accomplish.

Another clear indicator of success is the ***recruitment of productive center faculty by other institutions***. This year, two center faculty, ***Dr. Seong-Ho Lee*** and ***Dr. Nicholas Frank***, took positions at the University of Maryland, a top-25 institution, and Tufts University, respectively. Dr. Lee's impressive work in nutritional approaches to cancer prevention earned him a tenure-track assistant professor position in the Department of Nutrition and Food Science. Dr. Frank, who is world-renowned for his equine laminitis work, is now the chair of the Department of Clinical Sciences (the veterinary school's largest department) and professor of large animal internal medicine.

Research Funded* Externally FY 2011

Investigator	Federal	Industry	Foundation/ Private	Totals
Baek, Seung Joon	$199,929			$199,929
Brian, David	$352,193			$352,193
Cui, Mei-Zhen	$361,159			$361,159
Frank, Nicholas		$7,080	$41,490	$48,570
Godkin, James	$349,503			$349,503
Kania, Stephen		$5,000	$46,466	$51,466
Lee, Seong-Ho	$70,470			$70,470
Moustaid-Moussa, Naima	$159,481		$43,540	$203,021
Oliver, Stephen	$500,000	$643,440		$1,143,440
Phillips, Jeffrey	$94,590			$94,590
Rouse, Barry	$691,948			$691,948
Schuller, Hildegard	$1,054,344			$1,054,344
Wang, Hwa-Chain Robert	$190,598			$190,598
Xu, Xuemin	$456,782		$133,333	$590,115
Totals	**$4,480,997**	**$655,520**	**$264,829**	**$5,401,346**

*Represents FY 2011 receipts for active grants

Research Expenditures FY 2011

Investigator	Federal	Industry	Foundation/ Private	Totals
Baek, Seung Joon	$163,892			$163,892
Brian, David	$324,651			$324,651
Frank, Nicholas			$22,937	$22,937
Godkin, James	$98,854			
Kania, Stephen		$2,832	$4,413	$7,245
Lee, Seong-Ho	$70,180			$70,180
Moustaid-Moussa, Naima	$188,137		$21,768	$209,905
Oliver, Stephen	$7,027	$859,580		$866,607
Phillips, Jeffrey	$88,080			$88,080
Rouse, Barry	$366,132			$366,132
Schuller, Hildegard	$1,133,111			$1,133,111
Wang, Hwa-Chain Robert	$141,382			$141,382
Xu, Xuemin	$333,983		$89,162	$423,145
Totals	**$2,915,429**	**$862,412**	**$138,280**	**$3,916,121**

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, promotes new investigators' potential to develop competitive research programs, and promotes new collaborative ventures.

Research Advisory Committee's Three Main Criteria for Funding

- Scientific merit
- Potential to lead to external funding
- Relevance to the center's objectives

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 are new faculty who have received start-up funds. Junior members are expected to secure external funding within 2 years; members who fail to secure such funding will be placed on probation for 1 year. If, at the end of the probationary period, external funding has not been secured, the member will no longer be eligible for center funds.

Start-up funds – The center provided $72,500 in start-up funds for six faculty members to secure additional external funding. In the Department of Biomedical and Diagnostic Sciences, Dr. Marcy Souza received funds to support her public health and avian exotics research, and Dr. Bente Flatland received support for clinical pathology work. In the Large Animal Clinical Sciences Department, Dr. Reza Seddighi and Dr. Brian Whitlock used their center funds for large animal anesthesia and food animal field service research, respectively. Drs. Andrea Matthews and Jill Narak in Small Animal Clinical Sciences received support for radiation oncology work and neurology work, respectively.

Graduate student support – The center supported two partial stipends, four full stipends, full tuition (1), and partial tuition (1) for Comparative and Experimental Medicine graduate students of center faculty. These stipends allow the students to work at least quarter-time in faculty laboratories to perform research for their theses or dissertations.

Infrastructure and supplies – 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 Advisory Committee reviews requests based on three criteria: justification of need, current availability of equipment, and number of investigators who may benefit. In support of the UTCVM's research enterprise, the center purchased a balance for the Tumor Biology Laboratory ($1,115). Many COE and UTCVM faculty use this piece of equipment to weight chemicals and other compounds. In addition, the center partially funded a microscope ($1,924) for use in both teaching and research. The microscope is

$18,094 helped fund equipment, service contracts, and supplies

used most by the research groups of Drs. Baek, Cui, Lee, and Schuller to review various histologic preparations, generating in vivo data. Two new computers for research office staff members cost $2,607. The center also funded a service contract for one piece of equipment purchased previously with center funds. Service for a flow cytometer totaled $7,088. The flow cytometer is shared by center faculty members Dr. Barry Rouse and Dr. Madhu Dhar and is used almost daily.

Supplies for the multi-investigator stem cell project, described in detail on pp. 5 – 6, allowed for cell storage and incubation, as well as cell sorting to enumerate, enrich, and characterize cells (total $5,360). This equipment is also available for use by all UTCVM and center faculty members to run or set up experiments.

Training – To keep faculty abreast of new research techniques and to increase their chances of obtaining extramural funding, the center sponsors training opportunities. *Current Protocols in Cytometry* was purchased for Nancy Neilsen, who staffs the Tumor Biology Laboratory and provides flow cytometry services for UTCVM and center researchers. This best practices collection provides the latest techniques and protocols for flow cytometry.

Just over $1,300 went toward sponsorship to bring in the following guest speakers for the Comparative and Experimental Medicine graduate seminar course.

Jeffrey S. Elmendorf, PhD, Indiana University School of Medicine
Hui Zheng, PhD, Baylor College of Medicine
William P. Schiemann, PhD, Case Western Reserve University
Yueming Li, PhD, Sloan-Kettering Cancer Institute

The center also provided meals or refreshments during lunch-time training events held at the UTCVM. A Pfizer seminar on what pharmaceutical companies look for when partnering with academics was held in May ($87.71). In addition, $117.80 provided a graduate student lunch-and-learn opportunity during fall 2010 orientation.

Dissemination of research – Faculty are encouraged to share their research by speaking to professional groups, community groups, and civic groups. The center partially supported travel expenses for three faculty members to be able to attend national and international scientific meetings (total $2,337) in Alexandria, VA; Philadelphia, PA; and Santiago, Chile. One graduate student also received support to travel to a local meeting in Murfreesboro, TN ($410). A complete list of faculty publications and presentations for the 2010 calendar year can be found in the Publications and Presentations section (pp. 33 – 45).

Travel awards totaling $3,152 for four new investigators involved in the 2010 Comparative & Experimental Medicine and Public Health Research Symposium allowed them to disseminate their research at three different national meetings and one international meeting.

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. An example is shown below of Drs. Xuemin Xu and Mei-Zhen Cui, both of whom were featured in a short video produced by the University of Tennessee, Knoxville, Office of Communications and Marketing to promote the Life of the Mind book selection for the incoming freshmen class. Every freshman read the book *The Immortal Life of Henrietta Lacks*, which focuses on the story behind HeLa cells. Both Dr. Xu and Dr. Cui have used these cells in their research. The video may be viewed at *http://www.youtube.com/user/UniversityTennessee?blend=7&ob=5#p/u/6/_FaQ9Utx--E*.

Dr. Xuemin Xu (L) and Dr. Mei-Zhen Cui (R) speak about their use of HeLa cells on a video geared toward UT freshmen. All incoming freshmen read the book The Immortal Life of Henrietta Lacks*, a story about how the cells of Henrietta Lacks are still being used today after being the first human cells to be harvested and kept alive outside the body. One of Lacks's grandchildren, Ron Lacks, commented on the online video, saying "Thank you so much for talking about some of the different ways my grandmother's cells are being used. It really means a lot to the family."*

The three UTCVM news publications described below are available on the UTCVM Web site as well (*http://www.vet.utk.edu/publications/index.php*), which also provides an overview of the types of research conducted by UTCVM and center faculty.

L–R: The quarterly, in-house newsletter Discovery *keeps UTCVM researchers informed about each other's work and research-related policies and resources. The quarterly newsletter* Volunteer Vet *features research activities and results and is distributed to donors and employees. 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.*

Center of Excellence Summer Student Research Program

In an effort to foster interest in careers in biomedical research and enhance appreciation for scientific investigation, inquiry, and the acquisition of new knowledge, the center helped provide opportunities for both high school students and veterinary students to do research at the UTCVM.

Center faculty Drs. Cui and Xu participated in the Farragut High School Science Academy by allowing students from that Knoxville-area school to conduct research on site in their labs. One student learned about laboratory techniques in studying vascular smooth muscle cells and two more studied neuron science. The students then presented their results in a poster session at the high school. Two of the student participants from last year are currently seeking degrees at Duke University and Emory University.

In addition, 23 veterinary students gained research experience at the UTCVM during the summer. Students participated in laboratory and field research and attended weekly professional development seminars, during which guest speakers addressed topics such as career opportunities in research, compliance issues in laboratory animal care, science writing, and the grant proposal process. They also participated in the Comparative & Experimental Medicine and Public Health Research Symposium. Near the end of the 10-week program, the students presented their research findings to their colleagues and to UTCVM faculty.

Dr. Stephen Kania, a center faculty member, coordinated the program along with Dr. Linda Frank; Dr. Kania received a $4,000 grant from Morris Animal Foundation to help support the program. To maximize student participation, the program is open to both center and non-center faculty. During fiscal year 2011, three COE faculty participated in the program. The center will continue to encourage participation of its faculty.

$4,000 from Morris Animal Foundation helped fund the Summer Student Program

The students involved in the summer research program and a brief description of their activities follow:

Derek Adrian, 2nd year. *Faculty Mentors*: Dr. Stephen Kania and Dr. Christine Cain.
Hometown: Durham, NC. BS in zoology from North Carolina State University. *Summer Project*: Studied and measured antibody response in dogs with pyoderma (staphylococcal skin infection) compared with non-infected dogs. *Career Interest*: Obtaining a PhD and teaching physiology at the veterinary level.

Cassandra Couch Bates, 2nd year. *Faculty Mentor*: Dr. Madhu Dhar.
Nashville, TN. BS in animal science from Middle Tennessee State University. *Summer Project*: Culturing tissue to isolate equine stem cells. *Career Interest*: Mixed-animal private practice.

Amber Bowling, 3rd year. *Faculty Mentor*: Dr. Federica Morandi.
Jacksboro, TN. BS in animal science from the University of Tennessee. *Summer Project:* Retrospective

evaluation of thyroid tumors in dogs to determine if a correlation exists between the histopathological diagnosis and the scinitgraphic appearance of thyroid tumors. *Career Interest*: Veterinary radiology.

Gina Calvo, 2nd year. *Faculty Mentors*: Dr. Sarel Van Amstel and Dr. Christine Cocquyt.
Hendersonville, TN. BS in animal science from the University of Tennessee at Martin. *Summer Project*: Blood collection for a pharmacokinetic study of moxidectin in alpacas. *Career Interest*: Mixed-animal practice, with a focus on large animals.

Al Claiborne, 2nd year. *Faculty Mentors*: Dr. Charles Faulkner and Dr. Richard Gerhold.
Greeneville, TN. BS in business administration and logistics from the University of Tennessee. *Summer Project*: Survey of the parasites of small and medium mammals with samples from USDA, wildlife from Knox County, TN, and samples collected during the course of a lyme disease project in the Wildlife and Fisheries Science Department. *Career Interest*: Private practice ownership.

Hannah DeBusk, 2nd year. *Faculty Mentors*: Dr. Deb Miller, Dr. Matt Gray, Dr. Melissa Kennedy, and Dr. Becky Wilkes.
Tazewell, TN. BS in veterinary technology from Lincoln Memorial University. *Summer Project*: Environmental persistence of an amphibian ranavirus subjected to ultraviolet radiation. *Career Interest*: Pathology.

Lee Emery, 3rd year. *Faculty Mentor:* Dr. Marcy Souza.
Odessa, FL. BS in biology from Stetson University. *Summer Project*: Pharmacokinetic study of the antifungal terbinafine in Hispaniolan Amazon parrots. *Career Interest*: Avian and exotics medicine.

Lauren Essick, 2nd year. *Faculty Mentor*: Dr. Olya Smrkovski
Johnson City, TN. BA in French from Furman University. *Summer Project*: A retrospective study of canine mast cell tumor treatment with masitinib mesylate. *Career Interests:* Small animal medicine, pain management, alternative medicine, companion animal behavior, animal welfare, and the human-animal bond.

Deb Haines

Michelle Gates, 2nd year. *Faculty Mentors*: Dr. Deb Miller and Dr. Richard Gerhold.
Rockaway, NJ. BS in animal and veterinary science from Clemson University. *Summer Project*: Took necropsy samples from 24 coyotes from north Georgia that were provided from a Georgia Predator Removal Program. Samples included ticks, fresh tissue from major organs, fecal samples, heartworms, and intestinal worms. Counted, sexed, and measured adult heartworms and looked for microfilaria on a stained blood slide. *Career Interests*: Wildlife and exotic animal medicine or small animal medicine.

Diana Gibbs, 3rd year. *Faculty Mentor*: Dr. Deb Miller.
Chicago, IL. BS in biology and BA in theater from Mary Baldwin College; MS in wildlife science at North Carolina State University. *Summer Project*: Examined 200 slides of tadpole sections for necrosis and viral inclusions in the kidney, liver, and spleen. *Career Interests*: Zoo animals, exotic species, pathology, neurology, behavior, nutrition, and acupuncture.

Tea Gluhak, 3rd year. *Faculty Mentor*: Dr. Joseph Bartges
San Antonio, TX. BA in history and political science from Warren Wilson College. *Summer Project*: Studied effects of calcium oxalate/struvite preventive diets on urine saturation in cats and looked at *E. coli* bacterial isolates from previous urinary tract infection cases. *Career Interests*: Small animal practice and/or board certification in internal medicine.

Kristin Harrison, 2nd year. *Faculty Mentor:* Dr. Angela Lusby Witzel.
Montverde, FL. BS in animal sciences from the University of Florida. *Summer Project*: Determining the effects of metronidazole on nutrient digestion and energy use in healthy cats. *Career Interests*: Small animal medicine.

Monica Huerta, 3rd year. *Faculty Mentors*: Dr. Silke Hecht and Dr. Robert Reed.
Dickson, TN. BS in biochemistry and molecular biology from Rhodes College. *Summer Project*: Compared spinal cord and spinal canal measurements taken from magnetic resonance imaging (MRI) studies to measurements in cadaver specimens to establish anatomical reference ranges for spinal cord, spinal canal, and spinal cord-to-spinal canal diameter in normal dogs. Goal was to provide a reference to assist in the challenging diagnosis of diffuse, degenerative spinal cord diseases in dogs. *Career Interests*: Academia, radiology, and anatomy.

Jennie Jankovsky, 3rd year. *Faculty Mentors*: Dr. Shelley Newman and Dr. Kim Newkirk.
Talbott, TN. BS in biology from Youngstown State University. *Summer Project*: Cox-2 and c-kit expression in canine gliomas. *Career Interest*: Pathology.

Benjamin Kinney, 2nd year. *Faculty Mentors*: Dr. Steve Adair and Dr. Patricia Tithof.
Lagrange, TN. BS in biology from Hampton-Sydney College. *Summer Project*: Studying a class of phospholipases called PLA2s that have been indicated as having activity in regulating estrous cyclicity in the mare. Used a technique called immunoflorescence to examine these PLA2s in equine uterine tissues. *Career Interests*: Mixed-animal practice in a rural area; internal medicine.

Bridgid Lammers, 3rd year. *Faculty Mentor*: Dr. John New.
Atlanta, GA. BS in ecology from the University of Georgia. *Summer Project*: Disease prevalence and population control in the feral cat population of Knox County, TN. *Career Interests*: Exotics and aquatic animal medicine.

Anna Elizabeth McRee, 2nd year. *Faculty Mentors*: Dr. Ed Ramsay and Dr. Kim Newkirk.
Rock Hill, SC. BS in biology from Maryville College. *Summer Project*: Evaluation of liver lesions in exotic cats. *Career Interests*: Zoological and exotics medicine.

Ellen Messenger, 2nd year. *Faculty Mentor*: Dr. Jeffrey Phillips.
Franklin, TN. BE in biomedical engineering from Vanderbilt University. *Summer Project*: Characterize Her-2/neu expression in various types of cancers for dogs, cats, and horses. Her-2/neu overexpression may be used as a biomarker for therapeutics. *Career Interests*: Research that benefits both human and animal health while practicing in a small-animal clinic setting; responsible pet ownership and pet overpopulation.

Jessica Miner, 2nd year. *Faculty Mentors*: Dr. Brad Fenwick, Dr. David Bemis, and Dr. Becky Wilkes.
Boone, NC. BS in biology from Appalachian State University. *Summer Project*: Developing an in vitro model of *Moraxella bovis,* which is implicated in infectious keratoconjunctivitis in cattle. *Career Interests*: Large animal medicine, infectious disease, veterinary public health, zoonotic infectious disease, outbreak investigation, and biosafety/bioterrorism.

Jenny Pope, 3rd year. *Faculty Mentor*: Dr. Shelley Newman.
Lexington, VA. BS in biology from Bridgewater College. *Summer Project*: Assisted the histology laboratory in trimming tissue; established normal organ weights for llamas, alpacas, goats, sheep, and birds; and reorganized slides on the virtual microscope with the microanatomy course. *Career Interest*: Veterinary pathology either at a diagnostic laboratory or a university.

Sherri Townley, 2nd year. *Faculty Mentor*: Dr. Maria Cekanova.
Johnson City, TN. BS in wildlife and fisheries science from the University of Tennessee. *Summer Project*: Immunohistochemistry (transitional cell carcinoma, squamous cell carcinoma, breast cancer), immunocytochemistry (transitional cell carcinoma), and cell line maintenance (transitional cell carcinoma). *Career Interests*: Reptile medicine/autoimmunity and nutrition research.

Alyson Wertz, 3rd year. *Faculty Mentor*: Dr. Patricia Tithof.
Knoxville, TN. BS in animal science from the University of Tennessee. *Summer Projec*t: Collected uterine biopsies from several mares at different points of the estrous cycle and used immunofluorescent staining techniques to identify enzymes in the tissue and determine if their expression changes over the timepoints studied. These enzymes are hypothesized to be linked to the uterine prostaglandins responsible for maintenance and destruction of the corpus luteum. Goal was to take the first of many steps to determine the mechanism of maternal recognition of pregnancy in the mare. *Career Interests*: Equine medicine and large animal theriogenology.

Kimberly White, 2nd year. *Faculty Mentors*: Dr. Karen Tobias and Dr. Becca Hodshon.
Black Mountain, NC. BS in biology and environmental studies from Montreat College. *Summer Project*: Client follow-up for a retrospective study of portosystemic shunts. *Career Interests*: Large animal or mixed animal practice.

Five-Year Benchmark Data

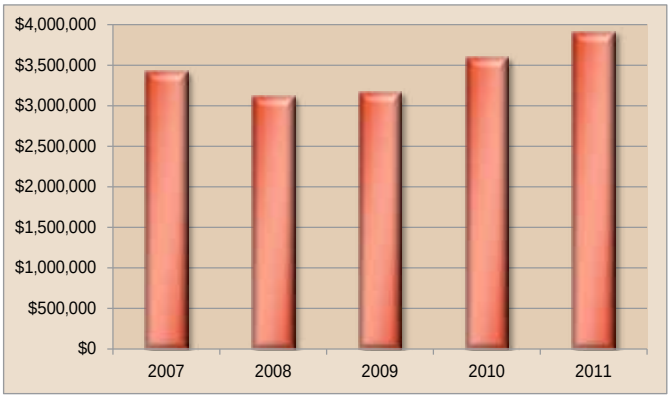


Fig. 2. *Research expenditures by fiscal year.*

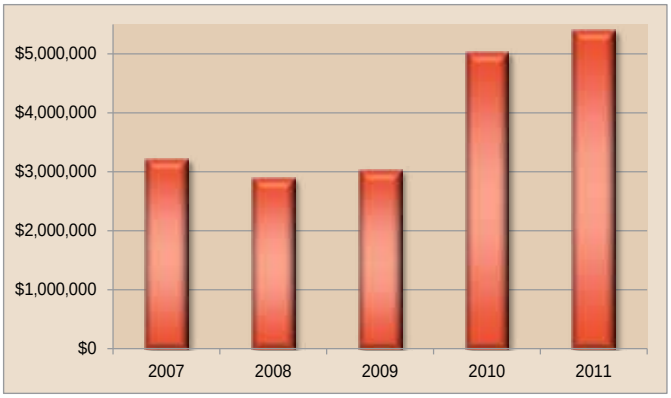


Fig. 3. *External research funding by fiscal year receipts.*

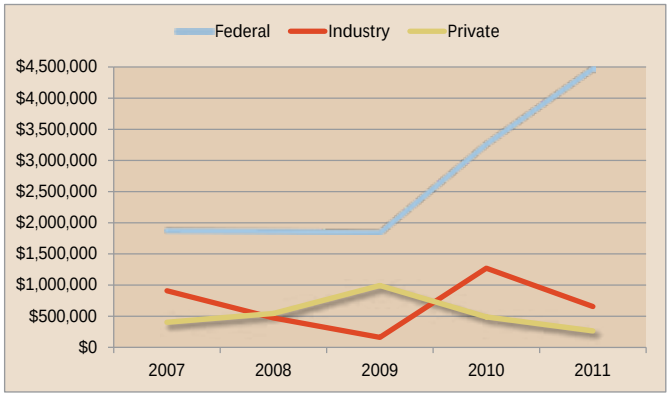


Fig. 4. *External research funding from the three major sources by fiscal year receipts.*

Benchmark Summary (2007-2011)

Average refereed articles per faculty member: 3

Federal funding increased: $2,582,108

Average return on investment: 7:1

Productivity among center faculty has been outstanding during the last 5-year period. From 2007-2011, center faculty published 287 articles in peer-reviewed journals and gave 194 presentations at national and international meetings.

Total research funding was up from $5.04 million in 2010 to $5.40 million in 2011; this upward trend is shown in Fig. 3. Federal funding increased dramatically from $1,898,889 in 2007 to $4,480,997 in 2011 (Fig. 4). Most of this comes from the National Institutes of Health, where the effects of diminishing federal budget allocations will no doubt negatively impact all our research programs.

Grant and contract expenditures per center faculty member had steadily decreased to a nadir of $155,000 in FY 2008 (Table 1). However, **expenditures per faculty member increased to $261,075 in FY 2011, exceeding the FY 2005 pre-downturn level of $222,000.** These indicators promote confident projections that the center is recovering vigorously.

The 5-year average return on the state's investment in the center is 7:1, the ratio of research expenditures to the state's appropriation. For comparison, benchmark data from 2007-2011 are summarized in Figs. 2 – 4.

Table 1. *Average expenditures per faculty member by fiscal year.*

Fiscal Year	$ Expenditures
2007	189,000
2008	155,000
2009	213,000
2010	239,800
2011	261,075

FUTURE Plans

The center successfully endured several years of sluggish federal and corporate funding and is poised to advance with an even greater commitment to livestock and human health. This year (FY11) the center will expend approximately $219,160 to fund nine projects. In addition, the center will continue to support core facilities and contribute to the purchase of essential research software and equipment. Already, external funding from center faculty is projected to be approximately $1.2 million in FY11.

The center will again be a major contributor to the Comparative & Experimental Medicine and Public Health (CEMPH) Research Symposium. The CEMPH Symposium provides a venue for new investigators (graduate students, postdocs, and research assistant professors) to gain experience presenting their research as oral presentations in scientific meeting format. The symposium grew from 15 student presentations at the inaugural 2007 event to over 80 presentations at the 2011 symposium with participants representing 22 UT departments and programs. More than 300 people attended the 2-day event. An additional goal of the symposium is to promote and facilitate the development of research collaborations among biomedical scientists from the different campuses of the university, a goal that closely parallels important objectives of the center.

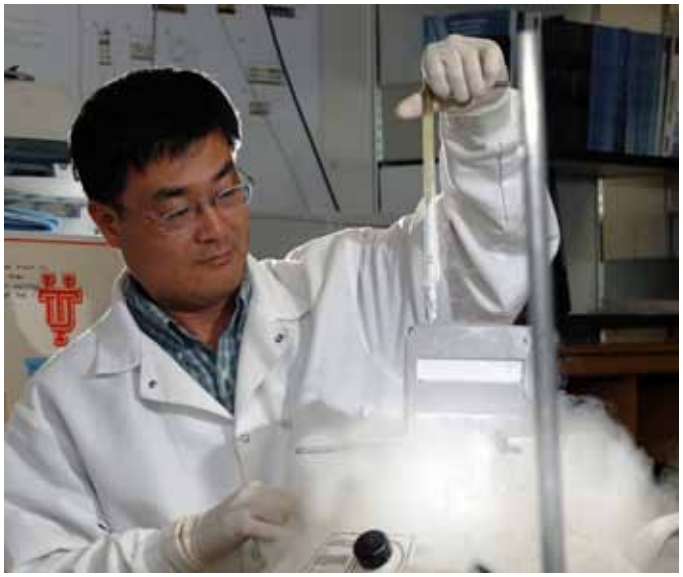
The center will continue to increase its involvement in research training of veterinary students and graduate students by providing increased opportunities for summer internships, matching travel grants, and stipend upgrades to help recruit and retain superior graduate students.

In addition, the UTCVM is aggressively pursuing initiatives in several different areas of research pertinent to the center. A primary goal of these initiatives is rapid movement of bench-level science to the clinic or farm, i.e., translational research. Established initiatives include investigations of equine and canine stem cells via the Alliance for Regenerative Medicine. Developments in this alliance include a collaboration with the Knoxville branch of the UT Health Sciences Center to generate and use custom biomaterial that will play an important role in tissue engineering. It is collaborations like this one and others that combine the three areas of animal, human, and environmental health to reinforce the concept of "One Health."

The center will continue to participate conceptually and materially in strategic planning to develop areas of investigative strength in the UTCVM and the Institute of Agriculture, as well as across the University of Tennessee campuses and with other regional universities.

Preventing and Slowing Colorectal Cancer Growth

Dr. Seung Joon Baek



Associate Professor

Biomedical and Diagnostic Sciences

PhD, University of Maryland

12 refereed publications in 2010

In addition to center funds, Dr. Baek's research is supported by the National Institutes of Health.

The American Cancer Society estimates that colorectal cancer is the third-deadliest cancer in both men and women. Over 1 million Americans are assumed to be living with this cancer.

Colorectal tumors typically begin as noncancerous polyps. Dr. Seung Joon Baek's research team wants to see these polyps become an endpoint by finding ways to prevent the polyps from turning cancerous.

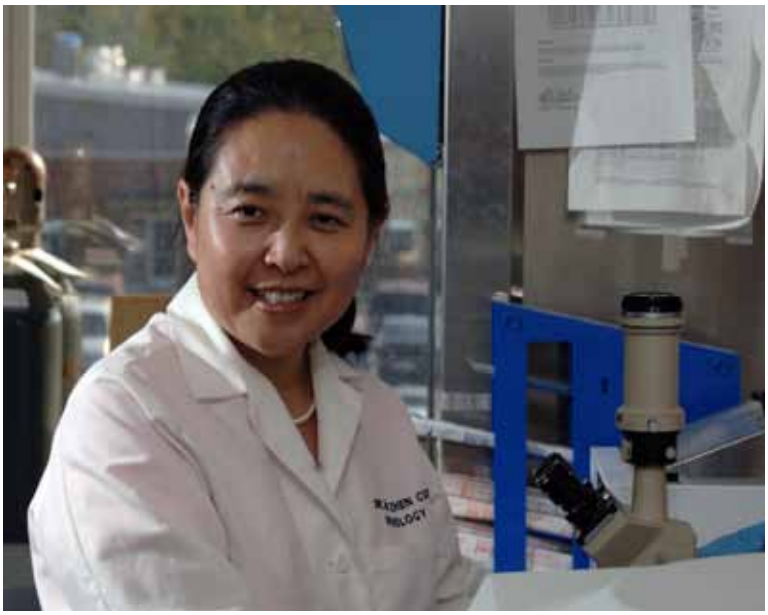
Several projects in Dr. Baek's laboratory address colorectal cancer prevention and intervention via natural remedies. For example, one project focuses on noni fruit (*Morinda citrifolia* L.). Noni is a tropical plant found in Southeast Asia, and Dr. Baek has found that one of its compounds, Damnacanthal, inhibits cancer cell growth.

In another project, he is looking at how resveratrol stalls the progression of colorectal cancer. Resveratrol is a component of the skin of red grapes and other fruits and is currently available as a nutritional supplement. Dr. Baek has discovered that resveratrol works by modulating specific genes in cancer cells, thereby causing cell death.

Dr. Baek's work builds a basic foundation for future clinical trials using these natural compounds to prevent and slow colorectal and potentially other types of cancer.

Preventing and Treating Atherosclerosis

Dr. Mei-Zhen Cui



Associate Professor

Biomedical and Diagnostic Sciences

PhD, Tokyo Institute of Technology, Japan

2 refereed publications in 2010

In addition to center funds, Dr. Cui's research is supported by the National Institutes of Health.

When oxidized, low-density lipoprotein (LDL), the so-called "bad cholesterol" found in the blood, produces lysophosphatidic acid (LPA), this LPA accumulates in high concentrations, contributing to the formation of lesions in arteries and leading to atherosclerosis.

This form of heart disease causes the intima of the arterial walls to thicken, narrowing the pathway for blood flow to the heart and brain. An estimated one in three adults in the United States was living with cardiovascular disease in 2008, and Tennessee was one of the top five states in stroke and heart attack-related deaths.

Dr. Mei-Zhen Cui has been investigating how LPA contributes to arterial wall thickening, specifically the proliferation and migration of smooth muscle cells that build up inside the wall. She theorizes that CYR61, an LPA-induced protein highly expressed in atherosclerotic lesions, contributes to smooth muscle cell proliferation and migration, and she seeks to determine how CYR61 is regulated.

Research performed in Dr. Cui's lab will help clinical scientists in developing prevention and treatment measures for people living with heart disease and thereby reduce the mortality associated with it, as well as decrease the estimated $503 billion cost to society each year.

Dr. James Godkin

Professor

Animal Science

PhD, University of Massachusetts

2 refereed publications in 2010

In addition to center funds, Dr. Godkin's research is supported by the U.S. Department of Agriculture.

Miscarriage within the first 3 weeks of pregnancy is a major cause of reproductive failure in cattle, sheep, and other large ruminant species. Ineffective signaling between the embryo and the maternal reproductive tract is responsible for most of these pregnancy failures, which can be costly for farmers. According to an article in the *Journal of Dairy Science*, each pregnancy loss cost an average of $555 in 2006.

Dr. James Godkin recently discovered that melatonin, a naturally-occurring compound in animals, may contribute to the maintenance of pregnancy in these livestock. He found that the ruminant placental membranes synthesize melatonin, and the uterine endometrium expresses receptors for melatonin. By giving pregnant cattle melatonin during the critical period of early embryonic survival (days 7–16), Dr. Godkin hopes to improve their embryos' survival rates. His results could lead to commercialization for a melatonin supplement specifically for cattle and other ruminants.

Shattering Methicillin Resistance

Dr. Stephen Kania

Professor

Biomedical and Diagnostic Sciences

PhD, University of Florida

9 refereed publications in 2010

In addition to center funds, Dr. Kania's research is supported by the American Kennel Club Canine Health Foundation, Discover Life in America, and Morris Animal Foundation.

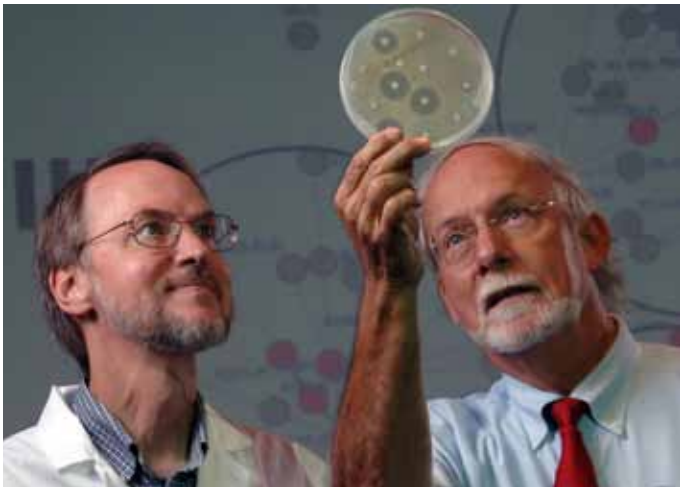
Dr. David Bemis

Professor

Biomedical and Diagnostic Sciences

PhD, Cornell University

5 refereed publications in 2010



It took only 2 years (1959-1961) for some penicillin-resistant staphylococci bacteria to become resistant to the antibiotic methicillin. The continued spread of methicillin resistance has become a serious public health concern; methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) is particularly concerning because it may be a source for interspecies spread of resistance genes. Evidence indicates these resistant genes occur as clonal populations within CDC-defined regions of the United States, potentially affecting humans, pets, and livestock.

As a next step in their continued project, Dr. Stephen Kania and Dr. David Bemis are examining key regulatory features that may affect the emergence and maintenance of MRSP populations. Their studies include determining the regulatory components that control genes' encoding resistance to penicillins. Methicillin resistance makes it difficult to treat pyoderma skin infections because of the limited number of antibiotics available, but Dr. Kania and Dr. Bemis hope that by characterizing MRSP, they can eventually develop ways to prevent the spread of resistance and perhaps develop a vaccine.

Dr. Seong-Ho Lee

Research Assistant Professor

Biomedical and Diagnostic Sciences

PhD, Korea University

6 refereed publications in 2010

In addition to center funds, Dr. Lee's research is supported by the National Institutes of Health.

Tolfenamic acid is a non-steroidal anti-inflammatory drug (NSAID) commonly used to treat migraines. However, it has also been found to induce growth arrest and death of colorectal cancer cells. Dr. Seong-Ho Lee seeks to determine the mechanisms by which tolfenamic acid mediates this anticancer activity.

So far, Dr. Lee has discovered that tolfenamic acid activates the protein ESE-1, which binds to specific DNA sequences. Depending on its cellular location, ESE-1 plays a significant role in colorectal cancer cell death, and ESE-1 seems to be a promising target in chemoprevention. Considering these results, Dr. Lee's studies could eventually lead to clinical studies for developing drugs that target ESE-1.

In addition, Dr. Lee is examining the beneficial effects of capsaicin, found in hot chili pepper, as a natural remedy for colorectal cancer.

Dr. Hildegard Schuller

Distinguished Professor

Biomedical and Diagnostic Sciences

PhD, University of Veterinary Medicine, Hannover, Germany

DVM, Justus Leibig University, Germany

3 refereed publications in 2010

In addition to center funds, Dr. Schuller's research is supported by the National Institutes of Health.

Stress motivates some of us to get things done, but increases in stress hormones enhance our vulnerability to numerous diseases. In particular, stress may be a potent driving force in cancer development and progression. The American Cancer Society's 2011 statistics show that low socioeconomic status, which often creates chronic stress, is associated with higher incidence and mortality of all cancers.

With her unique project, Dr. Hildegard Schuller is examining how chronic stress and chronic nicotine exposure work together to hinder cancer prevention measures. Nicotine alone and stress hormones alone activate a signaling messenger, cAMP, that is important in many regulatory biological processes but also perhaps in the growth of some cancers. An inhibitor in the central nervous system known as gamma-aminobutyric acid (GABA) normally counterbalances the activity of this pathway. However, the combination of the effects of smoking and stress virtually shuts down GABA production. It is Dr. Schuller's belief that treatment with GABA will reverse all negative effects of cAMP signaling by restoring the body's ability to repair itself.

Breast Cancer: An Ounce of Prevention

Dr. Hwa-Chain Robert Wang

Professor

Biomedical and Diagnostic Sciences

PhD, University of Virginia

DVM, National Chung-Hsing University, Taiwan

2 refereed publication in 2010

In addition to center funds, Dr. Wang's research is supported by the National Institutes of Health.

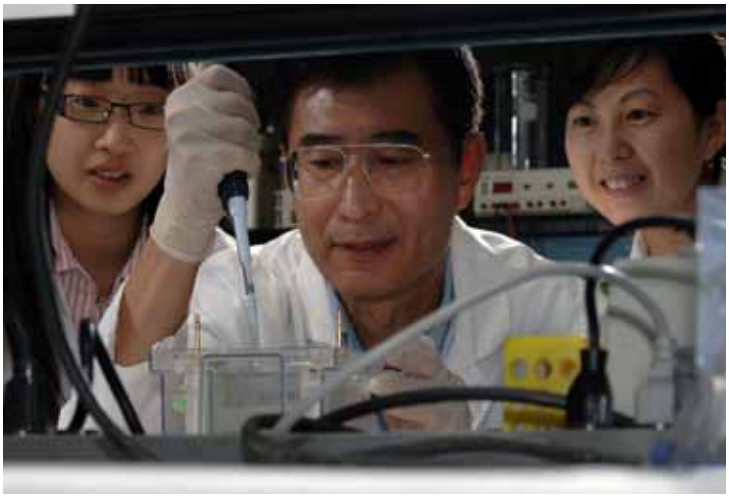
Excluding cancers of the skin, breast cancer is the most common type of cancer among women in North America, and chronic exposure to carcinogens found in the environment accounts for more than 70% of breast cancers. Dr. Hwa-Chain Robert Wang has developed a cell model that mimics this chronic exposure so that potential prevention methods can be tested. In particular, Dr. Wang is using his model to study tumor stem-like cells, which, like regular stem cells, can self renew and differentiate into other cell types. However, these stem-like cells differ in that they propagate tumor cells.

To prevent and treat breast cancer, his focus is on natural substances like green tea and grape seed extract. Thus far, he has determined that these two extracts are able to suppress the effects of the cancer-causing substances B[a]P (found in cigarette smoke and food cooked at high temperatures) and NNK (found in tobacco).

Completion of this research will aid developers of dietary supplements in creating treatments and preventives for breast cancer, as well as influence dietary regimens in those at risk for cancer and those living with cancer.

Remembering Alzheimer's Disease

Dr. Xuemin Xu



Professor

Biomedical and Diagnostic Sciences

PhD, Tokyo Institute of Technology, Japan

2 refereed publications in 2010

In addition to center funds, Dr. Xu's research is supported by the National Institutes of Health and the American Health Assistance Foundation.

Tennessee's renowned women's basketball coach Pat Summitt was recently diagnosed with early-onset Alzheimer's disease, putting this devastating condition under even more national scrutiny. In 2011, it was estimated that 5.4 million Americans had Alzheimer's disease, and as our population ages, the disease will likely become more frequent. This predicted, dramatic rise in Alzheimer's occurrence makes understanding the disease all the more important.

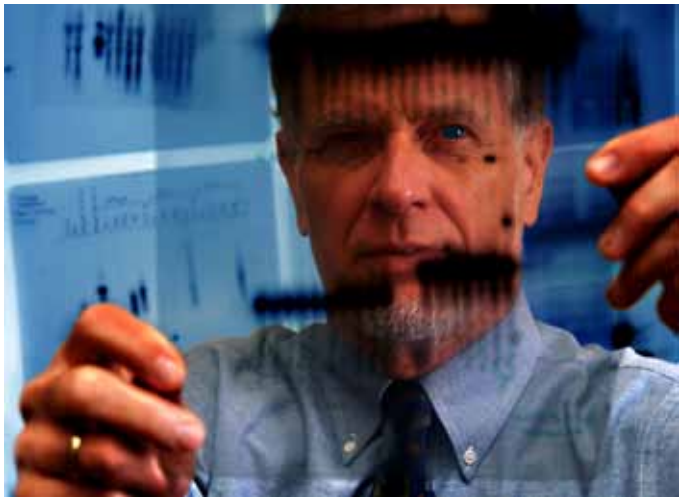
The mechanisms that cause neuron death associated with Alzheimer's disease are still not well understood, but one of the proposed mechanisms is apoptosis, which is a genetically-determined process of cell self-destruction.

Dr. Xuemin Xu's research group believes that presenilin-associated protein (PSAP) may relay apoptotic signals, and thus may play an important role in the neuronal degeneration found in Azheimer's disease. Using a genetically-engineered strain of yeast, Dr. Xu was able to determine that PSAP acts through interaction with the death receptor DR6. Receptors like DR6 transmit apoptotic signals on the cell surface.

The long-term goal of his studies is to determine PSAP's role in order to further the foundation for future clinical research aimed at preventing and treating this devastating disease.

Turning Off the Coronavirus Switch

Dr. David Brian



Professor

Biomedical and Diagnostic Sciences

DVM, PhD, Michigan State University

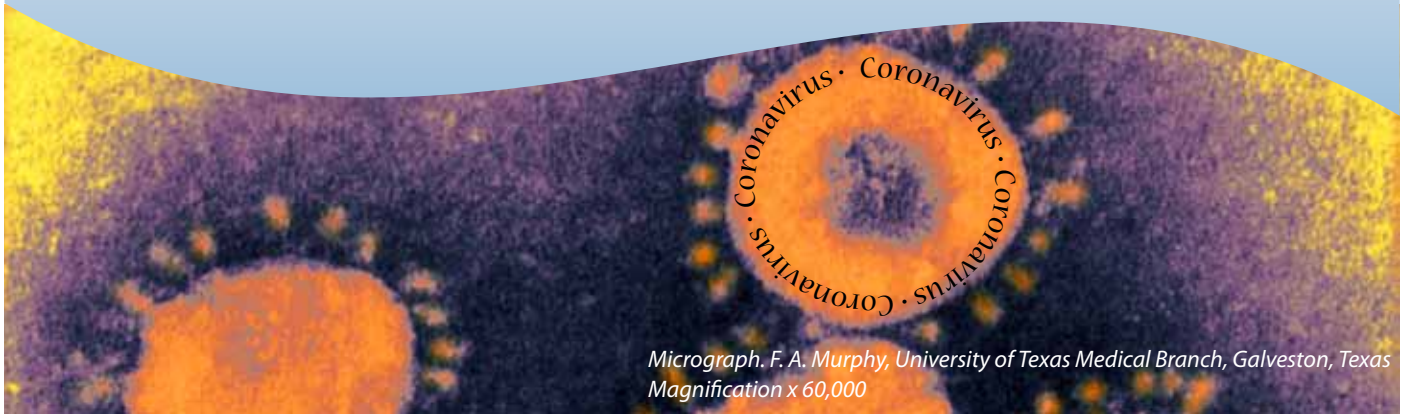
1 refereed publication in 2010

In addition to center funds, Dr. Brian's research is supported by the National Institutes of Health.

Coronavirus is a virus found in mammals (including humans) and birds that affects the respiratory and gastrointestinal tracts, as well as the central nervous system. It is responsible for the common cold and more serious illnesses like SARS (severe acute respiratory syndrome) in humans but also impacts the farm industry in swine, cattle, and chickens. Like other viruses, it contains a specific protein structure.

To his surprise, Dr. David Brian discovered that when cells are infected with coronavirus, the virus hijacks the cells' ability to build its own protein in favor of virus proteins. For years, scientists assumed that this hijacking process involved a "cap" site. This cap is a special tag at the end of an mRNA molecule where the virus enters. However, the coronavirus also seems to have a cap-independent mechanism, otherwise known as an internal entry site.

Dr. Brian has been working to characterize this entry site and determine if the virus or cell "switches" between cap-dependent and cap-independent entry. More knowledge of this riboswitch may allow scientists to exploit the regulation of the riboswitch in coronavirus-infected cells, and thus develop ways to treat the virus in animals and humans alike.



Micrograph. F. A. Murphy, University of Texas Medical Branch, Galveston, Texas
Magnification x 60,000

Measuring Glucose: How Sweet it Is

Dr. Nicholas Frank

Associate Professor

Large Animal Clinical Sciences

DVM, PhD, Purdue University

5 refereed publications in 2010

In addition to center funds, Dr. Frank's research is supported by the Grayson Jockey Club and Advantage Partners.

In horses, diagnosing insulin resistance is important because this resistance predisposes the animal to laminitis, an inflammatory condition that, in its worst form, causes the hoof wall to separate from the bone. If not treated appropriately, laminitis can result in permanent lameness, forced retirement, or euthanasia.

Insulin resistance is often diagnosed by measuring glucose concentration within a single blood sample, as with humans who do their own diabetic testing. Reference ranges for glucose and insulin concentrations are available for humans, but appropriate ranges have not been determined for horses.

Dr. Nicholas Frank hypothesizes that blood insulin concentrations are affected by factors other than insulin resistance, and these must be identified and quantified. He is focused on measuring hour-to-hour, day-to-day, and month-to-month variability in blood glucose and insulin levels in healthy and insulin-resistant horses. In addition, he is assessing the effects of diet by collecting and analyzing pasture grass and hay samples.

His ultimate goal is to improve the accuracy of diagnostic testing for insulin resistance in horses.

Stamping Out Obesity-related Disease

Dr. Naima Moustaid-Moussa

Photo by Phil Snow

Professor

Animal Science

PhD, University of Paris, France

2 refereed publications in 2010

In addition to center funds, Dr. Moustaid-Moussa's research is supported by the U.S. Department of Agriculture and the American Heart Association.

In 2010, over 30% of Tennesseeans were considered obese by the Centers for Disease Control. Obesity is associated with higher risk for certain types of cancer, diabetes, stroke, and heart disease. Doctors are now recommending their patients try to lower these risks through dietary changes and nutritional supplements that include soy isoflavones or omega-3 fatty acids.

Individually, these two compounds decrease inflammation and improve insulin sensitivity often associated with obesity. However, their synergistic effects when combined have not been fully explored. Dr. Naima Moustaid-Moussa hypothesizes that a combination of soy isoflavones and omega-3 fatty acids will be more beneficial at lower doses than either compound alone.

These studies will provide valuable insight into interactions among foods to improve human health.

Udderly Devastating: *E. coli* Mastitis

Dr. Stephen Oliver

Professor

Animal Science

PhD, The Ohio State University

2 refereed publications in 2010

In addition to center funds, Dr. Oliver's research is supported by Biotechnology Research & Development Corp., Fort Dodge Animal Health, Pfizer Animal Health, the U.S. Department of Agriculture, and other private industry.

Mastitis, an inflammatory condition of the udder, is the most common and most costly disease in dairy cattle. The disease creates discomfort for the animal (and in some acute cases, death), as well as abnormalities and lower yield in the milk the cow produces.

Dr. Stephen Oliver has been studying mastitis for over 30 years, and he has recently focused his attention on how *Escherichia coli* mastitis affects well-managed dairy farms. In these herds, where contagious pathogens are otherwise controlled, mastitis is typically chronic, with recurring episodes of symptoms varying in severity. Work from Dr. Oliver's laboratory shows that *E. coli* in chronic mastitis survives better than in acute mastitis. Dr. Oliver suspects this is because *E. coli* adheres and internalizes itself into the mammary epithelial cells, and the goal of his work is to identify virulence factors involved in this process. Virulence factors are what allow the bacteria to establish themselves within the host.

Detection of virulence factors is the first step in the design of effective vaccines for the control of this infectious disease.

Blueprinting Osteosarcoma

Dr. Jeffrey Phillips

Assistant Professor

Small Animal Clinical Sciences

DVM, PhD, Tufts University

1 refereed publication in 2010

In addition to center funds, Dr. Phillips's research is supported by the National Institutes of Health.

Each year, approximately 800 people in the United States are diagnosed with osteosarcoma. This cancer is highly aggressive, with very high rates of spread, and it occurs most commonly in the long bones (upper arm and leg) of teenagers during growth spurts.

Of the cancers that occur in both humans and dogs, osteosarcoma seems to be the most similar between species. Veterinarians see about 10,000 canine cases each year in the United States. Likely because of their long bones, Scottish deerhounds are particularly prone to osteosarcoma, and treating the disease in dogs has a similar outcome as in human patients.

Because the majority (>80%) of reported cases of osteosarcoma occur in the Scottish deerhound, Dr. Jeffrey Phillips is concerned with the genetic makeup of the breed. He has determined that a specific, dominant gene is responsible for this cancer, and thanks to these results, a genetic test can now identify deerhounds at risk for osteosarcoma. Eventually, these breakthroughs may be applied to predict human risk, as well.

Reducing Severity of Stromal Keratitis

Dr. Barry Rouse

Distinguished Professor

Biomedical and Diagnostic Sciences

BVSc, DSc, University of Bristol, England

PhD, University of Guelph, Canada

4 refereed publications in 2010

In addition to center funds, Dr. Rouse's research is supported by the National Institutes of Health.

Infection of the eye with herpes simplex virus-1 (HSV-1) results in a chronic, inflammatory reaction known as stromal keratitis, which can lead to blindness. Controlling inflammatory diseases is challenging, particularly if treatment begins late after initial infection.

Recent studies suggest that certain regulatory T cells (Tregs) can diminish the severity of keratitis lesions. However, these cells are not stable, and cells that were once suppressive can change and instead increase the severity of the disease. Dr. Barry Rouse's research aims at stabilizing these Tregs using epigenetics. Epigenetics is the study of heritable changes in genes that occur without changing the DNA sequence.

Epigenetic modifier drugs like trichostatin and azacytidine have been shown to increase the stability of Foxp3 Tregs; therefore, Dr. Rouse plans to determine the effect of these two drugs on maintaining this Treg stability in hopes that the drugs will eventually help control the severity and duration of lesions in patients with stromal keratitis.

Seung Joon Baek (p. 19)

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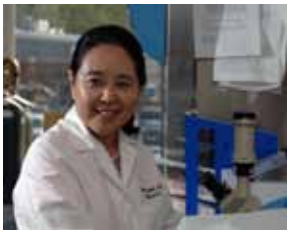

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Stephen Oliver (p. 30)

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Kerro Dego O, Almeida RA, Luther DA, **Oliver SP**. Gene expression profile of bovine primary mammary epithelial cells infected with *Escherichia coli* associated with acute or chronic bovine mastitis. Poster presented at: Conference of Research Workers in Animal Diseases; December 2010; Chicago, IL.

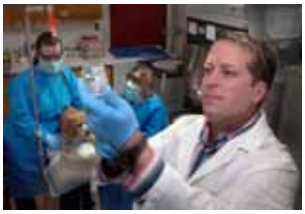
Oliver SP. Tennessee AgResearch: Issues and opportunities. Invited seminar presented at: The University of Tennessee Institute of Agriculture; March 2010; Knoxville, TN.

Oliver SP. Milk somatic cell counts from Tennessee dairies: Should we be concerned? Invited talk presented at: Joint Meeting of the UT AgResearch Dairy Advocacy Group and the Tennessee Farm Bureau Dairy Commodity Advisory Committee; Novebmer 2010; East Tennessee Research and Education Center, Little River Animal Environmental Research Unit, Walland, TN.

Lopez Benavides MG, Headrick SI, Lewis MJ, Gillespie BE, Moorehead J, Plunk JD, Traistaru C, Ahmed F, Hemling T, **Oliver SP**. Efficacy of two chorine dioxide-based postmilking teat disinfectants. Poster presented at: Annual Meeting of the National Mastitis Council: Technology Transfer Session; January 31–February 3, 2010; Albuquerque, NM.

Lopez Benavides MG, Headrick SI, Lewis MJ, Gillespie BE, Bauer LM, Johnson D, Lamar K, Traistaru C, Ahmed F, Hemling T, **Oliver SP**. Efficacy of two chorine dioxide-based barrier teat disinfectants. Poster presented at: Annual Meeting of the National Mastitis Council: Technology Transfer Session; January 31–February 3, 2010; Albuquerque, NM.

Jeffrey Phillips (p. 31)



Phillips JC, Lembcke L, Chamberlin T. A novel locus for canine osteosarcoma maps to CFA34, the canine orthologue of human 3q26. *Genomics* 2010;96:220–227.

Phillips J. Evaluation of tyrosinase expression in canine and equine melanocytic tumors. Oral presentation at: American College of Veterinary Internal Medicine Forum; June 2010; Anaheim, CA.

Phillips J. Genetics of osteosarcoma in the Scottish deerhound. Oral presentation at: American College of Veterinary Internal Medicine Forum; June 2010; Anaheim, CA.

Phillips J. Thermochemotherapy in the treatment of solid tumors. Oral presentation at: American College of Veterinary Internal Medicine Forum; June 2010; Anaheim, CA.

Phillips J. Thermochemotherapy for the palliation of solid tumors in large animals. Invited presentation at: Veterinary Cancer Society Annual Meeting; 2010; San Diego, CA.

Phillips J. Thermochemotherapy for the treatment of feline fibrosarcomas. Oral presentation at: Veterinary Cancer Society Annual Meeting; 2010; San Diego, CA.

Phillips J. Development of immunologic assays to measure response to xenogenic HuTyr DNA vaccination. Poster presented at: Merial Limited Seminar Series; 2010; Athens, GA.

Phillips J. Adding heat to improve outcome in small animal oncology. Oral continuing education presentation to: University of Tennessee December Conference; December 2010; Knoxville, TN.

Phillips J. Treatment of tumors in large animals. Invited lecture at: University of Tennessee December Conference; December 2010; Knoxville, TN.

Smrkovski O, Aknine G, **Phillips JC**. A novel method of localized hyperthermia delivery in conjunction with chemotherapy for the treatment of non-resectable canine and feline sarcomas: a pilot study [abstract]. Comparative & Experimental Medicine and Public Health Research Symposium; June 2010; Knoxville, TN.

Lembcke L, Noltenius C, Newman S, Blackford J, Grosenbaugh D, Leard T, **Phillips JC**. Tyrosinase expression in canine and equine melanocytic tumors [abstract]. Comparative & Experimental Medicine and Public Health Research Symposium; June 2010; Knoxville, TN.

Barry Rouse (p. 32)

Kaufman SHE, **Rouse BT**, Sacks D, eds. *The Immune Response to Infection*. Washington, DC: ASM Press;2010.

Belkaid Y, Sehrawat S, **Rouse BT**. Regulation of microbial immunity. In: Kaufman SHE, Rouse BT, Sacks D, eds. *The Immune Response to Infection*. Washington, DC: ASM Press;2010:109–120.

Sarangi P, **Rouse BT**. Herpetic keratitis. In: Levin LA, Albert DM, eds. *Ocular Disease: Mechanisms and Management*. Philadelphia: Saunders Elsevier;2010:91–97.

Sehrawat S, Reddy PJP, Rajasag NK, Suryawanshi A, Hirashima M, **Rouse BT.** Galectin-9/TIM-3 interaction regulates virus-specific primary and memory CD8 T cell responses. *PLoS Pathogens* 2010;6:e1000882.

Rouse BT, Sehrawat S. Immunity and immunopathology to viruses–What decides the outcome? *Nature Reviews Immunology.* 2010;10:514–526.

Araki K, Gangappa S, Dillehay DL, **Rouse BT**, Larsen CP, Ahmed R. Virus specific T cells generated in the presence of calcineurin-inhibitor 2010 FK506 causes lethal disease;Implications for transplantation. *Journal of Experimental Medicine* 2010;207:2355–2367.

Rouse BT, Lukacher AE. Some unmet challenges in the immunology of virus infections. *Discovery Medicine*. 2010;10:363–370.

Rouse BT. Tinkering with regulatory mechanisms to change the outcome of virus infection. Invited seminar at: University of British Columbia; March 31, 2010; Vancouver, BC, Canada.

Rouse BT. Immune regulation to viral infection. Invited lecture at: 4th Pasteur-AREVA Course on Anti-Viral Immunity; May 18, 2010; Shanghai, China.

Rouse BT. Invited seminar at: Areva Pasteur Research Institute; May 20, 2010; Shanghai, China.

Rouse BT. Invited seminar at: College of Veterinary Medicine, Agricultural University of Beijing; May 22, 2010; Beijing, China.

Rouse BT. Cornea angiogenesis. Invited expert roundtable discussant at: World Ophthalmology Congress; June 6, 2010; Berlin, Germany.

Rouse BT. Invited seminar at: College of Veterinary Medicine, Free University of Berlin; June 8, 2010; Berlin, Germany.

Rouse BT. Invited seminar at: Robert Koch Institute; June 7, 2010; Berlin, Germany.

Rouse BT. Invited participant: Kansas State University Center of Excellence for Emerging and Zoonotic Animal Diseases Advisory Meeting; June 28–29, 2010; Manhattan, KS.

Rouse BT. Invited seminar at: Medimmune; October 21, 2010; Palo Alto, CA.

Rouse BT. Invited seminar at: Kansas State University; December 17, 2010; Manhattan, KS.

Hildegard Schuller (p. 24)

Al-Wadei HAN, Al-Wadei MH, Masi T, **Schuller HM**. Chronic exposure to estrogen and the tobacco carcinogen NNK cooperatively modulates nicotinic receptors in small airway epithelial cells. *Lung Cancer* 2010;69:33–39.

Schuller HM, Al-Wadei HAN. Neurotransmitter receptors as central regulators of pancreatic cancer [invited review]. *Future Oncology* 2010;6:221–228.

Schuller HM. Beta-adrenergic signaling, a novel target for cancer therapy? [invited commentary on Powe DG, et al. Beta-blocker therapy reduces secondary cancer formation in breast

cancer and improves cancer specific survival]. *Oncotarget* 2010;1:466–469.

Schuller HM. Role of nicotinic acetylcholine receptors in lung cancer. Invited lecture at: American Thoracic Society International Conference; May 2010; New Orleans, LA.

Schuller HM. Effects of estrogen on nicotinic receptor-mediated responses to the nicotine derivative NNK. Invited lecture at: National Lung Cancer Partnership Annual Meeting; June 2010; Chicago, IL.

Schuller HM. Role of chronic nicotine in cancer of the lungs and pancreas. Invited lecture at: U.S. Food and Drug Administration public workshop: Risks and Benefits of Long-Term Use of Nicotine Replacement Therapy Products; October 2010; Arlington, VA.

Hwa-Chain Robert Wang (p. 25)

Song X, Rathore K, Siriwardhana N, Lin D, **Wang H-CR**. Grape seed proanthocyanidin suppression of breast cell carcinogenesis induced by chronic exposure to combined 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone and benzo[a]pyrene. *Molecular Carcinogenesis* 2010;49:450–463.

Choudhary S, Rathore K, **Wang H-CR**. FK228 and oncogenic H-Ras synergistically induce Mek1/2 and Nox-1 to generate reactive oxygen species for differential cell death. *Anti-Cancer Drugs* 2010;21:831–840.

Mukherjee A, **Wang H-CR**. To identify the role of HSD11B2 in cellular carcinogenesis. Poster presented at: The University of Tennessee/Oak Ridge National Laboratory Graduate School of Genome Science & Technology Annual Retreat; March 5, 2010; Knoxville, TN.

Rathore K, **Wang H-CR**. Identification of cancer stem cells during cancer progression and preventive role of green tea catechins. Poster presented at: The University of Tennessee/Oak Ridge National Laboratory Graduate School of Genome Science & Technology Annual Retreat; March 5, 2010; Knoxville, TN.

Choudhary S, **Wang H-CR**. Differential induction of reactive oxygen species by histone deacetylase inhibitors for mediating selective apoptosis of oncogenic H-Ras-expressing cells. Poster presented at: Experimental and Molecular Therapeutics 11, The 101st Annual American Association for Cancer Research Meeting; March 19, 2010; Washington, DC.

Rathore K, Choudhary S, Song X, Siriwardhana N, **Wang H-CR**. Biological, biochemical, and molecular targets for dietary catechin-induced suppression of breast cell chronic carcinogenesis. Poster presented at: Carcinogenesis 5, The 101st Annual American Association for Cancer Research Meeting; April 20, 2010; Washington, DC.

Choudhary S, **Wang H-CR**. Role of reactive oxygen species in histone deacetylase inhibitor-mediated selective apoptosis of oncogenic H-Ras-expressing cells [abstract]. Presented at: Comparative & Experimental Medicine and Public Health Research Symposium; June 14, 2010; Knoxville, TN.

Rathore K, Song X, Siriwardhana N, **Wang H-CR**. Targets for dietary grape seed extract-induced suppression of breast cell chronic carcinogenesis [abstract]. Presented at: Comparative & Experimental Medicine and Public Health Research Symposium; June 14, 2010; Knoxville, TN.

Wang H-CR. American veterinary college accreditation. Keynote presentation at: Eighth Annual Meeting for Deans of Chinese Veterinary Medical Colleges; August 2010; Changchun City, China.

Wang H-CR. Veterinary education in the USA. Invited presentation at: Xinjiang Agricultural University, College of Veterinary Medicine; October 2010; Urumqi City, Xinjiang Province, China.

Wang H-CR. Reactive oxygen species-mediated selective apoptosis of oncogenic Ras-expressing cancer cells. Invited presentation at: Xinjiang Agricultural University, College of Veterinary Medicine; October 2010; Urumqi City, Xinjiang Province, China.

Wang H-CR. ROS-mediated selective apoptosis of oncogenic Ras-expressing cancer cells. Invited presentation at: BIT's 8th Annual Congress of International Drug Discovery Science and Technology; October 2010; Beijing, China.

Wang H-CR. Reactive oxygen species-mediated selective apoptosis of oncogenic Ras-expressing cancer cells. In-

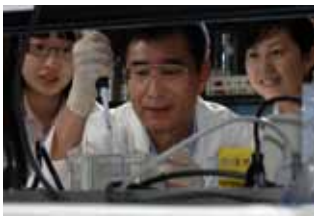
vited presentation at the: National Institute of Cancer Research/National Institutes of Health Research; October 27–28, 2010; Tainan City, Taiwan.

Wang H-CR. Reactive oxygen species-mediated selective apoptosis of oncogenic Ras-expressing cancer cells. Invited presentation at the China Medical University; October 29, 2010; Taichung City, Taiwan.

Wang H-CR. Reactive oxygen species-mediated selective apoptosis of oncogenic Ras-expressing cancer cells. Invited presentation at: Veteran General Hospital Medical Research Center; November 1, 2010; Taipei City, Taiwan.

Wang H-CR. Veterinary education in the USA and UTCVM. Invited presentation at: Hanoi University of Agricultural Faculty of Veterinary Medicine and the U.S. CDC; November 4, 2010; Hanoi, Vietnam.

Xuemin Xu (p. 26)



Wang K, Cai L, Hao F, **Xu X**, Cui M-Z, Wang S. Distinct cell responses to substrates consisting of poly(ε-caprolactone) and poly(propylene fumarate) in the presence or absence of crosslinks. *Biomacromolecules* 2010;11:2748–2759.

Hao F, Tan M, Wu D, **Xu X**, Cui M-Z. Lysophosphatidic acid induction of interleukin 6 secretion from aortic smooth muscle cells via LPA1 regulated, PKC dependent and p38alpha mediated pathway. *American Journal of Physiology-Heart and Circulatory Physiology* 2010;298:H974–983.

Xu X. A possible mechanism of how oxLDL contributes to Alzheimer's disease. Invited lecture presented at: South East Lipid Research Conference; October 2010; Pine Mountain, GA.

Xu X. Molecular mechanism of presenilin-mediated pathogenesis of Alzheimer's disease. Invited lecture at: Temple University School of Medicine; June 30, 2010; Philadelphia, PA.

Xu X, Dong Y, Tan J, Mao G, Cui M-Z. Oxidized LDL in Alzheimer's disease. Poster presented at: Keystone Symposia Bioactive Lipids: Biochemistry and Diseases; June 2010; Kyoto, Japan.

Cui M-Z, Hao F, Wu DD, **Xu X**. LPA receptor 1-mediated activation of PKC and p38α MAPK is required for lysophosphatidic acid induction of interleukin 6 secretion from vascular smooth muscle cells. Poster presented at: Keystone Symposia Bioactive Lipids: Biochemistry and Diseases; June 2010; Kyoto, Japan.

*Publications and presentations listed are for the 2010 calendar year. The reporting method for this report was changed in 2009 to more accurately reflect the total number of publications and presentations by including all items from the previous calendar year. Past reports included only items from the current calendar year through the publication date of the report. Some items may be duplicated between individual investigators.

Research Funded Externally – Detail

Investigator	Project Title	Funding Agency	Project Period	2011 Receipts	2011 Expenditures
Baek, Seung Joon	PPAR-gamma ligands in colorectal cancer	National Institutes of Health	06/01/06–05/31/12	$199,929	$163,892
Brian, David	Coronavirus RNA replication	National Institutes of Health	06/01/08–05/31/13	$352,193	$324,651
Cui, Mei-Zhen	Novel mechanism mediating LPA-induced smooth muscle cell and vascular responses	National Institutes of Health	06/15/11–05/31/15	$361,159	$0
Frank, Nicholas	Endotoxemia as a predisposing factor for laminitis	Grayson Jockey Club Research Foundation	04/01/10–09/30/11	$41,490	$22,937
	Pharmocokinetics and clinical application of Resvantage Equine in horses	Advantage Partners, Inc.	05/01/11–04/30/12	$7,080	$0
Godkin, James	Phospholipase A regulation of uterine and conceptus lipid mediators	USDA	10/14/09–08/13/12	$349,503	$98,854
Kania, Stephen	Characterization of staphylococci isolated from bears in the Great Smoky Mountains National Park	Discover Life in America, Inc.	04/01/10–03/31/11	$5,000	$2,832
	Bacteriophage in methicillin-resistant *Staphylococcus* from canine skin infections	Morris Animal Foundation	06/01/10–08/31/10	$4,000	$2,445
	Genomic resources for the control of canine pyroderma	AKC Canine Health Foundation	01/01/11–12/31/12	$42,466	$1,968
Lee, Seong-Ho	Combinational anti-cancer effects of capsaicin and 3,3'-diindolylmethane in colorectal cancer	National Institutes of Health	07/01/09–06/30/12	$70,470	$70,180
Moustaid-Moussa, Naima	Systems genetics in nutrition and obesity research	USDA	09/01/09–08/31/10	$10,000	$0
	Epidemiologic tools to assess obesity-related energy and nutrient intakes	USDA	06/15/09–06/14/11	$149,481	$73,169
	Metabolic effects of caloric restriction in mice overexpressing angiotensinogen in adipose tissue	American Heart Association	07/01/09–06/30/11	$43,540	$21,768
	Utilizing a competitive, creative, after-school program as a model for nutrition and physical activity education program	USDA	02/01/08–02/14/12	*$0	*$114,968

Oliver, Stephen	Confidential	Private Industry	02/18/09–08/31/11	$93,440	$714,591
	Funding of a rapid, sensitive, in-the-field foodborne pathogen detection system	Biotechnology Research & Development Corp.	07/01/10–09/30/12	$500,000	$144,989
	Characterization of immune response & protection following experimental challenge in dairy cows vaccinated with *Streptococcus uberis* adhesion molecule	USDA	02/15/11–12/31/11	$500,000	$7,027
	Tennessee Quality Milk Initiative	Fort Dodge Animal Health Global Research	10/01/07–12/31/12	$50,000	$0
	Efficacy and field safety of Spectramast LC for intramammary treatment of clinical mastitis due to *Staphylococcus aureus* or *Streptococcus uberis*	Pfizer Animal Health	08/05/08–08/09/11	*$0	*$0
Phillips, Jeffrey	Preclinical comparison of 3 indenoisoquinolines candidates in tumor-bearing dogs: A Pilot study of topotecan in dogs with lymphoma	National Institutes of Health	01/01/10–12/31/10	$94,590	$88,080
Rouse, Barry	Mechanisms in herpetic keratitis	National Institutes of Health	01/01/08–12/31/12	$335,412	$252,767
	T-Regulatory cells in HSV immunity and immunopathology	National Institutes of Health	02/01/11–01/31/16	$356,536	$113,365
Schuller, Hildegard	The GABA-B receptor is a novel drug target for pancreatic cancer	National Institutes of Health	05/01/09–04/30/13	$264,476	$291,004
	Modulation of cancer prevention by social stress	National Institutes of Health	09/30/09–08/31/12	$500,000	$496,809
	GABA-BR-mediated prevention of pancreatic cancer	National Institutes of Health	09/28/09–08/31/14	$289,868	$345,298
Wang, Hwa-Chain Robert	Carcinogenesis cellular model for identifying preventive agents	National Institutes of Health	09/27/07–08/31/10	*$0	*$12,886
	Green tea catechins in precancerous prevention	National Institutes of Health	09/01/08–08/31/11	$190,598	$128,496
Xu, Xuemin	The role of the new zeta cleavage in ABeta formation	National Institutes of Health	04/01/07–03/31/12	$277,202	$333,983
	Vascular risk factors in Alzheimer's disease	American Health Assistance Foundation	04/01/09–03/31/12	$133,333	$89,162
	Role of presenilin-associated protein (PSAP) in apoptosis and Abeta formation	National Institutes of Health	04/15/11–03/31/13	$179,580	$0
				$5,401,346	**$3,916,121**

*No-cost extension granted, resulting in no new funds in the current year.
Expenditure amounts, if any, are from carry-over from the previous year.

CENTERS OF EXCELLENCE/CENTERS OF EMPHASIS

ACTUAL, PROPOSED, AND REQUESTED BUDGET

College of Veterinary Medicine — **Center of Excellence in Livestock Diseases and Human Health**

	FY 2010-11 Actual			FY 2011-12 Proposed			FY 2012-13 Requested		
	Matching	Appropr.	Total	Matching	Appropr.	Total	Matching	Appropr.	Total
Expenditures	250,909	501,817	**752,726**	304,089	608,178	**912,267**	261,050	522,100	**783,150**
Salaries									
Faculty	26,671	53,342	**80,013**	7,024	14,047	**21,071**	7,375	14,750	**22,125**
Other Professional	34,780	69,561	**104,341**	51,732	103,463	**155,195**	54,318	108,637	**162,955**
Clerical/ Supporting	34,386	68,772	**103,159**	35,818	71,637	**107,455**	37,609	75,219	**112,828**
Assistantships	23,443	46,887	**70,330**	13,804	27,608	**41,412**	14,494	28,988	**43,483**
Total Salaries	**119,281**	**238,561**	**357,842**	**108,378**	**216,755**	**325,133**	**113,797**	**227,593**	**341,390**
Longevity	1,013	2,027	**3,040**	0	0	**0**	0	0	**0**
Fringe Benefits	23,665	47,330	**70,995**	27,407	54,815	**82,222**	28,778	57,555	**86,333**
Total Personnel	**143,959**	**287,918**	**431,877**	**135,785**	**271,570**	**407,355**	**142,574**	**285,149**	**427,723**
Non-Personnel									
Travel	5,541	11,083	**16,624**	4,417	8,833	**13,250**	4,638	9,275	**13,913**
Software	2,419	4,838	**7,258**	0	0	**0**	0	0	**0**
Books & Journals	138	277	**415**	0	0	**0**	0	0	**0**
Other Supplies	61,173	122,347	**183,520**	127,639	255,278	**382,917**	89,778	179,555	**269,333**
Equipment	1,702	3,403	**5,105**	13,333	26,667	**40,000**	0	0	
Maintenance	2,451	4,902	**7,354**	10,000	20,000	**30,000**	10,500	21,000	**31,500**
Scholarships	8,466	16,931	**25,397**	5,865	11,730	**17,595**	6,158	12,317	**18,475**
Consultants	0	0	**0**	0	0		0	0	**0**
Renovation	0	0	**0**	0	0		0	0	**0**
Insurance, Cont & Sp Svc	24,536	49,072	**73,607**	6,717	13,433	**20,150**	7,053	14,105	**21,158**
Media / Communication	283	566	**849**	0	0		0	0	**0**
Legal, Prof. Fees / Group Arranged Food & Lodging / Commercial Svc / Seminar Conf. Reg.	240	480	**720**	333	667	**1,000**	350	700	**1,050**
Total Non-Personnel	**106,950**	**213,899**	**320,849**	**168,304**	**336,608**	**504,912**	**118,476**	**236,952**	**355,428**
GRAND TOTAL	**250,909**	**501,817**	**752,726**	**304,089**	**608,178**	**912,267**	**261,050**	**522,100**	**783,150**
Revenue									
New State Appropriation		555,602	**555,602**		499,482	**499,482**		522,100	**522,100**
Carryover State Appropriation		54,911	**54,911**		108,696	**108,696**			**0**
New Matching Funds	277,801		**277,801**	249,741		**249,741**	261,050		**261,050**
Carryover from Previous Matching Funds	27,456		**27,456**	54,348		**54,348**			**0**
Total Revenue	**$305,257**	**$610,513**	**$915,770**	**$304,089**	**$608,178**	**$912,267**	**$261,050**	**$522,100**	**$783,150**