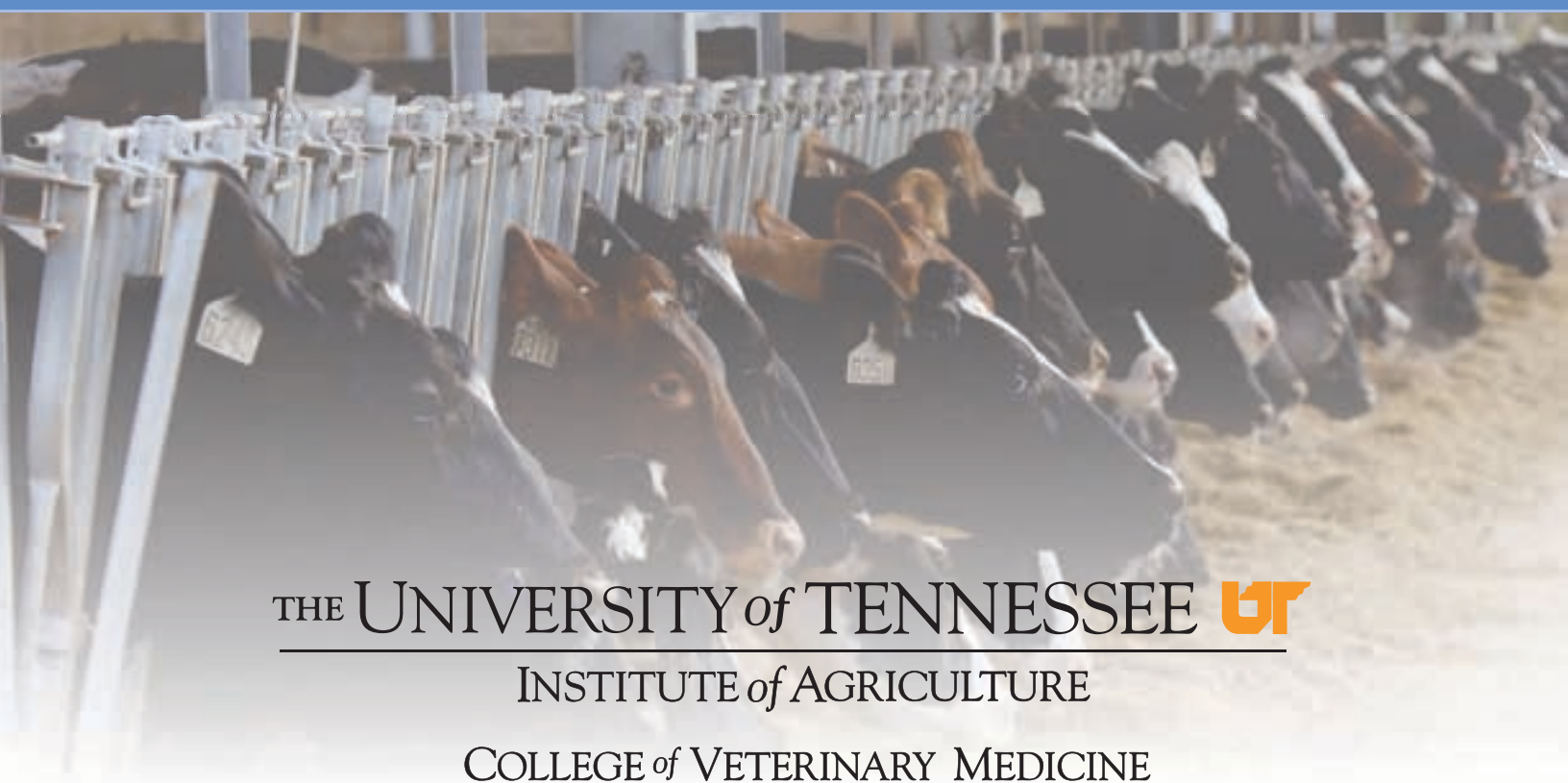




2013 Annual Report

Center of Excellence

in Livestock Diseases and Human Health



THE UNIVERSITY of TENNESSEE 

INSTITUTE of AGRICULTURE

COLLEGE of VETERINARY MEDICINE

Our Mission

- 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
- Develop new strategies for the diagnosis, treatment, and prevention of disease

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

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Message from the Dean

We are pleased to present the 2013 annual report for the Center of Excellence in Livestock Diseases and Human Health. This marks the 30th year the center has been able to make an investment in both (1) new investigators who show professional promise and (2) established investigators for the conception of novel and innovative lines of research.

When the College of Veterinary Medicine proposed the center to Tennessee's state government in 1984, administrators looked to focus on the college's strengths in human health research with comparative models and farm animal health research. For 30 years, we have been able to maintain these strengths, and center faculty continue to strive for answers to difficult yet important research questions related to the center's focus areas.

Within this report, you will see highlights of such faculty research projects funded by the center in fiscal year 2013. During 2013, the center supported the efforts of 12 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. The opening of our new Large Animal Hospitals will further facilitate such research.

Benchmark data are also included for fiscal years 2009–2013. Research funding steadied, and the return on investment, as the ratio of research expenditures to the state appropriation for the center, was 4.1:1.

Center faculty continue to garner national and international recognition for their research and scholarship. During calendar year 2012, center faculty published 51 peer-reviewed articles and gave 45 presentations at regional, national, and international meetings.

Despite increased fiscal challenges faced by our center faculty, we are extremely proud of their efforts and continued success; we hope you enjoy this summary presentation of center activities and accomplishments.



Dr. Jim Thompson, Dean

Center of Excellence

in Livestock Diseases and Human Health

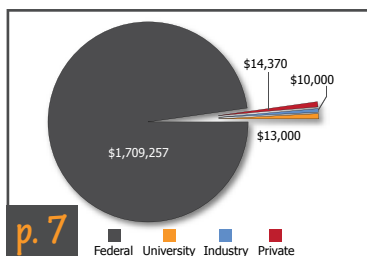
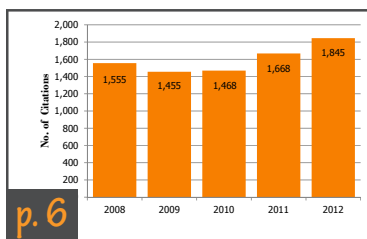


THE UNIVERSITY of TENNESSEE 
INSTITUTE OF AGRICULTURE
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In accordance with the requirements of Title VI of the Civil Rights Act of 1964, Title IX of the Education Amendments of 1972, Section 504 of the Rehabilitation Act of 1973, and the Americans with 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.

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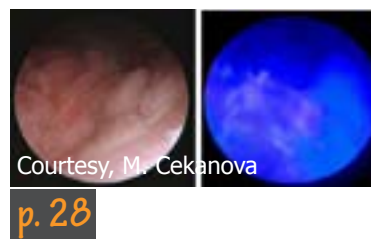
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- 38 Barry Rouse

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Special Thanks

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Emily Dyke

Becky Greene

Kim Rutherford

Kathy Yates

Comparative Summary of Accomplishments

Benchmark	2013 12 faculty	2012 12 faculty
Publications	n (mean)*	n (mean)†
Peer-reviewed articles	51 (4.25)	39 (3.25)
Books or book chapters	0 (0)	2 (0.17)
Abstracts or posters	41 (3.42)	63 (5.25)
Presentations		
International	30 (2.5)	9 (0.75)
National	10 (0.83)	40 (3.33)
State or local	5 (0.42)	14 (1.17)
Research monies		
External funding	\$1,746,627 (\$145,552)	\$2,466,712 (\$205,559)
Research expenditures	\$2,057,499 (\$171,458)	\$2,332,888 (\$194,407)
Return on investment	4.1:1	4.7:1

*Publications and presentations based on 2012 calendar year; research monies based on 2013 fiscal year.

†Publications and presentations based on 2011 calendar year; research monies based on 2012 fiscal year.



L-R: Drs. Hwa-Chain Robert Wang, Amy LeBlanc, Xuemin Xu, and Seung Joon Baek

Accomplishments

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. 26–37).

During the 2012 calendar year, the 12 center faculty each averaged 4 peer-reviewed publications (51 total) and 3 presentations at prestigious national and international meetings (40 total). Figure 1 shows the number of times 2013 center faculty publications have been cited by others over the last six calendar years. These numbers tell us that scientists worldwide have evaluated center faculty work positively and used it to stimulate, validate, and/or support their own work in similar fields. Therefore, citations are indicators of the quality of faculty work.

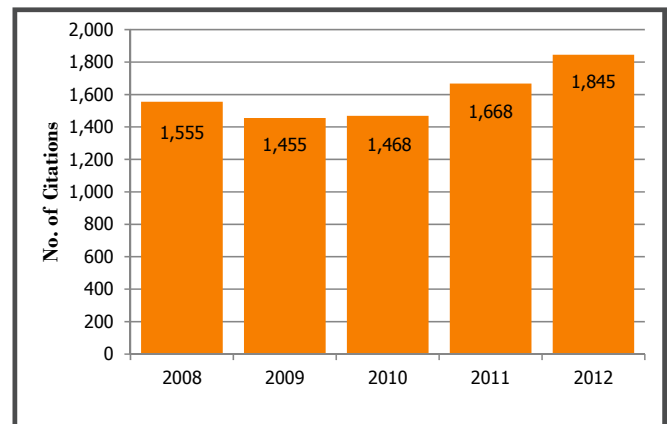


Fig. 1. Number of times 2013 center faculty publications were cited by others from calendar years 2008 to 2012 (excludes self-citations).

Particularly noteworthy articles in 2012 were by Drs. David Brian, Barry Rouse, Hildegard Schuller, and Hwa-Chain Robert Wang. Drs. Brian and Rouse published articles in the *Journal of Virology*. Dr. Rouse's work was also published in the *Journal of Immunology*. Both Drs. Schuller and Wang had articles published in *Carcinogenesis*. All these journals have an impact factor above 5.0. The impact factor is frequently used as a measure of a journal's importance in its field. The higher the number, the more times articles published in the journal have been cited in a particular year. See Publications and Presentations (pp. 40–48) for more details.

External Funding:
\$1,746,627

New Grants:
\$786,471

The return on the state's investment in the center was 4.1:1, calculated as ratio of expenditures from extramural funding to center appropriation. This calculation means that for every \$1 of center funds spent, center faculty returned over \$4 in extramural funding. Extramural funding totaled

\$1,746,627 this year, while expenditures for the year were \$2,057,499.

Figure 2 shows the percentage breakdown of external funding by source. The funding includes a new, multi-year award for Dr. Barry Rouse totaling \$2,464,341 over the course of the project, and new, one-year awards for Drs. Maria Cekanova, Shigetoshi Eda, Stephen Kania, and Amy LeBlanc, totaling \$304,071. See "Research Funded Externally" and "Research Expenditures" on p. 12 for the fiscal year 2013 data summary.

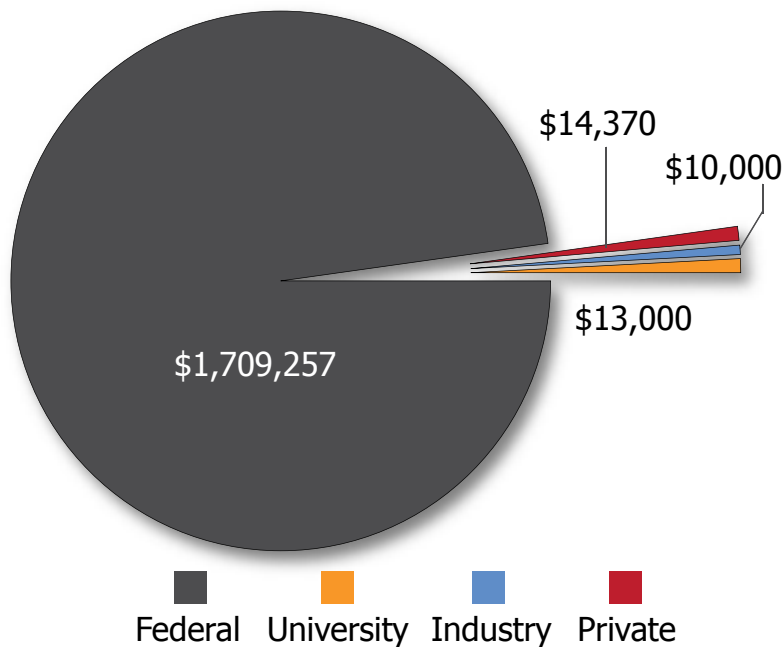


Fig. 2. FY 13 external funding by source.

Total = \$1,746,627.

Introduction

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 and unique role in developing these focused areas of strength in both the University of Tennessee College of Veterinary Medicine (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 has served as director of the center since October 1, 2012, having served as interim director since February 2011. Dr. Stephen Kania chaired the Research Advisory Committee responsible for selecting 2013 funded proposals. Ms. Misty Bailey produces the annual report, and Ms. Kim Rutherford oversees submissions of faculty proposals for funds.



L-R: McEntee, Kania, Bailey, Rutherford

Our Story: 1984-2013



The Center of Excellence for the Study of Livestock Diseases and Human Health, as it was originally called, began operations at the start of the new fiscal year in July 1984 with a \$250,000 grant from the Tennessee Better Schools Program. At the time, it was one of 14 centers established by the Tennessee Higher Education Commission (THEC) and was one of three centers targeted by THEC to have the greatest potential to bring national recognition to Tennessee.

By 1989, THEC had designated the center as “accomplished”; this designation, then earned by only four centers in the university, meant the center had met or exceeded all projected objectives and had achieved the recognition THEC predicted.

This year marks the 30th anniversary for the center, and to commemorate, we asked some of our most frequently center-funded faculty to recall their most proud research accomplishments.

State names center ‘accomplished’

The University of Tennessee College of Veterinary Medicine’s Center for Excellence in Human Health and Livestock Diseases has been designated an “accomplished center” by the Tennessee Higher Education Commission (THEC).

Mastitis in Dairy Cows

Dr. Stephen Oliver (seen on p. 9, top left):

"Center support resulted in the generation of the necessary preliminary data that allowed us to be competitive at the national level. Our research on identification and characterization of *Streptococcus uberis* virulence factors resulted in the discovery of a molecule that we refer to as *Streptococcus uberis* Adhesion Molecule or SUAM. SUAM is a novel bacterial protein involved in the pathogenesis of *Strep. uberis* mastitis. SUAM has several potential applications, including use as an antigen/vaccine for the prevention of *Strep. uberis* mastitis in dairy cows, and use as a therapeutic in the treatment of cows with mastitis.

This discovery resulted in the submission of U.S. Non-Provisional Patent and PCT International Patent applications. SUAM now has patent protection in the United States, several countries in the European Union, Canada, Mexico, New Zealand, Australia, and Brazil. From 2004 to 2011, we received over \$1 million from USDA for research on SUAM projects. We are in deliberations with a commercial partner to continue to develop SUAM technology. The center has been very meaningful to me as a research scientist and has helped move the science forward more expeditiously."

Setting Interpretive Standards for Methicillin-Resistance

Drs. David Bemis (R) & Stephen Kania (L):

"Center-sponsored work led to a change in the way the Clinical Laboratory Standards Institute (CLSI) interprets methicillin resistance in *Staphylococcus pseudintermedius* isolated from dogs. The CLSI is an internationally-recognized organization that sets standards and publishes guidelines for all aspects of diagnostic laboratory operations. As a result of our center work, the CLSI document outlining susceptibility testing guidelines was altered to enable detection of a considerable number of strains that had previously tested negative due to the original interpretive criteria being based on *S. aureus*."



Discovering Ways to Better Treat Coronaviruses in Animals

Dr. David Brian (seen on p. 9, top right):

"My work on coronaviruses began when I arrived at the UTCVM in 1976, a time when coronaviruses were known as serious pathogens in domestic animals but minor pathogens in humans

(common cold, mostly); little was known about how coronaviruses replicate inside cells. Our goal was to identify targets for new therapeutic agents. We tackled coronavirus replication by studying the pig and cow coronaviruses that belong to separate coronavirus subgroups. Our major contribution came in 1989: the discovery that coronavirus messenger RNAs, unlike those in other known viruses, behave (in part) as mini replicons and undergo rapid amplification. Rapid amplification aids survival of this virus with the largest known RNA genome. This discovery was first presented at an International Coronavirus Conference in Cambridge, England, and was later published in the *Proceedings of the National Academies of Science U S A* (Coronavirus subgenomic minus-strand RNAs and the potential for mRNA replicons. 1989;86:5626–30). The finding changed the working model for how virologists think coronaviruses replicate and identified new potential target sites for blocking virus replication. Today, we know that there are several serious veterinary and human coronavirus pathogens. These include the recently-discovered SARS and MERS coronaviruses, which are zoonotic and harbored in bat reservoirs. Our lab remains focused on identifying potential targets for therapeutic agents against coronaviruses.”

Bovine Viral Diarrhea

Dr. Leon Potgieter

Dr. Potgieter was frequently funded by the center immediately after its inception in 1984. From 1995 to 2001, he was appointed as the assistant director of the center. When asked about the role the center played in his research, he talked about how “BVD had a primary role in enhancing the severity of other respiratory infections in cattle. The Center of Excellence helped with equipment and supplemental funding to continue our research program for the development of a ‘safe’ vaccine for the disease. Some of our COE funding went toward purchasing the first PCR [polymerase chain reaction] machine in a UT campus laboratory. I went to the Keystone Symposium in Colorado to learn PCR technique and then to a conference in North Carolina to learn DNA sequencing. Now, PCR is a necessity in every lab.”

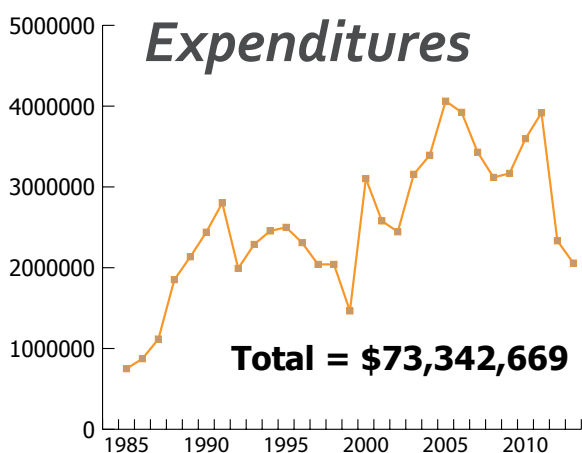


Fig. 3. Expenditures from extramural funding since the inception of the center.

COE Faculty Have Published:
2,443 peer-reviewed articles
303 books or book chapters

Presented:
3,339 talks or posters

Funding & Expenditures

Research Funded* Externally FY 2013

Investigator	Federal	Industry	Foundation/ Private	University	Totals
Cekanova, Maria	\$200,000			\$13,000	\$213,000
Cui, Mei-Zhen	\$347,480				\$347,480
Eda, Shigetoshi			\$3,700		\$3,700
Kania, Stephen		\$10,000	\$10,670		\$20,670
LeBlanc, Amy	\$79,701				\$79,701
Rouse, Barry	\$801,683				\$801,683
Schuller, Hildegard	\$280,393				\$280,393
Totals	\$1,709,257	\$10,000	\$14,370	\$13,000	\$1,746,627

*Represents FY 2013 receipts for active grants

Research Expenditures FY 2013

Investigator	Federal	Industry	Foundation/ Private	University	Totals
Baek, Seung Joon				*\$34,442	\$34,442
Brian, David	\$277,902				\$277,902
Cekanova, Maria	\$3,420		\$16,133	\$7,258	\$26,811
Cui, Mei-Zhen	\$286,898				
Eda, Shigetoshi			\$1,128		\$1,128
Kania, Stephen		\$10,000	\$24,912		\$34,912
LeBlanc, Amy	\$78,657				\$78,657
Rouse, Barry	\$687,985				\$687,985
Schuller, Hildegard	\$469,570				\$469,570
Xu, Xuemin	\$114,982		\$44,210		\$159,192
Totals	\$1,919,414	\$10,000	\$86,385	\$41,700	\$2,057,499

*Federal flow-through (National Institutes of Health)

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.

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.

Research Advisory Committee's Three Main Criteria for Funding

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

Bridge funds

The center provided \$92,235 in bridge funding to support Dr. Madhu Dhar and Dr. Cristina Lanzas while they pursue additional sources of external funding.

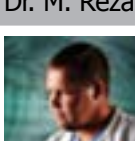
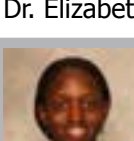
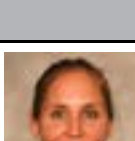
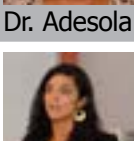


In fiscal year 2013, Dr. Dhar was funded by Morris Animal Foundation and the Physician's Medical Education and Research Foundation. She had five publications published in peer-reviewed journals, including three articles in the *FASEB Journal*, which has an impact factor of 5.704. Her research focuses on harvesting and using adult equine stem cells in horse rehabilitation and healing.



Dr. Lanzas' research interests include developing and applying mathematical and epidemiological approaches to study the dynamics and control of infectious diseases caused by zoonotic and gastrointestinal pathogens in human and animal populations. She published in *PLoS One* in calendar year 2012. *PLoS One* is one of the oldest and most well-respected open-access journals. Open-access journals provide free content to all readers rather than charging subscription fees.

The center provided \$138,333 in start-up funds for 13 junior faculty members to secure additional external funding in 2013.

Start-up Funds					
Faculty Member	Area of Research	\$ Amount	Faculty Member	Area of Research	\$ Amount
Biomedical & Diagnostic Sciences			Small Animal Clinical Sciences		
 Dr. Richard Gerhold	Wildlife parasitology, including <i>Trichomonas gallinae</i> in birds	25,000	 Dr. Erica Fields	Radiation oncology, including optimizing contrast-enhanced, multidetector abdominal CT in sedated canine patients	1,250
Large Animal Clinical Sciences					
 Dr. Marc Caldwell	Production animal medicine, infectious diseases of livestock	8,333	 Dr. Sara Frazier	Oncology, including effects of pioglitazone, rosiglitazone, carboplatin, mitoxantrone, and doxorubicin to treat canine cancers	24,500
 Dr. Karen McCormick	Large animal clinical medicine, including testing blood coagulation variation in horses	5,000	 Dr. Sophy Jesty	Cardiology, including heart disease in dogs, cats, and horses and specifically arrhythmias in the exercising animal	5,000
 Dr. M. Reza Seddighi	Pharmacokinetics/dynamics of anesthetic drugs with emphasis on the potency of inhalational anesthetics	10,000	 Dr. Nathan Lee	Palliative care for cancer patients; developing new radiation therapy protocols for small animal patients with various tumor types	5,000
 Dr. Brian Whitlock	Large animal field service medicine and food animal theriogenology (reproduction medicine)	25,000	 Dr. Elizabeth May	Bacterial skin and ear infections, staphylococcal bacteria and mechanisms of resistance, hair coat disorders in Schipperkes	5,000
			 Dr. Adesola Odunayo	Emergency and critical care	5,000
 Dr. Katie Tolbert	Feline gastrointestinal disease as a translational model for human disease	15,000	 Dr. Valeria Tanco	Large and small animal theriogenology	2,500

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 in 2013, the center funded tests and certifications for two fume hoods in research laboratories in the college (\$200). Such tests ensure that faculty and staff who use these hoods are safe from harmful fumes and other potentially dangerous airborne substances; they also protect research cells by preventing their contamination. A total of \$1,103.16 was paid for carbon dioxide gas to be used in incubators in the Tumor Biology Laboratory, as well as for liquid nitrogen to maintain frozen cells. Faculty members Dr. Madhu Dhar, Dr. Maria Cekanova, and Dr. Casey LeBlanc benefit from this laboratory equipment.

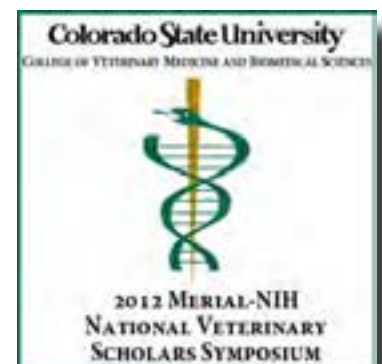
\$2,903 helped fund equipment, service contracts, and supplies

Various supplies for the Tumor Biology Laboratory totaled \$1,600; however, cell sorter services provided by laboratory manager Nancy Neilsen for numerous faculty throughout the college and university earned the center \$2,025 in income to more than offset the cost of supplies.

Training

To keep faculty, staff, and students abreast of new research and techniques and to increase our competitiveness in obtaining extramural funding, the center sponsors training and continuing education opportunities.

Dr. Stephen Kania received center funds to travel with two students in the Summer Student Research Program to present their work at the 2012 Meriel-NIH Veterinary Scholars Program Symposium in Ft. Collins, CO, at Colorado State University. By attending this meeting, Dr. Kania was able to make an essential contact with a National Institutes of Health director for sponsored training programs, and as a direct result, drafted two applications to support pre- and post-doctoral students. If one of these is awarded, the entire research enterprise at the UTCVM will be enriched.



In further support of the Summer Student Research Program, the center provided meals (\$137.93) during the student/faculty matching session, as well as during one of the students' professional development sessions.

Ms. Rachel Dutkosky, one of the students in the 2012 Summer Student Research Program, received travel funds (\$688) to present a poster at the American College of Veterinary Pathology Conference in December 2012. The poster was a result of her work with Dr. Marcy Souza and Dr. Kim Newkirk: evaluating the effectiveness of a subcutaneous implant to treat white nose syndrome in captive bats.

Likewise, Mr. Christopher Lee Emery, also a 2012 summer student, presented his work at the Association of Avian Veterinarians annual conference, which took place in August 2012 in Louisville, KY. Emery won the Student Manuscript Competition, which funded his conference registration. The center provided other travel-associated costs (\$664.10). Emery's work was on the pharmacokinetics of nebulized terbinafine in Hispaniolan Amazon parrots.

Center faculty member Dr. Maria Cekanova met with Dr. Lawrence Marnett's cancer research group at Vanderbilt University to discuss current progress and future studies for clinical development of fluorocoxib use in humans and domestic animals. The meeting included Dr. Christopher Contag from Stanford University's School of Medicine and Dr. William C. Kruka, executive vice president for corporate development and imaging business head unit at Perkin Elmer. Dr. Cekanova received center travel support (\$600) to give a presentation about her progress using fluorocoxib A in dogs and cats with cancers. *Cekanova is shown at right with Dr. Joseph Bartges using the technique on a client-owned cat. >>>*



Dr. Cekanova was also partially funded by the center to present a poster at the Veterinary Cancer Society's annual conference in Las Vegas, NV.

The center also provided \$1,503 for a tuition waiver for one student in the Comparative and Experimental Medicine graduate program for 3 hours of coursework in summer 2013.

Comparative & Experimental Medicine and Public Health Research Symposium



The center was a major sponsor of the Comparative & Experimental Medicine and Public Health Research Symposium, which brought together researchers from 17 different departments for a 2-day-long event that included special seminars on diagnosis of and outbreak investigations into fungal infections, translational disease intervention strategies, and one health.

Featured was Dr. Ralph Tripp (above, center) of the Department of Infectious Diseases at the University of Georgia College of Veterinary Medicine. Also featured were Dr. Marion Kainer of the Tennessee Department of Health and Dr. David Bemis, professor at the UTCVM and center co-investigator. Ms. Channa Palmer, lead university recruiter for the Oak Ridge National Laboratory, gave an overview of postdoctoral opportunities available at ORNL. The symposium culminated with an awards banquet and guest speaker Dr. Marcy Souza, known for her research on infectious and zoonotic diseases of exotic pets and wildlife.

Fifty-five researchers from the Institute of Agriculture presented talks, including heavy participation by members of the Biomedical and Diagnostic Sciences and Small Animal Clinical Sciences departments. They were among 76 new scientists to present, and at the end of the 2 days, the institute was able to boast seven winners of travel awards.

The center sponsored five of the 2012 award winners to present at four national scientific meetings during fiscal year 2013. Dr. Ricardo Videla presented at the American Association of Immunologists meeting in Honolulu, HI. Dr. Tinting Xu traveled to San Antonio, TX, to present at the 52nd Annual Meeting of the Society of Toxicology. Dr. Maria Cekanova went to Las Vegas, NV, to present a poster and oral presentation to the Veterinary Cancer Society, and Dr. Eman Anis presented at the Conference of Research Workers in Animal Disease in Chicago.

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. It remains an entirely unique, cross-campus, cross-disciplinary venue for presenting new research data on the Knoxville campuses of the university.

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

Dissemination of Research

Faculty are encouraged to share their research via speaking engagements for professional groups, community groups, and civic groups. A complete list of faculty publications and presentations for the 2012 calendar year can be found in the Publications and Presentations section (pp. 38–49).



Through scientific conferences, Center of Excellence faculty share their research with a worldwide audience. The map above showcases where their research was presented in 2012.

Dissemination of Research

In addition to faculty speaking engagements, 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 UTCVM has a recurring spot on local NBC affiliate **WBIR, Channel 10's** "Live at Five at Four" news show. Within the last 2 years, UTCVM has also launched a **Facebook** page and a new **VolVet Connect** alumni e-newsletter. At the end of July 2013, the Facebook page had 3,122 "likes" from individuals from seven different countries. Page administrators post clinical and research information for users. VolVet Connect contains items of note aimed at DVM alumni, including UTCVM research news, and continuing education and networking opportunities. UTCVM is also on **Twitter** (1,362 followers), has a **YouTube** channel with 65 subscribers and 3,062 views since its inception in 2012, and a **Pinterest** presence with 68 followers.



Our researchers are also occasionally featured in **Tennessee Alumnus** and **Tennessee Land, Life & Science**, tri-annual and bi-annual magazines produced by the University of Tennessee and the UT Institute of Agriculture, respectively. The center itself was featured in the spring 2012 issue of Tennessee Land, Life & Science (see Fig. 4).

The 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.



Fig. 4. The center was featured in the spring 2012 issue of Tennessee Land, Life & Science, a bi-annual magazine produced by the UT Institute of Agriculture.

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 once again helped provide opportunities for veterinary students to do research at the UTCVM.

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.

\$10,000 from Merial helped fund the Summer Student Program

The center funded 19 student salaries. A grant from Morris Animal Foundation funded one student. Dr. Stephen Kania, a center faculty member, coordinated the program along with Dr. Linda Frank; they received a \$10,000 grant

from Merial to help support the program. From Merial, four additional student salaries were funded in summer 2013; these students also received travel funds from Merial to present their work as posters at the 2013 Merial-NIH Veterinary Scholars Program Symposium in East Lansing, MI, at Michigan State University. Three center-sponsored students attended the symposium, as well (see below). From 2008–2012, 30 peer-reviewed publications were produced as a result of past summer students' work.

To maximize student participation, the program is open to both center and non-center faculty. During fiscal year 2013, five junior members participated in the program. The center will continue to encourage participation of its faculty.



L-R: Jose Grenet, Marissa Torre, Jessica Chin, Patrick Reilly, Kimberly Pompo, Brooke Giff, and Erin Felty at the 2013 Merial-NIH Veterinary Scholars Program Symposium. Photo: Courtesy, S. Kania

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

Victoria J. Balvin, 2nd year. **Faculty Mentor:** Dr. Brian Whitlock.

Bethesda, OH. BS in pre-veterinary studies and animal science from the University of Findlay, Findlay, OH. **Summer Project:** Studied the effects of betahydroxy-butyrate on luteinizing hormone in wethers. **Career Interests:** Food animal and equine medicine, field service.

Jessica Chin, 2nd year. **Faculty Mentor:** Dr. Angela Witzel.

Brooklyn, NY. BS in biology from Trinity College, Hartford, CT. **Summer Project:** Retrospective study of dual absorptiometry x-ray (DEXA) scan data, which differentiates between bone mineral content, fat body mass, and lean body mass. Goal was to determine what portion of excess body weight in overweight and obese dogs and cats can be attributed to fat body mass versus lean body mass. Data will be useful in calculating energy needs and drug dosages for overweight pets because fat body mass does not metabolize drugs. **Career Interests:** Small animal or exotic medicine.

Emily Credit, 3rd year. **Faculty Mentor:** Dr. Julie Albright.

Pittsford, NY. BA in organismal biology from Keuka College, Keuka Park, NY. **Summer Project:** Compiled data on how puppies develop and their use of different toys in play behavior. **Career Interests:** Small animal medicine.

Mary Dell Deweese, 3rd year. **Faculty Mentor:** Dr. Karen Tobias.

Germantown, TN. Studied animal science at the University of Tennessee, Knoxville, TN. **Summer Project:** Predicting tracheal diameter using radiographs. Success would enable surgeons to obtain an ideal stent size pre-operatively, increasing survival time of dogs undergoing surgery to treat tracheal collapse. **Career Interests:** Surgery.

Carrie Dobey, 2nd year. **Faculty Mentor:** Dr. Richard Gerhold.

Lawrenceville, GA. MS in wildlife biology from the University of Tennessee, Knoxville, TN; BS in biology from North Georgia College, Dahlonega, GA. **Summer Project:** Helped validate a recently-developed PCR test to detect *Parelaphostrongylus tenuis* (brain worm) in domestic and wild hooved animals. Evaluated which lesions can be used to detect *P. tenuis* DNA when the worm itself is not present. **Career Interests:** Pathology and small animal surgery.

Blake Everett, 2nd year. **Faculty Mentors:** Dr. Agricola Odoi and Dr. David Bemis.

Lewisburg, TN. BS in animal science from Middle Tennessee State University, Murfreesboro, TN. **Summer Project:** Compared three antibiotic-impregnated disks both singly and in combination to detect methicillin resistance in *Staphylococcus pseudintermedius* in dogs. **Career Interests:** Mixed-animal practice and surgery.

Sloane Everett, 2nd year. **Faculty Mentor:** Dr. Rebecca Wilkes.

Collierville, TN. BS in biological sciences from the University of Missouri, Columbia, Missouri. **Summer Project:** Used PCR to analyze genomic differences between *Tritrichomonas foetus* in cats vs. the same species in cattle. Evaluated the genetic differences between three strains of *Trichimonas gallinae* from band-tailed pigeons. **Career Interests:** Laboratory animal medicine, pathology, research.

Erin Felty, 2nd year. **Faculty Mentors:** Dr. Angela Witzel and Dr. Nancy Howell.

Collierville, TN. BS in biology from the University of Tennessee at Chattanooga, Chattanooga, TN. **Summer Project:** Evaluated the quality of



veterinary nutrition programs at other veterinary colleges by surveying recent graduates' perceived level of adequacy in nutrition knowledge, and gathered information about nutrition curriculum and requirements at U.S. veterinary schools.

Career Interests: Feline medicine, small animal internal medicine, nutrition, and pathology.

Jose Grenet, 2nd year. **Faculty Mentor:** Dr. Edward Ramsay.

Memphis, TN. BA in neuroscience and Latin American studies from Vanderbilt University, Nashville, TN. **Summer Project:** Studied epidemiological risk factors associated with red panda neonatal mortality to provide recommendations for captive red panda husbandry in order to improve neonatal survival. **Career Interests:** Conservation medicine, international medicine, zoo and wildlife medicine.

Brooke Griff, 2nd year. **Faculty Mentor:** Dr. Debra Lee Miller.

Virginia Beach, VA. BS in zoology, North Carolina State University, Raleigh, NC. **Summer Project:** Evaluated the gray whale epidermis microscopically and measured mercury, selenium, and stable isotope levels to determine the effect of their different levels on the epidermis. **Career Interests:** Zoological and wildlife medicine.

Benton Harvey, 3rd year. **Faculty Mentor:** Dr. Brian Whitlock.

Nashville, TN. BS in neuroscience, College of William & Mary, Williamsburg, VA. **Summer Project:** Collected over 800 blood samples from beef cattle in each Southeastern state to complete a survey of anaplasmosis and to complete a write-up of data from PCR and cELISA tests. **Career Interests:** Veterinary mission work in Central or South America.

Lauren Henderson, 2nd year. **Faculty Mentor:** Dr. Richard Gerhold.

Hendersonville, TN. BS in animal science from the University of Tennessee, Knoxville. **Summer Project:** Collected samples and extracted DNA to analyze heart tissue samples of raccoons, opossums, and feral hogs in southern Appalachia for *Toxoplasma gondii* and *Trypanosoma cruzi*. **Career Interests:** Wildlife rehabilitation and conservation medicine, public health, international medicine, zoonotic disease research.

Nicole Laia, 3rd year. **Faculty Mentor:** Dr. Jacqueline Whittemore.

Morgan Hill, CA. BS in biochemistry from California Polytechnic State University, San Luis Obispo, CA. **Summer Project:** Determining if administration of a probiotic helps prevent antibiotic-associated diarrhea in cats being given oral clindamycin. **Career Interests:** Small animal practice.

Jacob Malugin, 2nd year. **Faculty Mentor:** Dr. Valeria Tanco.

Culleoka, TN. BS in veterinary science from the University of Tennessee at Martin, Martin TN. **Summer Project:** Evaluated the effects of gonadotropin-inhibitory hormone on luteinizing hormone surge and ovulation in dairy heifers.

Career Interests: Mixed-animal practice (50/50 small and large animals), reproduction, and surgery.



Brooke Griff

Courtesy, S. Kania

Kelly Miller, 2nd year. **Faculty Mentor:** Dr. David Bemis.

Kingsport, TN. BS in animal science from the University of Tennessee, Knoxville. **Summer Project:** Studied antimicrobial effects of Yerba mate tea extracts on methicillin-resistant staphylococci obtained from samples submitted to the UTCVM. Concentrations of tea extract as low as 20 mg/mL successfully killed all strains of bacteria tested. **Career Interests:** Dermatology, radiology, feline internal medicine, community practice.

Kristen Niemann, 2nd year. **Faculty Mentor:** Dr. Rebecca Wilkes.

Youngsville, NY. BA in biology from Elmira College, Elmira, NY. **Summer**

Project: Evaluated several different efficient delivery methods for the treatment of feline herpes using RNA interference.
Career Interests: Small animal medicine and research.

Kimberly Pompo, 2nd year. **Faculty Mentor:** Dr. Rebecca Trout-Fryxell.
Syracuse, NY. BS in biology with medical concentration from Le Moyne College, Syracuse, NY. **Summer Project:** Collected ticks from UT Research and Education Centers across the state to determine the distribution of *Anaplasma marginale* within ticks. Bovine anaplasmosis has emerged in East Tennessee. It is an often fatal disease of humans and ruminants (including cattle). **Career Interests:** Mixed-animal practice, zoo or wildlife medicine.

Brianna Potter, 3rd year. **Faculty Mentor:** Dr. Sophy Jesty.
Ramona, CA. BS in general biology from the University of California, San Diego, La Jolla, CA. **Summer Project:** Hypothesized that long-term, intense exercise can cause arrhythmias in the heart. Rarely, ventricular arrhythmias can cause sudden cardiac death in high-level athletes. Performed heart pacing protocols by exercising dogs on a treadmill. **Career Interests:** Cardiology specialization.

Patrick Reilly, 2nd year. **Faculty Mentor:** Dr. Debra Lee Miller.
Collierville, TN. BAS in biology from the University of Memphis, Memphis, TN. **Summer Project:** Tested for differences in two ranavirus isolates among four host wood frog populations, as well as tested whether individual tadpoles infected with ranavirus can act as a superspreader. **Career Interests:** Wildlife research.

Mike Robbins, 3rd year. **Faculty Mentor:** Dr. Martha Cline.
Medina, OH. BS in pre-veterinary medicine from the University of Findlay, Findlay, OH. **Summer Project:** Analyzed how different water bowls affect drinking habits in cats and if the bowl type makes a difference in urine concentration and the likelihood of certain stone formation. **Career Interests:** Small animal nutrition, academic medicine.

Shannon Shuttle, 2nd year. **Faculty Mentor:** Dr. Madhu Dhar.
New Ipswich, NH. BS in biology from the University of Southern Maine, Portland/Gorham, ME; studies in biology at Elmira College, Elmira, NY. **Summer Project:** Analyzed data from skin biopsy samples for a wound healing study in horses. Assisted with adult stem cell injections and biopsy sampling. **Career Interests:** Mixed-animal practice, incorporating research.

Alicia Thomas, 3rd year. **Faculty Mentor:** Dr. Olya Smrkovski.
Midlothian, VA. BS in biochemistry from Virginia Tech University, Blacksburg, VA. **Summer Project:** Retrospective study on canine hemangiosarcoma. Collected specific information from patient medical records. Wrote and submitted an abstract for the Veterinary Oncology Conference. **Career Interests:** Small animal private practice, oncology or surgery residency.

Marissa Torre, 2nd year. **Faculty Mentor:** Dr. Stephen Kania and Dr. Linda Frank.
Inwood, NY. BS in biology from Binghamton University in Binghamton, NY. **Summer Project:** Studied the diagnostic efficacy of real-time PCR on dermatophytosis. Extracted DNA from feline samples and tested them via real-time PCR and then compared the results to the gold standard, which is fungal culture, for each of the samples. **Career Interests:** Private practice, small animal medicine internship.



Courtesy, S. Kania

Five-Year Benchmark Data

**External Funding by Source
(FY 09–13)**

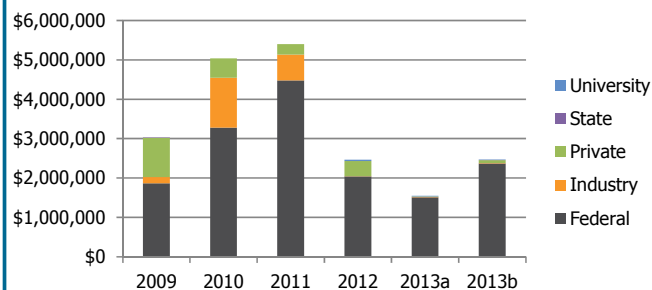


Fig. 5. External research funding by fiscal year. Column 2013b shows FY 13 funding from investigators supported by the center from FY 10–13.

**External Funding by Source
(FY 09–13)**

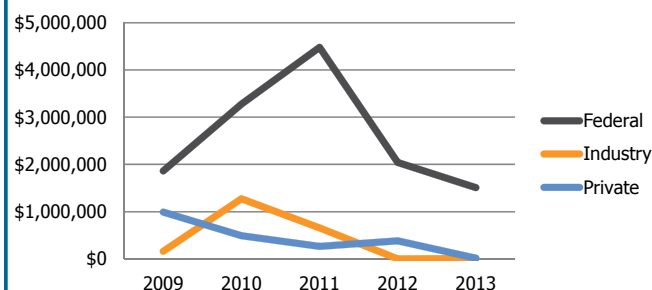
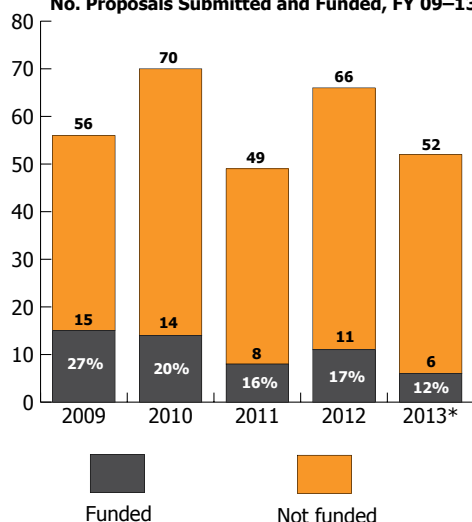


Fig. 6. External research funding from the three major sources of fiscal year receipts.

No. Proposals Submitted and Funded, FY 09–13



Over the past 5 years, center faculty have submitted 293 extramural grant proposals. Of those, 54 have been funded, and eight await decisions by the funding agencies. The 5-year funding rate for center faculty-submitted proposals is 18% (Fig. 7). This success rate is in line with

Fig. 7. Number of proposals submitted by center faculty and success rate for fiscal years 2009 to 2013. *Eight proposals are still awaiting decision by the funding agency.

Productivity among center faculty has been stable during the last 5-year period. From 2009-2013, center faculty published 255 articles in peer-reviewed journals and gave 207 presentations at national and international meetings.

Total research funding was down from \$2.5 million in 2012 to \$1.75 million in 2013 (Fig. 5); this downturn is a direct result of decreased federal support for our nation's research efforts and increasing competition for these diminishing funds. Figure 6 shows federal funding from 2009 to 2013.

It is also important to note that center support may not garner extramural funding in the same year, potentially requiring years for the necessary preliminary studies to mature, and requiring additional time for the application cycle. For instance, when considering external research funding for 2013 obtained by investigators supported by the center during the previous 3 years, and not just 2013 (Fig. 5), it is apparent that such funding for these most recently supported faculty was considerably higher.

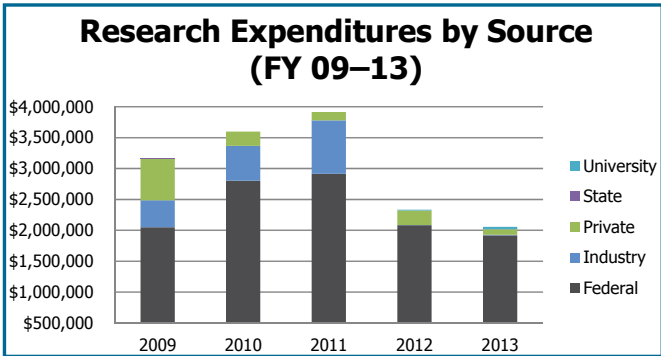


Fig. 8. Research expenditures by fiscal year.

the overall National Institutes of Health success rate for the same time period (17.6%).

Expenditures per faculty member were \$171,458 in FY 2013. Over the past 5 years, the mean expenditure amount per faculty member has been \$215,948. The 5-year average return on the state’s investment in the center is 5.5:1, the ratio of research expenditures to the state’s appropriation. For comparison, benchmark data from 2009-2013 are summarized in Figs. 5–8.

Benchmark Summary (2009-2013)

Average refereed articles per faculty member: 4

Federal funding total: \$11,769,436

Average return on investment: 5.54:1

The center successfully endured several years of sluggish federal funding and is poised to advance with an even greater commitment to livestock and human health. This year (FY14) the center will expend approximately \$204,088 to fund 11 projects. In addition, the center will continue to support core facilities and contribute to the purchase of essential research software and equipment. Already, 2014 center faculty have secured approximately \$375,000 in external funding.

In recent years, the center has emphasized comparative medicine and human health and has contributed significantly to innovation and scientific literature in these areas. In fact, center faculty are responsible for a large proportion of federal biomedical research funds granted across all Knoxville campuses of the University of Tennessee, in particular those funds from the National Institutes of Health. While these programs are anticipated to continue and grow with center support, we are also looking forward to a larger emphasis on livestock health research to bring our agricultural mission into greater focus. With the opening of both a new Equine Hospital and a new Farm Animal Hospital, the College of Veterinary Medicine is poised to be an academic and professional leader in the study of livestock infectious disease, tissue repair, and reproductive health. In addition, the research emphasis of the newly-hired department head in the UTCVM Large Animal Clinical Sciences Department, Dr. David Anderson, will ensure our faculty actively seek opportunities to positively influence livestock research.



The Equine Hospital, half of UTCVM's new Large Animal Hospital, opened in spring 2013. The Farm Animal Hospital opened in fall 2013.

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 nearly 80 presentations at the 2013 symposium with participants representing 17 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.

Additionally, we 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.



Dr. Seung Joon Baek

Associate Professor, Biomedical and Diagnostic Sciences

PhD, University of Maryland

6 refereed publications in 2012

327 article citations in 2012

In addition to center funds, Dr. Baek's research is supported by the University of Maryland (National Institutes of Health flow-through).

Co-investigator: Dr. Robert Donnell

Ways to Prevent and Treat Colorectal Cancer

Colorectal cancer is the third-most common cancer in the United States, and it is the third deadliest, with more than 140,000 new cases each year. Obesity and chronic inflammation may increase the risk of colon cancer.

Nonsteroidal anti-inflammatory drug activated gene-1 (NAG-1) is a gene that exhibits anti-inflammatory, anti-obesity, and anti-tumorigenic activities. How this gene accomplishes these activities is poorly understood and is the subject of Dr. Baek's research.

Dr. Baek's preliminary data suggest that NAG-1 is somehow linked to a signaling pathway that has already been determined to play an important role in obesity/inflammation-related colorectal cancer. By changing the way the body expresses NAG-1, this pathway—termed TGF-beta signaling—may also be altered. By manipulating these potentially connected processes, we can become one step closer to finding a way to prevent or treat colorectal cancer.



Dr. Maria Cekanova

Research Assistant Professor, Small Animal Clinical Sciences

MS, RNDr, PhD, University of Pavol Jozef Safarik, Slovakia

1 refereed publication in 2012

66 article citations in 2012

In addition to center funds, Dr. Cekanova's research is supported by the Winn Feline Foundation, The Physician's Medical Education and Research Foundation, UT-Battelle–Oak Ridge National Laboratory, and Vanderbilt University Medical Center.

Co-investigators: Drs. Lawrence Marnett & Jashim Uddin, Vanderbilt University; Drs. Joseph Bartges & Alfred Legendre

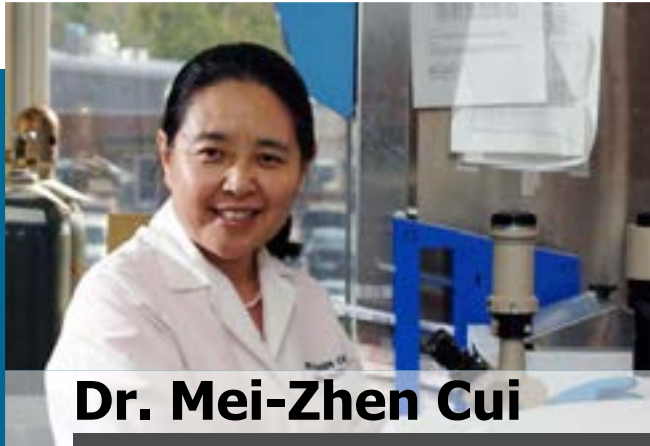
Early Bladder Cancer Detection

Like people, as dogs age, their risk for developing cancer increases. The early detection of cancer is imperative for diagnosis and treatment of human and canine patients to increase survival and quality of life. In her study, Dr. Cekanova is evaluating a new optical imaging agent, fluorocoxib A, for use in detecting cyclooxygenase-2 (COX-2)-expressing, naturally-occurring urinary bladder tumors in dogs as a model for human cancers.

Fluorocoxib A accumulates in tumors and generates fluorescence, which can then be used to detect the tumors during endo/cystoscopy, a minimally-invasive procedure that allows clinicians to examine the bladder, urethra, colon, small intestine, esophagus, mouth, and nose.

Results from this pre-clinical study will improve the identification of COX-2-expressing tumors in dogs and have an immediate veterinary application; the results can then be translated for use in humans, who will develop over a million new cases of cancer in 2013 in the United States alone.

The dual images in the Table of Contents show fluorocoxib A uptake in tissues during a cystoscopy procedure in a dog.



Dr. Mei-Zhen Cui

Professor, Biomedical and Diagnostic Sciences

PhD, Tokyo Institute of Technology, Japan

4 refereed publications in 2012

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

Co-investigator: Dr. Stephen Kania

Using Foam Cells to Fight Atherosclerosis

Atherosclerosis, a chronic inflammatory disease, results in part from the accumulation of modified lipoproteins in the arterial wall and formation of lipid-laden "foam cells." These foam cells surround fatty deposits (usually cholesterol) on blood vessel walls and help form plaques (build-ups).

Lysophosphatidic acid (LPA) is abundant in atherosclerotic plaques, and Dr. Cui's research group recently discovered that LPA helps induce foam cell formation. Understanding how LPA mediates foam cell formation is the focus of her current investigation.

Because LPA regulates a range of physiologic and pathologic processes, it is emerging as a target for a new class of therapeutics for cardiovascular disease. Dr. Cui's research is the first step in developing new ways to treat atherosclerotic lesions and thus prevent unnecessary deaths from heart attacks.



Professor, Biomedical and Diagnostic Sciences

PhD, University of Florida

4 refereed publications in 2012

178 article citations in 2012

In addition to center funds, Dr. Kania's research is supported by the American Kennel Club Canine Health Foundation, Winn Feline Foundation, and Merial Limited.

Co-investigator: Dr. David Bemis

Host Immunity to *Staphylococcus pseudintermedius*

Staphylococcus pseudintermedius is the primary cause of pyogenic skin infections in dogs and is responsible for numerous other canine infectious diseases. The resistance to multiple classes of antibiotics that has developed throughout our geographic region (estimated at 30% by Dr. Kania's group) has left few therapeutic choices.

Recognizing that conventional antibiotic therapy will no longer be an option, control strategies are shifting to new approaches, like Dr. Kania's project to determine how dogs' immune systems fight *S. pseudintermedius* and reveal *S. pseudintermedius* vulnerabilities toward the long-term goal of developing new, effective treatments.

These results will translate to human medicine since the problems encountered in dogs with *S. pseudintermedius* are analogous to those seen with *S. aureus* in humans.

The red petri dish image in the Table of Contents shows *Staphylococcus pseudintermedius* growth.

Stress and Pancreatic Cancer



Dr. Hildegard Schuller

Distinguished Professor, Biomedical and Diagnostic Sciences

PhD, College of Veterinary Medicine, Hannover, Germany; DVM, Justus Liebig University, Giessen, Germany

10 refereed publications in 2012

323 article citations in 2012

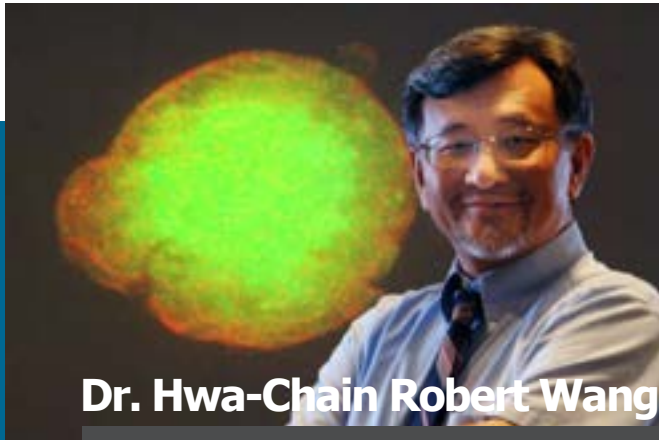
In addition to center funds, Dr. Schuller's research is supported by the National Institutes of Health.

Smoking, psychological stress, and alcohol consumption are all known risk factors for pancreatic ductal adenocarcinoma (PDAC). These risk factors simultaneously *sensitize* the nicotinic acetylcholine receptors (nAChRs) that *stimulate* PDAC and *desensitize* the nAChRs that *inhibit* PDAC.

Dr. Schuller's goal is to determine the ways in which this pathologic process works. Her data emphasize the role of two types of molecules on a cell's surface that receive chemical signals from outside the cell. These receptors appear to contribute to PDAC via the activation of multiple signaling pathways by stress neurotransmitters.

Dr. Schuller's results could lead to clinical trials and eventually to improving survival rates of PDAC patients and preventing the development of PDAC in individuals at risk.

Intervening in Obesity-associated Breast Cancer



Dr. Hwa-Chain Robert Wang

Professor, Biomedical and Diagnostic Sciences

PhD, University of Virginia; DVM, National Chung-Hsing University, Taiwan

3 refereed publications in 2012

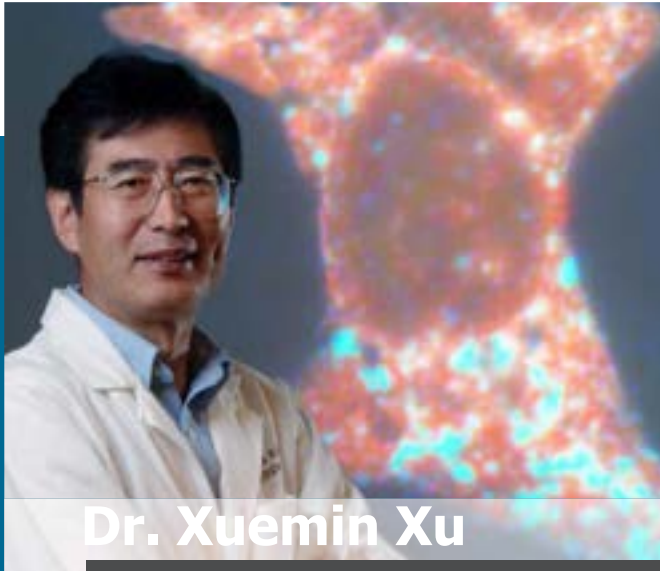
17 article citations in 2012

Co-investigators: Drs. Robert Donnell, Agricola Odoi, and Ling Zhao

During summer 2013, the American Medical Association officially declared obesity a disease. Over 35% of women in the United States are considered obese. Growing evidence indicates a link between obesity and increased risk for developing breast cancer. Sorting through the details of this link and developing methods for intervention are the foci of Dr. Wang's research.

Using an in vitro cell model created in his laboratory, Dr. Wang studies the effects of cumulative exposures of carcinogens B[a]P and PhIP on normal and pre-cancerous breast cells. Exposure to these carcinogens comes from various places, including from smoke (burning wood and cigarettes) and red meat cooked at high temperatures (like grilled meats).

Studies suggest that carcinogens like B[a]P and PhIP may also induce carcinogenesis of obesity-involved cells. Dr. Wang is assessing the ability of certain types of carcinogen-exposed cells to increase the likelihood of breast cells becoming cancerous, as well as agents (like green tea catechins) capable of blocking such cancer progression.



Dr. Xuemin Xu

Professor, Biomedical and Diagnostic Sciences

PhD, Tokyo Institute of Technology, Japan

5 refereed publications in 2012

46 article citations in 2012

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

Co-investigator: Dr. Shelley Newman

Dissecting the Intracacies of Alzheimer's Disease

Apoptosis, a type of cell death regulated by the body, is believed to be a springboard for the neuronal degeneration that leads to Alzheimer's disease. Determining the way this process happens is the focus of Dr. Xu's research.

Dysfunction in mitochondria, the powerhouse of the cell, can lead to apoptosis, and Dr. Xu wants to know how that connection may lead to Alzheimer's disease. In his laboratory, they are studying PSAP, a cellular protein expressed in the mitochondria in neurons in the brain. Dr. Xu has found that when PSAP is overexpressed, cells undergo apoptosis associated with mitochondrial dysfunction.

Therefore, his goal is to determine the pathological role of PSAP in order to lead to new therapeutic targets for treatment and prevention of Alzheimer's disease.



Dr. Raul Almeida

Research Associate Professor, Animal Science

PhD, MSc, Iowa State University;
DVM, Universidad del Litoral,
Veterinary Medicine, Argentina

3 refereed publications in 2012

99 article citations in 2012

Co-investigators: Drs. Loren Hauser,
ORNL; Arnold Saxton and Oudessa
Kerro Dego; Mr. Douglas Luther

Role of *Streptococcus uberis* in Dairy Cattle Mastitis

Mastitis occurs worldwide and is characterized by inflammation of mammary tissue, which severely affects milk production and quality. In the dairy industry, mastitis is the most costly disease of dairy cattle, costing U.S. dairy producers over \$2 billion annually. Mastitis is caused by bacterial pathogens, and among them *Streptococcus uberis* is showing an alarming increasing prevalence.

In spite of this, how *S. uberis* affects mammary tissue to cause mastitis is still not understood and is the focus of Dr. Almeida's research. Thus far, he has identified a list of genes associated with early bacterial infection events, and his immediate goal is to describe the roles of three of these genes in relation to *S. uberis*.

The long-term goal of this research is to develop vaccines to prevent or control *S. uberis* mastitis to not only minimize the negative financial impact but also to improve the health and comfort of dairy cattle.



Dr. David Brian

Professor, Biomedical and Diagnostic Sciences

PhD, DVM, Michigan State University

1 refereed publication in 2012

30 article citations in 2012

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

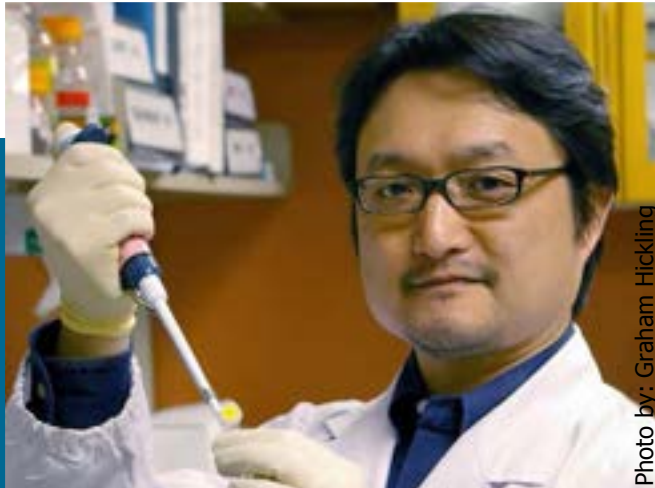
Co-investigator: Dr. Yu-Pin Su

Halting Bovine Coronavirus Replication

Coronaviruses cause common upper respiratory and gastrointestinal infections in mammals and birds, including humans and livestock. One type of coronavirus causes severe acute respiratory syndrome (SARS) (discovered in 2002) and another is the more recently-found (in 2012) Middle Eastern respiratory syndrome (MERS), which is seen in bats in the wild.

Both the SARS and MERS coronaviruses are zoonotic, and in humans, infections cause high death rates (approaching 10% and 50%, respectively). Coronaviruses may also be a cause of multiple sclerosis in humans.

Coronaviruses harbor the largest, single-stranded RNA virus genome known. Dr. Brian's group studies how the coronavirus genome replicates with the goal of characterizing the inter-molecular steps required for reproduction. These steps involve RNA-RNA interactions, protein-RNA interactions and protein-protein interactions. Once characterized, these interactive sites may be useful targets for anti-coronaviral drug design.



Dr. Shigetoshi Eda

Associate Professor, Forestry, Wildlife and Fisheries

PhD, MS, Tokyo University of Pharmacy and Life Science, Japan

3 refereed publications in 2012

60 article citations in 2012

In addition to center funds, Dr. Eda's research is supported by the Physician's Medical Education and Research Foundation.

Co-investigators: Drs. Jayne Wu, Maria Prado, and Brian Whitlock

On-site Diagnosis of Johne's Disease in Dairy Cattle

The U.S. Department of Agriculture describes Johne's disease (JD) as "a contagious, chronic and usually fatal infection that affects the small intestine of ruminants." It is caused by a hardy bacteria related to the agents of leprosy and tuberculosis. The disease is causing significant economic loss to the global dairy industry.

Dr. Eda's research group seeks to develop an on-site (cow-side) device for diagnosis of JD on dairy farms. The current method suffers from low sensitivity to detect the infection, high cost, and delayed diagnosis. These drawbacks discourage farmers from testing their herds.

Dr. Eda is using nano-scale science in a diagnostic device about the size of a smart phone. The protocol is now being optimized and validated to maximize the test's sensitivity and specificity. So far, a provisional patent application has been submitted for the device.



Dr. Amy LeBlanc

Associate Professor, Small Animal
Clinical Sciences

DVM, Michigan State University

5 refereed publications in 2012

55 article citations in 2012

In addition to center funds, Dr.
LeBlanc's research is supported by
UT-Battelle–Oak Ridge National
Laboratory.

Co-investigator: Dr. Shruthi Naik

Using Viruses to Kill Tumor Cells

Dr. LeBlanc's research group is using a technique known as oncolytic virotherapy as a new form of cancer treatment. This promising experimental approach to cancer treatment uses viruses that target specific cancer cells.

This strategy has demonstrated success in preclinical studies, and work is underway to determine which cancers seem most likely to respond to these viruses. The results produced in dogs will be translatable to humans.

In collaboration with researchers at Mayo Clinic, who develop, manufacture, and study recombinant vesicular stomatitis virus and other oncolytic viruses, Dr. LeBlanc's team has determined a well-tolerated dose of a novel oncolytic virus in dogs in preparation for clinical trials in pet dogs with cancer.

Dr. LeBlanc will also characterize viral shedding and assess the dog's ability to neutralize the virus through a natural immune response.

If successful, application of this strategy will help eliminate the requirement for long-term, potentially toxic and expensive chemotherapy.



Dr. Barry Rouse

Distinguished Professor, Biomedical
and Diagnostic Sciences

PhD, MSc, University of Guelph,
Canada; BVS, University of Bristol, UK

6 refereed publications in 2012

533 article citations in 2012

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

Bringing Clarity to Immunopathogenesis of Corneal Disease

For optimal vision, the cornea must be transparent so light goes to the retina without interruption. To maintain transparency, the cornea normally suppresses all tissue-damaging inflammatory and immune reactions.

However, this control system breaks down in response to some events, such as herpes simplex virus-1 (HSV-1) infection of the cornea. This infection can result in stromal keratitis (SK), which is the most common infectious cause of blindness in developed countries.

A key feature of SK is the establishment of new blood vessels in the cornea (angiogenesis), but how virus infection results in angiogenesis is poorly understood and is the focus of Dr. Rouse's research.

Publications & Presentations



Raul Almeida (p. 34)

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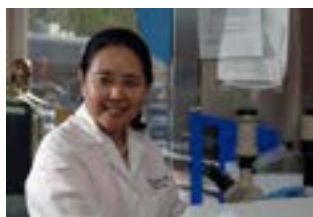
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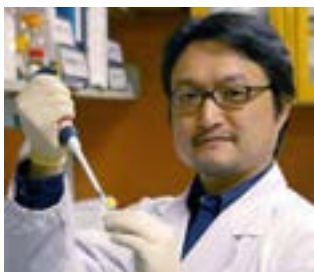
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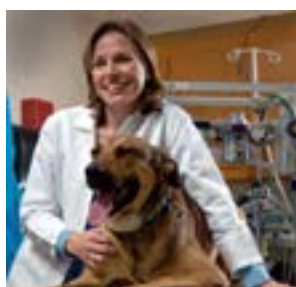
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Barry Rouse (p. 38)

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Rouse BT. Critical events in the pathogenesis of herpetic stromal keratitis [invited seminar]. University of Illinois College of Medicine at Chicago. Chicago, IL. October 2012.

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Hildegard Schuller (p. 31)

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Hwa-Chain Robert Wang (p. 32)

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Wang H-CR. Intervention of chronically-induced breast cell carcinogenesis [invited talk]. Institute of Biomedical Sciences, Academia Sinica. Taipei City, Taiwan. August 2012.

Wang H-CR. Horse care at UTCVM. Xinjiang Provincial Veterinary and Animal Husbandry. Urumqi City, Xinjiang Province, China. August 2012.

Wang H-CR. The structure and function of the Association of American Veterinary Medical Colleges [invited keynote talk]. Tenth Annual Meeting for Deans of Chinese Veterinary Medical Colleges. Urumqi City, China. August 2012.

Wang H-CR. Intervention of cellular carcinogenesis [invited talk]. North West Agricultural and Forestry University, College of Animal Science and Veterinary Medicine. Yangling City, Shaanxi Province, China. October 2012.

Wang H-CR. Teaching molecular & cell biology and biochemistry in cancer research [invited talk]. North West Agricultural and Forestry University, College of Innovation Experiment. Yangling City, Shaanxi Province, China. October 2012.

Wang H-CR. American veterinary education [invited talk]. Hanzhong City Centre for Animal Disease Control. Hanzhong City, Shaanxi Province, China. October 2012.

Wang H-CR. Veterinary education in the USA [invited talk]. Hanzhong City Centre for Animal Disease Control. Hanzhong City, Shaanxi Province, China. October 2012.

Wang H-CR. Intervention of cellular carcinogenesis [invited talk]. Guangdong Ocean University. Zhanjiang City, Guangdong Province, China. October 2012.

Wang H-CR. Research approaches of molecular biology, cell biology, and biochemistry for studying biologi-

cal and pathological events [invited talk]. Guangdong Ocean University. Zhanjiang City, Guangdong Province, China. October 2012.

Wang H-CR. Teaching molecular & cell biology and biochemistry in cancer research [invited talk]. Guangdong Ocean University. Zhanjiang City, Guangdong Province, China. October 2012.

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*Publications and presentations listed are for the 2012 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	2013 Receipts	2013 Expenditures
Baek, Seung Joon	Prevention of colorectal cancer by tolfenamic acid	University of Maryland (National Institutes of Health flow-through)	7/01/11–6/30/15	\$0*	\$34,442
Brian, David	Coronavirus RNA replication	National Institutes of Health	6/01/08–5/31/13	\$0 [†]	\$277,902
Cekanova, Maria	New staging techniques & evaluation of therapies for oral squamous cell carcinomas	Winn Feline Foundation	2/18/10–7/30/12	\$0*	\$7,964
	Role of estrogen receptor beta in breast cancer	The Physician's Medical Education and Research Foundation	9/01/11–3/21/13	\$0 [†]	\$8,169
	Potential use of neutron imaging for biomedical and biological application	UT-Battelle, LLC–Oak Ridge National Laboratory	8/03/11–8/02/12	\$0*	\$0
	Detection of COX-2 expressing canine tumors by new optical imaging tracer	Vanderbilt University Medical Center	11/01/11–6/30/13	\$13,000	\$7,258
	Investigation of a novel approach to forensic analysis using neutron imaging techniques	UT-Battelle, LLC–Oak Ridge National Laboratory	1/28/11–9/30/13	\$0*	\$3,420
	Evaluation of neutron radiography and computed tomography for detection of cancer using COX-2-targeted boronated contrast agents	Oak Ridge National Laboratory/ Spallation Neutron Source/U.S. Department of Energy	6/01/13–10/30/13	\$200,000	Beam time only; no monetary expenditures
Cui, Mei-Zhen	Novel mechanism mediating LPA-induced smooth muscle cell and fascular responses	National Institutes of Health	06/15/11–05/31/13	\$347,480	\$286,898

Investigator	Project Title	Funding Agency	Project Period	2013 Receipts	2013 Expenditures
Eda, Shigetoshi	A portable and rapid assay system to detect levels of circulating D-dimer protein	The Physician's Medical Education and Research Foundation	11/21/12–11/30/13	\$3,700	\$1,128
Kania, Stephen	Genomic resources for the control of canine pyoderma	AKC Canine Health Foundation	1/01/11–12/31/12	\$0 [†]	\$16,723
	Effectiveness of small interfering RNA (siRNA) to inhibit feline coronavirus replication	Winn Feline Foundation	1/01/12–12/31/14	\$0*	\$8,189
	Detection of dermatophytosis in cats by PCR	Winn Feline Foundation	5/01/13–4/30/14	\$10,670	\$0
	Veterinary student research program	Merial Limited LLC	5/01/13–9/01/13	\$10,000	\$10,000
LeBlanc, Amy	Imaging properties and toxicity of selected near-IR dyes in dogs	UT-Battelle, LLC–Oak Ridge National Laboratory	9/26/12–4/10/13	\$79,701	\$78,657
Rouse, Barry	Mechanisms in herpetic keratitis	National Institutes of Health	1/1/13–12/31/16	\$482,400	\$380,175
	T-Regulatory cells in HSV immunity and immunopathology	National Institutes of Health	2/02/11–1/31/16	\$319,283	\$307,810
Schuller, Hildegard	The GABA-B receptor is a novel drug target for pancreatic cancer	National Institutes of Health	5/01/09–4/30/13	\$0*	\$252,042
	Modulation of cancer prevention by social stress	National Institutes of Health	9/30/09–8/31/12	\$0 [†]	\$0
	GABA-BR-mediated prevention of pancreatic cancer	National Institutes of Health	9/01/09–8/31/14	\$280,393	\$217,528
Xu, Xuemin	The role of the new zeta cleavage in Abeta formation	National Institutes of Health	4/01/07–3/31/14	\$0 [†]	\$70,913
	Vascular risk factors in Alzheimer's disease	American Health Assistance Foundation	4/1/09–3/31/14	\$0 [†]	\$44,210
	Role of presenilin-associated protein (PSAP) in apoptosis and Abeta formation	National Institutes of Health	4/15/11–3/31/13	\$0 [†]	\$44,069
Totals				\$1,746,627	\$2,057,499

*All funds were awarded in year 1.

[†]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.

Schedule 7
Center of Excellence in Livestock Diseases and Human Health
ACTUAL, PROPOSED, AND REQUESTED BUDGET

	FY 2012-13 Actual			FY 2013-14 Proposed			FY 2014-15 Requested		
	Matching	Appopr.	Total	Matching	Appopr.	Total	Matching	Appopr.	Total
Expenditures	187,289	374,577	561,866	261,661	523,321	784,982	274,744	549,487	824,231
Salaries									
Faculty	6,264.46	12,529	18,793			0	0	0	0
Other Professional	47,832	95,665	143,497	54,823	109,662	164,484	57,564	115,145	172,708
Clerical/ Supporting	34,282	68,565	102,847	37,514	75,028	112,543	39,386	78,784	118,170
Assistantships	8,084	16,169	24,253	6,111	12,222	18,333	6,416	12,834	19,250
Total Salaries	96,464	192,927	289,391	98,448	196,912	295,360	103,366	206,763	310,128
Longevity	1,085	2,170.28	3,255	891	1,782	2,672	935	1,871	2,806
Fringe Benefits	23,195	46,389	69,584	18,040	36,080	54,120	18,940	37,886	56,826
Total Personnel	120,743	241,487	362,230	117,379	234,774	352,153	123,241	246,519	369,760
Non-Personnel									
Travel	3,887	7,773.28	11,656	8,330	16,661	24,991	8,746	17,495	26,241
Software	1,013.33	2,027	3,040			0	0	0	0
Books & Journals				533	1,066	1,599	559	1,119	1,678
Other Supplies	43,312	86,623	129,935	110,132	220,265	330,397	115,628	231,290	346,917
Equipment	2,162	4,323	6,485			0			0
Maintenance	941.12	1,882	2,823	762	1,523	2,285	800	1,600	2,399
Scholarships	2,309	4,618	6,927	2,329	4,657	6,986	2,445	4,890	7,335
Consultants			0			0			0
Services	8,544	17,088	25,632	19,775	39,550	59,325	20,762	41,530	62,291
Total Non-Personnel	62,167	124,334	186,502	141,861	283,722	425,583	148,939	297,923	446,862
GRAND TOTAL	182,911	365,821	548,732	259,240	518,496	777,736	272,180	544,442	816,623
Revenue									
New State Appropriation		505,110	505,110		523,321	523,321	0	549,487	549,487
Carryover State Appropriation		231,207	231,207		371,802	371,802			0
New Matching Funds	252,555		252,555	261,661		261,661	274,744		274,744
Carryover, Prev. Matching Funds	115,604		115,604	185,901		185,901			0
Total Revenue	368,159	736,317	1,104,476	447,562	895,123	1,342,685	274,744	549,487	824,231