Center for Veterinary Health Sciences – FY2012 Research Abstracts

DEPARTMENT OF VETERINARY PATHOBIOLOGY

***In Vitro* Assessment for Antimicrobial Activity - Part A: Bacteria and Fungi.** IDIQ Drug Screening Contract.
The purpose of the contract is to provide NIAID with a broad and flexible range of *in vitro* assay capabilities for human infectious diseases of human importance caused by infectious agents. The broad scope will allow NIAID to respond to changing priorities as scientific and public health needs shift, including rapid responses to public health emergencies. The scope of work encompasses any type of *in vitro* assay work needed for infectious disease research, to include routine screening of products and development of new *in vitro* assays and database management of work. The services provided under this and other similar contracts will assist NIAID in accomplishing its goal of developing medical products to counter emerging, re-emerging and other infectious diseases, as well as agents of bioterrorism. Co-investigators are Christina Bourne, Ph.D., Phil Bourne, Ph.D., and Ken Clinkenbeard, Ph.D., D.V.M.
Sponsors: NIH/NIAID/DMID, Contract HHSN272201100020I. June 1, 2011 – May 31, 2018.
PI/PD: William W. Barrow

Broad-spectrum Antifolates for Treatment of Drug Resistant *Bacillus anthracis* – Research Grant
This is a multidisciplinary partnership grant involving the Departments of Veterinary Pathobiology (CVHS-VP) and Chemistry at OSU, Sapient Discovery (San Diego, CA), and Lovelace Respiratory Research Institute (LBERI) (Albuquerque, NM). Co-Investigators are Christina Bourne, Ph.D. and Phil Bourne, Ph.D. (CVHS-VP), Darrell Berlin, Ph.D. and Richard Bunce, Ph.D. (Chemistry/OSU), Kal Ramnarayan, Ph.D. (Sapient), and Michelle Valderas, Ph.D. (LBERI). The goal is to develop a new assemblage of antimicrobials for the treatment of inhalation anthrax. The iterative process will involve a combination of traditional drug design methods, including crystallography, molecular biology and medicinal chemistry as well as *in silico* discovery tools and animal models.
Sponsors: NIH/NIAID/DMID**,** Grant RO1-AI090685-01, July, 2010-June, 2015.
PI/PD: William W. Barrow

Bovine Respiratory Disease: Risk Factors, Pathogens, Diagnosis, and Management
The project determines changing patterns, geographical differences, risk factors, and management practices related to bovine respiratory disease. The influence of various bacteria and viruses is studied. In addition, the pharmacokinetics and efficacy of newer therapies and new-generation vaccines are evaluated. The host-pathogen relationships are characterized at the molecular level.
Sponsor: Oklahoma Agricultural Experiment Station
PI/PDs: Anthony W. Confer, Robert W. Fulton, Sahlu Ayalew

***M. haemolytica* Chimeric Protein Vaccine for Delivery of Multiple Outer Membrane Protein and Leukotoxin Antigens**
Using immunoproteomic approach, outer membrane protein antigens that are important in stimulating immunity to *M. haemolytica* were identified and sequenced. The genes were then cloned and expressed for functional studies of antibodies to these important antigens. Studies will incorporate new epitopes into chimeric vaccines to stimulate immunity against the bacterium.
Sponsors: USDA CSREES, National Research Initiative Competitive Grant
PI/PDs: Anthony W. Confer, Sahlu Ayalew

Comparison of *Mannheimia haemolytica* Isolates from Cattle in Australia with U.S. Isolates
Mannheimia haemolytica is the most common bacterial agent of bovine respiratory disease. This study is examining *M. haemolytica* isolates from across the United States to isolates obtained from Australia, with the goal of determining whether vaccine products licensed for use in the US may be expected to be effective in other geographic regions. Genotyping techniques as well as antigenic comparisons will be made to determine diversity and effectiveness of immune response to the vaccine at neutralizing the isolates.
Sponsor: Pfizer Animal Health
PI/PDs: Anthony W. Confer, Jared D. Taylor

Prevalence of *Brucella canis* Infection in a Fighting Pit Bull Population
Brucella canis, the causative agent of canine brucellosis, is a zoonotic disease that causes abortion and infertility in dogs and flu-like illness, lymphadenopathy and recurrent fevers in humans. This study proposes to determine the prevalence of *B. canis* infection, using serology and polymerase chain reaction, among a population of >400 fighting pit bulls and associated breeding animals. This could assist in determining the public health risk of dogfighting operations and unregulated dog breeding operations.
PI/PD: Tamara Gull

Characterization of Tick Genes Involved in the Tick Developmental Cycle and Transmission of the Cattle Pathogen, *Anaplasma marginale*
The vectorial capacity of ticks for *Anaplasma marginale* is most likely dependent upon both tick cell and pathogen interactions that involve pathogen adhesion proteins, tick cell receptors and a series of tick cell proteins that mediate the trafficking of the pathogen throughout ticks. In this research we will identify and characterize genes differentially expressed in tick cells in response to infection with *A. marginale*. These key genes will then be tested as vaccine antigens aimed at reducing the vectorial capacity of ticks for transmission of *A. marginale*.
Sponsor: Oklahoma Agricultural Experiment Station
PI/PDs: Katherine M. Kocan, José de la Fuente, Edmour F. Blouin

Tick Gene Expression and Developmental Cycle of *Anaplasma phagocytophilum*
Anaplasma phagocytophilum is a tick-borne pathogen that causes emerging disease in humans, human granulocytic anaplasmosis. In this research we will describe the development cycle of *Anaplasma phagocytophilum* in its tick vector, *Ixodes scapularis*. We will then determine the impact of silencing selected differentially-expressed genes identified previously by RNA interference on the pathogen and transmission.
Sponsor: OSU Center for Veterinary Health Sciences, Research Advisory Committee
PI/PDs: Katherine M. Kocan, José de la Fuente, Edmour F. Blouin.

Walter R. Sitlington Endowed Chair in Food Animal Research
Funds generated by this endowed chair support the overall Tick and Tick-borne Pathogen Vaccine Development Laboratory for the conduct of the various research projects.
Sponsor: Center for Veterinary Health Sciences
PI/PD: Katherine M. Kocan

Baboon Research Resource Program
Baboons are an important animal species used in biomedical research. This program will develop a breeding colony of baboons in Oklahoma and supports research aimed at improving the breeding

efficiency of baboons in captivity, defining viruses that naturally infect baboons, and improving the basic well-being and behavior of captive-bred baboons.
Sponsor: NIH, NCRR
PI/PDs: Richard Eberle, Jean d'Offay, Mason Reichard
Physiological Sciences: Dianne McFarlane
OUHSC: Gary White

Development of an SPF Baboon Colony
Indigenous viruses can have a major adverse effect on the results of biomedical research studies using animals, particularly where immunosuppression is involved. This program supports derivation of a colony of baboons that are free of all known herpesviruses and most retroviruses.
Sponsor: NIH, NCRR
PI/PDs: Richard Eberle
OUHSC: Gary White

Bovine Viral Diarrhea Disease Virus (BVDV) Vaccines: Antibody Response to Heterologous BVDV Strains
The study will determine the range of heterologous immunity in calves receiving modified live virus (MLV) or killed BVDV vaccines. Currently there are two recognized antigenic types and several subgenotypes of BVDV: BVDV1a,2a,1b, and 2b.. The study will determine if these vaccines induce antibodies to these four BVDV subtypes..
Sponsors: Novartis Animal Health, Pfizer Animal Health, Fort Dodge Animal Health
PI/PDs: Robert W. Fulton, Anthony W. Confer

Bovine Viral Diarrhea Virus: Diversity of BVDV Strains and Impact on Diagnosis, Vaccinations, and Control Programs
Bovine viral diarrhea viruses (BVDV) isolates from persistently infected (PI) cattle will be obtained from feedlot cattle. The isolates will be subtyped by sequencing a region of the 5'-UTR. Subgenotypes to be detected will include those of worldwide ePI/PDdemiology. The BVDV subgenotypes expected in North America are: BVDV1a, 1b, 2a, and 2b. Molecular diagnostic tests including reverse transcriptase PCR and real time PCR will be evaluated to detect these diverse BVDV subgenotypes in peripheral blood, serums and ear notch samples of infected animals. Cytopathic BVDV 1b strains as potential vaccine strains will be sequenced to permit detection by genomic tests allowing diffentiation of vaccine strains from field strains in vaccinated animals. The prevalence of PI/PD animals in Oklahoma beef herds will be determined using immunohistochemistry and antigen capture ELISA (ACE) on ear notches. The PI/PD strains will be subtyped. Vaccination records will be obtained to determine use of BVDV vaccines or lack thereof in herds with PI/PD animals. Potentially new subtypes may warrant additional subtypes in the vaccines.
Sponsor: Oklahoma Agricultural Experiment Station
PI/PDs: Robert W. Fulton, Anthony W. Confer
Veterinary Clinical Sciences: D.L. Step

Antibiotic Administration and Vaccination with Live Bacterial Vaccine in Calves
This study will determine if an antibiotic given calves that have been administered avirulent *Mannheimia haemolytica* and *Pasteurella multocida* vaccine will decrease the immune responses to the immunogens. Calves will receive Micotil antibiotic and Once PMH *Mannheimia haemolytica* and *P. multocida* vaccine. The calves' sera will be tested for *M. haemolytica* and *P. multocida* antibodies.

Sponsor: ELANCO Animal Health, Division of Eli Lilly and Company
PI/PDs: Robert W. Fulton, Anthony W. Confer

Evaluation of Viral Vaccine Containing Infectious Bovine Rhinotracheitis Virus (IBRV), Bovine Viral Diarrhea Virus 1 and 2 (BVDV), Parainfluenza -3V (PI/PD-3V), and Bovine Respiratory Syncytial Virus (BRSV) in Preventing Infection and Respiratory Disease in Cattle
The purpose of the study will be to determine if pre-weaning vaccination of ranch calves with viral vaccine: (1) reduces respiratory disease; and (2) reduces transmission of viruses in calves moved from auction markets and commingled with the fresh calves under feedlot conditions.
Sponsors: Fort Dodge Animal Health, Schering Plough Animal Health, BI Animal Health
PI/PDs: Robert W. Fulton, Anthony W. Confer

Rapid Diagnosis of Viruses Involved in Bovine Respiratory Diseases
The purpose of the study will be to determine if use of reverse transcriptase PCR testing aids in the diagnosis of viruses involved in bovine respiratory disease. Samples including nasal swabs, serums, and lung samples collected at necropsy will be tested for viruses using the PCR tests for bovine viral diarrhea viruses, bovine herpesvirus 1, bovine respiratory syncytial virus, and bovine coronavirus. The tests results will be compared to use of standard tests including cell culture isolation for viruses. Genomic tests have advantages as cell culture tests are not often rewarding for viral identification. A higher recovery rate for these viruses is expected by PCR.
Sponsors: Oklahoma Agricultural Experiment Station, 1433 Animal Health Research
PI/PD: Robert W. Fulton

Efficacy of an Experimental IBR-BVD-PI/PD3-BRSV-VL5 Vaccine in Protecting Pregnant Heifers and Fetuses Against a Bovine Viral Diarrhea Virus Type 1b Challenge
This objective of this study is to demonstrate efficacy of an IBR, BVDV, PI/PD3V, BRSV, Campylobacter fetus, and leptospiral bacterin prebreeding vaccine in protecting pregnant heifers and their fetuses against challenge exposure to seeder calves persistently infected with BVDV 1b at approximately 75 days of gestation.
Sponsor: Pfizer Veterinary Medicine Research and Development
PI/PDs: Robert W. Fulton
OADDL: Bill J. Johnson
Veterinary Clinical Sciences: DL Step
Animal Science: Clint Krehbiel

Bovine Coronavirus: Role in Respiratory Disease
Bovine respiratory diseases (BRD) also referred to as “Shipping Fever” represents significant losses to cattlemen. There are several viruses contributing to the BRD which has a polymicrobial etiology. These include bovine herpesvirus, parainfluenza -3 virus, bovine respiratory syncytial virus, and bovine viral diarrhea viruses along with *Mannheimia haemolytica, Pasteurella multocida, Histophilus somni*, and *Mycoplasma spp*. The bovine coronavirus (BCV) has emerged as another virus which contributes to BRD. Measuring the BCV role in BRD has been hampered by lack of tools for the study of this virus both in vitro and in animal studies. The purpose of this study will be to develop means of propagating the BCV in cell cultures, developing and validating a serologic test for BCV antibodies to demonstrate active infections, developing an immunohistochemistry assay to detect BCV in infected cells and tissues, and a challenge model to demonstrate the disease induced by BCV. An attempt will be made to develop live and inactivated BCV vaccines for cattle.

Sponsors: Oklahoma Agriculture Experiment Station, USDA Section 1433 Animal Health Research Funds
PI/PDs: Robert W. Fulton, Anthony W. Confer, Richard Eberle
Veterinary Clinical Sciences: D.L. Step

Bovine Coronavirus in Respiratory Disease: Methods of Study, Pathogenesis, and Development of Challenge Model for Efficacy Studies
Bovine coronavirus (BCV) represents an infectious agent contributing to bovine respiratory disease (BRD) in cattle. This study will investigate the role of BCV in clinical cases of BRD by viral isolations from clinically ill cattle, and the use of serology to detect active infections in commingled cattle under feedlot conditions. Serologic tests will include ELISA and viral neutralization tests to detect BCV antibodies. BCV isolated from affected cattle will be characterized as BCV and propagated with viral quantification. A challenge model will be developed to measure infectivity and pathology caused by BCV in susceptible cattle. This challenge model will be used to measure resistance to BCV in cattle immune and susceptible to BCV.
Sponsor: Pfizer Veterinary Medicine Research and Development
PI/PDs: Robert W. Fulton, Anthony W. Confer, Richard Eberle
Veterinary Clinical Sciences: D.L.Step

Bovine Herpesvirus-1: Molecular Characterization of Vaccine, Reference, and Field Strains
Bovine herpesvirus-1 (BHV-1) represents significant virus infections in cattle with significant losses due to respiratory, fetal (abortions), and genital tract diseases. Vaccines are available, with the MLV type the most commonly used for control programs. Often BHV-1 is recovered from clinically ill cattle shortly after vaccination. Tests are needed to differentiate the MLV vaccine strains from field strains. This project will use molecular procedures including viral sequencing and PCR to characterize BHV-1. The entire genome of 15 BHV-1 strains including: reference strains, vaccine strains, and selected field isolates will be sequenced. The viral genomes will be evaluated with selected regions used for PCR and sequencing will be performed on the respective regions derived from the PCR product. The entire viral genome results will be compared to the published viral genome for the BHV-1 Cooper reference strain. Variable regions will be identified for the selection of the PCR primers.
Sponsor: Novartis Animal Health
PI/PDs: Robert W. Fulton, Jean M. d'Offay, Richard Eberle

Epidemiology of American Canine Hepatozoonosis: The Susceptiblitiy of Selected Prey of Carnivores to Infection with Hepatozoon Americanum and the Role of Vertical Transmission
Amblyomma maculatum has been identified as the definitive host and vector of *Hepatozoon americanum* in dogs throughout the southern U.S. Transmission to dogs, an obligate intermediate host, occurs through ingestion of the infected tick. However, dogs are rarely infested with any of the 3 feeding stages of the tick. Immature ticks, stages that acquire the parasite, feed preferentially on smaller mammals and ground-dwelling birds; therefore, dogs are an unlikely source of infection for the tick definitive host. A naturally reservoir for the parasite has not been identified. However, cystozoites, a quiescent, infectious stage of the parasite, develops in the tissues of experimentally exposed laboratory rodents, making canine exposure through predation of infected prey (potential paratenic or facultative intermediate hosts of *H. americanum*) a possible mode of transmission. The primary goals of this research are: 1) to determine the natural vertebrate reservoirs for *Hepatozoon americanum*, 2) to determine the susceptibility of select vertebrate species known to be preferred hosts of immature *Amblyomma maculatum* to infection with *H. americanum*, 3) to determine the susceptibility of common prey of canids to infection with *H. americanum*, 4) to determine if vertical transmission from canine dam to offspring occurs and 5) to test the efficacy of the coccidiostat, decoquinate, as a preventive for

infection of *A*. *maculatum* and transport hosts. Experimental transmission trials to laboratory raised rodents, birds and lagomorphs will be conducted. Comparisons of *Hepatozoon* isolates from wild-caught vertebrates to canine isolates will be made through morphology, histopathology and DNA sequencing. Vertical transmission will be investigated through the natural birth of puppies from a chronically infected carrier dog and monitoring of the offspring by weekly DNA analysis of the puppies' blood. Identifying the natural reservoirs of the parasite and methods of transmission will help implement preventative measures for susceptible dogs to a non-curable, potential fatal parasitic disease.
Sponsor: OSU Center of Veterinary Health Sciences, Research Advisory Committee
PI/PDs: Eileen M. Johnson, Kelly E. Allen, Roger J. Panciera, Susan E. Little, Sidney A. Ewing

Canine Schistosomiasis: An Emerging Disease in Oklahoma
Canine schistosomiasis, caused by *Heterobilharzia americana*, is a debilitating and often fatal disease of dogs in southern states bordering the Gulf of Mexico. Recent reports indicate that the natural range for this fluke is expanding due to the migration or translocation of infected raccoons, a natural host and reservoir for the parasite. Reports of infections in dogs or wildlife in Oklahoma have not been published. Recently the infection has been diagnosed by local veterinarians in dogs (2) from a Tulsa neighborhood. Collaborative field investigation of the Tulsa neighborhood for infected dogs and for the snail intermediate host in a retention pond frequented by animals in the neighborhood have been ongoing. Eight dogs have been diagnosed and suitiable pulmonate snails have been collected from the retention pond. Schistosome cercariae released from snails collected from the retention pond are being tested for *H. americana* DNA. Examination of raccoons collected from the surrounding area should help verify introduction and establishment of this trematode infection in Northeastern Oklahoma.
Sponsor: None
PI/PDs: Todd Yeagley, Eileen Johnson, Mason Reichard, Matt Bolic, Sharon Snowden

Effects of Temperature Changes, Contaminants, and Collection Methods on Culture and PCR Identification of *Tritrichomonas foetus* from Naturally Infected Bulls
With recent changes in regulations for the testing of bulls for *T*. *foetus* before sale or movement has identified diagnostic complications related to collection methods, handling of commercial culture pouches (TF InPouch®) and testing methods used by veterinary diagnostic laboratories nationwide. A study was conducted to investigate the effects of Oklahoma temperature extremes, contaminants and collection methods on recovery and growth of the protozoan organism in the commercial media, and the stability of the organism's DNA under adverse conditions. Time interval between prepucial collections and 2 collection methods were also evaluated using a naturally infected bull to determine impact on recovery, culture, and PCR detection of the organism. Hot and cold temperature extremes were detrimental to survival of the protozoan in the culture pouches after 4 hours. Detection of the parasite through PCR amplification of DNA in culture media held at environmental temperature extremes was successful, indicating that the DNA remained stable under these conditions. Fecal bacteria interfered with growth of the parasite in the culture media. Less than a two week rest interval between prepucial collections reducedisolation of the parasite.
Sponsor: OSU Center of Veterinary Health Sciences, Research Advisory Committee
PI/PDs: Brenda Love, Stacy Blaylock, Emily Cooper, Eileen Johnson
OADDL: Grant Rezabek, Emily Cooper, Bill Johnson
Veterinary Clinical Sciences: John Gilliam

Timing of Transmission of Tick-borne Disease Agents
This project examines the transmission dynamics at play as tick borne disease agents move between vertebrate hosts and vector ticks.
Sponsor: Bayer Animal Health
PI/PD: Susan E. Little

Infection and Exposure Rates for Rickettsial Agents in Dogs
Rikettsial agents, including *Rickettsia* spp. and *Ehrlichia* spp., commonly infect dogs in areas of the US where lone star ticks predominate. This project seeks to document the extent to which dogs become infection with rickettsial agents following natural infestations in endemic areas with an ultimate goal of developing strategies to interrupt those infections.
Sponsor: Bayer Animal Health
PI/PD: Susan E. Little

Assembly of Human Respiratory Syncytial Virus (HRSV)
HRSV infects virtually every person on the planet and presents a serious, worldwide, disease burden. Available therapies are not adequate, and a better understanding is needed of the virus life cycle. In this project, the molecular mechanisms of virus assembly are investigated, and the role of the viral matrix and transmembrane glycoproteins therein determined. With an improved understanding of virus assembly, the project aims to: 1) control the virion assembly process such that the quality of anti-HRSV vaccine preparations can be improved, and 2) create new concepts for antiviral therapies.
Sponsor: Oklahoma Center for the Advancement of Science and Technology (OCAST)
PI/PD: Tom Oomens

Efficacy of Nucleoside Analogs for Treatment of Monkey B Virus Infection in Mice
Monkey B virus (BV, *CercoPI/PDthecine herpesvirus-1*) is an α-herpesvirus indigenous to macaque monkeys that cause serious, often fatal disease when transmitted to humans. TyPI/PDcally, BV infections involve researchers and animal technicians that work with macaque monkeys and acquire the infection via bites or scratches from monkeys shedding BV; therefore, BV is the major occupational biohazard concern for persons working with and around macaque monkeys. The optimal therapy for human BV infections remains unknown. The goal of this project is to use a murine BV model system to compare several existing anti-herpetic drugs to identify the one that is most efficacious.
Sponsor: ACLAM Foundation
PI/PDs: Jerry Ritchey, Richard Eberle
Physiological Sciences: Lara Maxwell

Diversity of Bacterial Isolates from the Nares of Healthy and Sick calves
The project will determine the genetic diversity of bacteria isolated from nasal passages of both healthy calves and those suffering from bovine respiratory disease (BRD). The goal is to determine whether a single clone typically dominates or if a variety of strains of a given species can be expected. If most or all isolates represent a single clone, culture of nasal swabs may be used in both diagnostic and research efforts of BRD. If a variety of strains are frequently present, nasal swabs would have limited usefulness, as it is not practical to examine all strains present in each calf.
Sponsor: Oklahoma State University Center for Veterinary Health Sciences
PI/PDs: Jared D. Taylor, Anthony W. Confer
Veterinary Clinical Sciences: D. L. Step

Magnetic Resonance Imaging (MRI) Characteristics and Treatment Aspects for Gliomas in Animal Models

Brain tumors are the most common solid tumor in children, with high grade gliomas accounting for ~10% of pediatric brain tumors. Standard approaches to therapy for high grade pediatric gliomas have provided only modest improvements to progression-free survival and overall survival. Most patients diagnosed with pediatric glioblastoma (pGBM) eventually progress, with no effective cure currently available. This study will focus on assessing if the anti-cancer agent, OKN-007 (OKlahoma Nitrone 007), is active against pGBM in pre-clinical models (nude mice orthotopically implanted with human high-grade pediatric glioma cells), and may be considered an effective therapy against pGBM.
We will assess the ability of OKN-007 to reduce tumor growth in pGBM xenografts (nude mice), by characterizing growth patterns with magnetic resonance imaging (MRI), and assessing anti-cancer activity via tumor markers.
Sponsor : Oklahoma Center for Neurosciences - Translational Neuroscience Research Initiative
PI/PDs: Patricia Coutinho de Souza
OMRF: Debra Saunders, Nataliya Smith; Charity Njoku
College of Veterinary Medicine: Sonia Crochik
University of Oklahoma Health Sciences Center: Rheal Towner

DEPARTMENT OF PHYSIOLOGICAL SCIENCES

Distribution and Localization of Sulfotransferases in Rat Endocrine Glands

This research project investigates the roles that sulfotransferasess play in the endocrine system. It focuses on the distribution and localization of hydroxysteroid sulfotransferases in rat endocrine glands. Rats and cultured cells will be used for these studies.
Sponsor: Oklahoma State University
PI/PD: Guangping Chen

Effect of Selected Nutritional Components on Immunity to *Haemonchus* in Small Ruminants

Internal parasitism causes a significant loss in the small ruminant industry of Oklahoma and other regions of the USA and worldwide. The proposed project will address this problem through characterizing the mechanisms of immune responses and attempting to manipulate specific cytokine expression to enhance resistance to parasites in small ruminants. The outcome of this research will lead to a better understanding of the interrelationship between immunity and parasitism and a precise immunity-enhancing strategy for parasite control in ruminants.
Sponsor: United States Department of Agriculture
PI/PDs: Guangping Chen
Langston University: Zaisen Wang

Dopamine Receptors Mediated Gene Regulation Mechanism of Sulfotransferases

This project focuses on mechanisms underlying dopamine (DA) regulation of human (Hep G2 cell) and rat sulfotransferases through hepatic dopamine receptor (DR) pathways. The specific aims to be carried out in this application are as follows: (1) Investigation of the different DR subtype in HepG2 cell, primary rat hepatocytes, and rat liver. (2) Investigation of DR agonists and antagonists on regulation of SULTs in hepatocytes and rat liver, through Gain and Loss of Function strategy, using western blot assay, real-time PCR, transgenic techniques, siRNA techniques, specific DR gene knockout methods and so on. (3) Validation of the DR pathway mechanism in regulation of hepatic SULTs *in vivo* by determination of pharmacokinetics of acetaminophen and moxifloxacin, which are probe drugs of SULT1A1 and SULT2A1

respectively. This study will investigate the new physiological functions of DR and new mechanisms of SULTs regulation based on hepatic dopamine receptor-linked signaling pathways.
Sponsor: National Science Foundation of China
PI/PDs: Guangping Chen
Peking University: Tianyan Zhou

Microstrucure and FRET of Fluorescent DNA Probe Based on Inorganic Nanoparticles
Nanotechnology methods are used to mimic the cell signal transduction pathways. Fluorescent DAN probes are used for the investigation of the signal transduction.
Sponsor: National Science Foundation of China
PI/PDs: Guangping Chen
Polytechnical University: Zhao Dai

Capacity for Respiratory-based Thermoregulation in Brachycephalic Breeds
Brachycephalic dogs are believed to be less capable of thermoregulation due to the conformation of their upper airways, leading many airlines to prohibit shipping of these dogs. This study will objectively characterize the thermoregulatory capacity of these dogs relative to dogs with longer noses to determine more precisely the appropriate guidelines for shipping.
Sponsor: American Kennel Club Canine Health Foundation
PI/PD: Michael Davis

Muscle Adaptations Permitting Fatigue-resistant Exercise
Exercise capacity is limited by either the ability to supply muscle with substrates for the production of energy, or the ability of the body to eliminate the waste products of energy production. In the case of endurance exercise, the availability of macromolecules for oxidation is typically the limiting factor in a thermoneutral environment. This study will determine the mechanisms by which availability of macromolecular substrates can be increased to facilitate improved exercise endurance.
Sponsors: Army Research Office Division of Life Sciences, Department of Defense
PI/PDs: Michael Davis, Guangping Chen
Department of Biochemistry: Peter Hoyt
Michigan State University: Ray Geor
University of Melbourne: Kenneth W. Hinchcliff
University of Guelph: Arend Bonen
Department of Veterinary Clinical Sciences: Ken Bartels

Combinatorial Drug Screening to Identify Strategies to Enhance Ground Troop Readiness at High Altitude
Acute exposure to high altitude confers a disadvantage to individuals needing to perform physical tasks, when compared to individuals who have acclimatized to high altitude. The goal of this study is to develop novel compounds that will accelerate the acclimatization process to low ambient oxygen levels, with subsequent improvement in exercise performance.
Sponsor: DARPA-DSO (Subcontract through University of Colorado)
PI/PDs: Michael Davis, Lara K. Maxwell
Veterinary Pathobiology: Jerry Ritchey

Physiology and Pathophysiology of Equine Athletic Performance
Superior athletic performance in horses requires optimal physiological adaptation in the musculoskeletal and cardiopulmonary systems, and improvements in these systems often lead to improved

performance. Conversely, disease in these systems will invariably cause decreased performance, and in some cases the exercise itself is the cause of the disease. The goals of this program are to investigate the mechanisms underlying the physiological adaptation to exercise in horses, identify methods that will improve the horse's adaptation to exercise, and determine strategies that can prevent exercise-induced disease. (2729)
Sponsors: Oklahoma Agricultural Experiment Station, Oxley Chair in Equine Sports Medicine
PI/PD: Michael Davis

IDD 2.0: Building a Better Canine Warfighter
Dogs are increasingly being used as warfighters tasked with assignments ranging from attack/patrol to explosive detection. Deployment places a considerable amount of physiological stress on the dogs, and there is currently minimal information as to the magnitude of this stress and how to adapt the dogs to this stress successfully. This study will develop conditioning and monitoring programs to prepare canine warfighters for the stress of deployment, including the proper type of athletic conditioning, heat tolerance, and dietary support. It will also develop field-implementable protocols for monitoring the successful adaptation of the dogs to deployment stress.
Sponsors: Office of Naval Research, Department of Defense
PI/PD: Michael Davis

The Role of P2X7R-mediated Purinergic Signaling in Alveolar Epithelial Cell Death
The goal of this predoctoral fellowship is to study functional roles of P2X7R in alveolar epithelial cells.
Sponor: American Heart Association, South Central Affiliate, predoctoral fellowship #09PRE2300211
PI: Yujie Guo (Mentor: Lin Liu)

Activation of Wnt/beta-catenin signaling inhibits inflammation during acute lung injury
The goal of this student seed grant is to investigate the role of Wnt signaling in lung inflammation during ALI.
Sponsor: Center of Veterinary Health Sciences, Oklahoma State University
PI: Yujie Guo (Mentor: Lin Liu)

Genetic Modifiers of Organ Dysfunction in PKD
This proposal's focus is on the role that proteoglycans and inflammation have on renal and liver dysfunction in polycystic kidney disease. These experiments utilize available multiple mouse models from collaborators in combination with mutant mice we've made to examine lesion severity.
Sponsor: Oklahoma Center for Advancement of Science and Technology
PI/PD: Myron Hinsdale

Extracellular Determinants of Polycystic Kidney Disease Severity
The focus of this grant is to study the role that proteoglycan levels have in lesion severity in PKD and specifically autosomal recessive polycystic kidney disease.
Sponsor: National Institutes of Health
PI/PD: Myron Hinsdale

Adult Stem Cell Proteoglycans and Emphysema
The focus of this grant is to study the role that stem cell extracellular matrix proteoglycans have in the healing process of lung disease.
Sponsor: Oklahoma Center for Adult Stem Cell Research
PI/PD: Myron Hinsdale

Impaired Myocardial Glucose Transport during Diabetes: The Novel Role of Calcium
The goal of this study is to understand how alterations in calcium homeostasis impair glucose transport in the heart during diabetes. We will also investigate the role of a calcium channel blocker therapy on calcium homeostasis and glucose transport in diabetic subjects.
Sponsor: National Institutes of Health, National Center for Research Resources
PI/PD: Véronique Lacombe

Investigation of Glucose Transport Pathways in Horses with Insulin Resistance
Insulin resistance, an impaired ability of insulin to stimulate glucose disposal into muscle and adipose tissue, is a significant health problem affecting both humans and animals. Recently there has been increased awareness and recognition of IR in horses. We will investigate the alterations in glucose transport in muscle and adipose tissue during insulin resistance. Findings from this study could unravel key aspects in the regulation of glucose transport and translate in the discovery of potential therapeutic targets for our equine patients.
Sponsor: United States Equestrian Federation
PI/PD: Véronique Lacombe

Investigation of the Regulation of Glucose Transport and Insulin Signaling Pathways in the Insulin-induction Model of Laminitis
Insulin resistance is a well-known risk factor for a painful, debilitating peripheral vascular limb disease in horses, namely laminitis, with many similarities to peripheral vascular disease and ischemic necrosis of the foot in human diabetics. We will investigate the alterations in glucose transport of striated muscle and lamellae in an equine model of insulin-induced laminitis. Findings from this study could translate in the discovery of potential therapeutic targets.
Sponsor: Animal Health Foundation
PI/PDs: Véronique Lacombe

Mechanisms of Alveolar Fluid Transport
The goal of this project is to investigate the roles of chloride channels of alveolar epithelial type I and type II cells in fluid secretion of fetal lungs, and in maintaining fluid homeostasis of adult and injured lungs.
Sponsor: National Institutes of Health R01 HL083188
PI/PD: Lin Liu

Role of MicroRNAs in Bronchopulmonary Dysplasia
The major goal of this project is to identify microRNAs involved in bronchopulmonary dysplasia using microRNA microarray and examine their functions.
Sponsor: National Institutes of Health R21HL087884
PI/PD: Lin Liu

MicroRNA Expression Profiling in Idiopathic Pulmonary Fibrosis
The goal of this project is to identify and characterize microRNAs changed in idiopathic pulmonary fibrosis using the IPF patient lung samples from the Lung Tissue Research Consortium.
Sponsor: National Institutes of Health R03HL095383
PI/PD: Lin Liu

MicroRNAs and Bovine Respiratory Disease
The goal of this project is to investigate the functions of microRNAs in bovine respiratory disease.
Sponsor: U.S. Department of Agriculture 2009-035505-05855
PI/PD: Lin Liu

Reprogramming of Adult Lung Cells for Cell-based Therapy
The goal of this grant is to convert adult lung cells into stem cells and use them for treating COPD.
Sponsor: Oklahoma Center for Adult Stem Cell Research
PI/PD: Lin Liu

Purchase of Shared Equipment for Testing Efficacy of Adult Stem Cell therapy
The goal of this project is to purchase the flexivent system to test how animals respond to adult stem cell therapy.
Sponsor: Oklahoma Center for Adult Stem Cell Research
PI/PD: Lin Liu

Regulation of VAMP-2 in Alveolar Type II Cells by MicroRNA-206
The goal of this project is to investigate the regulation of lung surfactant secretion by microRNA-206.
Sponsor: American Heart Association, South Central Affiliate
PI/PD: Lin Liu

Regulation of Placenta Growth Factor by Hemodynamics and Reactive Oxygen Species
The goal of this research project is to investigate fundamental mechanisms regulating a key arteriogenic growth factor called placenta growth factor (PLGF) as a basis for developing new, noninvasive treatments for ischemic cardiovascular disease. A variety of *in vitro* and *in vivo* model systems are being used to identify key regulatory mechanisms controlling PLGF expression in health and disease.
Sponsor: National Institutes of Health
PI/PD: Pamela G. Lloyd

Endothelial Progenitor Cell Survival and Function in Emphysema: Role of VEGF-A/PLGF Signaling
The goal of this project is to determine whether altered VEGF-A/PLGF ratios contribute to EPC homing, migration, and/or survival in lungs of mice with experimental emphysema.
Sponsor: Oklahoma Center for Adult Stem Cell Research (OCASCR)
PI/PD: Pamela G. Lloyd

Nuclear Receptor Gene Expression in the Bovine Preimplantation Embryo Produced in Vitro
The central hypothesis of this work is that specific patterns of early gene expression in the cumulus-oocyte complex during the maturation phase affects subsequent developmental capacity; these patterns are subject to influences of the local environment and can be characterized by examining the stimulatory effect of certain nutrient, including vitamin A (9-cis Retinoic Acid (RA). It follows that identification of the positive effects of 9-cis RA will provide a view of a transcript profile having positive influence on subsequent embryo development. The effect of 9-cis RA stimulation on maternal transcriptional activity and transcript profile, and the impact on the oocyte transcript profile will be separated by analysis of the cumulus cells alone, the oocyte alone, versus the cumulus-oocyte complex as a whole, using subtractive hybridization. These results are expected to yield a better understanding of the early transcriptional profile and those genes critical to developmental potential. Benefits may include targets for testing developmental potential of preimplantation embryos and better production methods. (2277)

Sponsor: Oklahoma Agricultural Experiment Station
PI/PD: Jerry Malayer

Pathogenesis, Diagnosis, Treatment, Prevention and Control of Livestock Diseases
This project covers agricultural and biomedical research funded by sources other than USDA that contributes to total research capacity of the OSU Center for Veterinary Health Sciences (CVHS). We are developing strategic alliances with partner institutions and the private sector and growing the supporting infrastructure. Consequently, publications are presented as evidence of progress and productivity. Expenditures for these non-USDA projects came from Federal, State and private funding sources, including biological and pharmaceutical corporations. (2061)
Sponsor: Oklahoma Agricultural Experiment Station
PI/PD: Jerry Malayer

Initiating Factors of Neurodegeneration
Parkinson's Disease and age are both characterized by a loss of functional dopamine-producing neurons. Several aging factors have been implicated in the development of dopaminergic neuronal loss including misfolding of a nerve protein known as alpha-synuclein (a-syn). The long-term goal of our research program is to understanding how aging results in the accumulation of misfolded a-syn and a loss of functional neurons and why the process is accelerated in those individuals with Parkinson's Disease using two novel animal models; spontaneous neurodegeneration in aged baboons and a highly prevalent neurodegenerative disease of aged horses.
Sponsor: National Institutes of Health-National Center for Research Resources 1K01RR023946-01A1
PI/PD: Dianne McFarlane

Assessment of Efficacy of a Long-acting Incretin Mimetic in Cats
The ability of a novel long acting incretin mimetic to regulate blood glucose concentration in experimentally induced diabetic cats is being tested.
Sponsor: Elanco Animal Health
PI/PD: Dianne McFarlane

Development of an Experimental Model of Feline Type 2 Diabetes
A novel experimental model that combines partial pancreatectomy, hormonal induction and nutritional modification for induction of type 2 diabetes mellitus in cats is being tested.
Sponsor: OSU-Center Veterinary Health Sciences
PI/PD: Dianne McFarlane

Metabolic Gene Expression and Mitochondrial Function in Horses with Equine Metabolic Syndrome
The cause of insulin resistance in the insulin sensitive tissue of horses with equine metabolic syndrome is unknown. To further understand the muscle abnormalities that lead to insulin resistance, expression of genes involved in metabolic function and antioxidant capacity in the skeletal muscle of horses with equine metabolic syndrome is being compared to that in normal horses.
Sponsor: American Quarter Horse Association
PI/PDs: Heidi Banse, Dianne McFarlane

Season Variation in Immune Function in Captive Baboons
Seasonal variation in immune response in young baboons housed outside will be compared to that of baboons housed indoors, with a consistent exposure to 12 hours of artificial light daily. This project is part of the Baboon Research Resource Program.

Sponsor: National Institutes of Health-National Center for Research Resources P40 RR12317
PI/PDs: Dianne McFarlane
OUHSC: Gary White

Presynaptic Modulation of Anticholinesterase Toxicity
The project evaluates the role of endocannabinoid signaling in differential toxicity of organophosphorus insecticides.
Sponsor: National Institute of Environmental Health Sciences
PI/PDs: Carey Pope, Jing Liu Pope

Counteracting Acute and Persistent Effects of Organophosphate Intoxication
This project evaluates long-term neurobehavioral deficits following acute diisopropylfluorophosphate intoxication and their modulation by drugs which enhance endocannabinoid signaling.
Sponsor: National Institute of Neurological Disorders and Stroke
PIs: Carey Pope, Jing Pope

Augmentation of Parasympathetic Tone with Pyridostigmine in Heart Failure
The objective of this project is to evaluate the therapeutic benefits of enhancing cholinergic signaling by the drug pyridostigmine on outcomes in human heart failure patients.
Sponsor: National Heart, Lung and Blood Institute
PI/PDs: Carey Pope, Lara Maxwell
New York University: Stuart Katz

CBPR on Pesticide Exposure & Neurological Outcomes for Latinos: PACE4
This project compares markers of pesticide exposures and neurological function in Latino agricultural workers.
Sponsor: National Institute of Environmental Health Sciences
PI/PDs: Carey Pope, Jing Pope
Wake Forest University: Tom Arcury

Role of miR-150 and its Target Glycoprotein NMB on the Pathogenesis of Bronchopulmonary Dysplasia
The goal of this postdoc seed grant is to investigate the functional role of miR-150 in the BPD.
Sponsor: Center of Veterinary Health Sciences, Oklahoma State University
PI: Dhananjay Shukla (Mentor: Lin Liu)
MiR-124a Regulates Fetal Alveolar Epithelial Maturation.
The goal of this student seed grant is to study how miR-124a regulates fetal lung development.
Sponsor: Center of Veterinary Health Sciences, Oklahoma State University
PI/PDs: Yang Wang (Mentor: Lin Liu)

The Functions of miRNAs in the Regulation of EMT
The goal of this student seed grant is to identify miRNAs that are involved in EMT.
Sponsor: Center of Veterinary Health Sciences, Oklahoma State University
PI/PDs: Xiao Xiao (Mentor: Lin Liu)

MicroRNA Profiling in Bovine Alveolar Macrophage
The goal of this student seed grant is to identify microRNA changed during LPS-stimulation in bovine alveolar macrophages.
Sponsor: Center of Veterinary Health Sciences, Oklahoma State University
PI/PD: Li Zhang (Mentor: Lin Liu)

DEPARTMENT OF VETERINARY CLINICAL SCIENCES

Veterinary Medicine Biomedical Laser Laboratory
Since the establishment of the Biomedical Laser Laboratory within the OSU Center for Veterinary Health Sciences, research to establish protocols for clinical applications in veterinary medicine has been a primary objective. In addition, the use of laboratory models has resulted in transfer of technology to both industry and human medicine. Work will continue concentrating on the clinical applications of biomedical lasers coupled with collaborative research protocols involving basic scientists (engineers, physicists) and clinicians.
Sponsors: McCasland Foundation, Kerr Foundation
PI/PD: Kenneth E. Bartels

Transrectal Near-infrared Optical Tomography for Prostate Imaging
This project is a collaboration between OSU colleges (School of Electrical and Computer Engineering and the Center for Veterinary Health Sciences), and the University of Oklahoma Health Sciences Center. It involves development of trans-rectal ultrasound probe using an animal model to image and differentiate malignant tumors in the prostate.
Sponsors: U.S. Army Prostate Cancer Research Program, Tomo Wave Laboratories, Kerr Foundation
PI/PDs: Kenneth E. Bartels, Reed Holyoak
Veterinary Pathobiology: Jerry W. Ritchey

Assessment of *Bdellovibrio bacteriovorus* Strain 109J as an Alternative Treatment for Infectious Bovine Keratoconjunctivitis
Pinkeye or infectious bovine keratoconjunctivitis (IBK) is associated with significant economic loss in the cattle industry. Although antibiotic therapy is the treatment of choice for IBK, treatment failures are common and current vaccines are not optimally effective. As a result, our laboratory has been actively investigating the therapeutic potential of *Bdellovibrio bacteriovorus* 109J (*B. bacteriovorus*), as a new treatment for IBK. The goal of this study is to evaluate the killing efficiency of *B. bacteriovorus* on various strains of *Moraxella bovis* and *Moraxella bovoculi* isolated from cattle with clinical signs of IBK in the state of Oklahoma.
Sponsors: Oklahoma State University's Veterinary Research Scholars program (supported by NIH, Merial Veterinary Scholars program, Morris Animal Foundation, Center of Veterinary Health Sciences)
PI/PDs: Melanie J. Boileau
Veterinary Pathobiology: Kenneth D. Clinkenbeard

The Effects of Intervertebral Disk Calcification in Chondrodystrophic Dogs on the Success of the Percutaneous Thoracolumbar Intervertebral Disk Ablation Procedure
Intervertebral disk disease results in herniation of the disk and variable neurologic impairment, with some dogs suffering permanent paralysis. The percutaneous laser disk ablation (PLDA) procedure has been recommended as a minimally invasive procedure to reduce the risk of recurrence in dogs with thoracolumbar disk disease. A holmium yttrium aluminum garnet (Ho:YAG) laser has been utilized for

the PLDA procedure and shown to significantly reduce the risk of recurrence, with recurrence seen at sites with calcified disks identified radiographically following the procedure. This study will evaluate the effects that intervertebral disk calcification has on laser-tissue interactions via measurement of optical tissue spectral reflection characteristics, evaluate the ability of radiographs to identify significant disk calcification based on histopathology and optical spectral characteristics, as well as determine if increasing the fluency (time / power) in the current laser protocol results in more successful ablation of calcified discs.
Sponsors: Kerr Foundation, McCasland Foundation, OSU Department of Veterinary Clinical Sciences
PI/PDs: Kenneth Bartels, Kelci McKeirnan, Melanie Breshears, Mark Rochat
Statistics: Mark Payton
Electrical and Computer Engineering: Daqing Piao, Katherine Jiang

A Comparison of Propofol and Propofol-Ketamine Anesthesia for Evaluation of Laryngeal Function in Healthy Dogs
Laryngeal paralysis is a common cause of upper airway obstruction in dogs. The disease is diagnosed via direct visualization of the arytenoid cartilages and their failure to abduct during inspiration. Multiple anesthetic protocols have been used to evaluate laryngeal function but the ideal protocol has yet to be identified. The purpose of the current study is to compare propofol to a combination of ketamine and propofol while observing laryngeal function in lightly anesthetized normal dogs. Forty-eight healthy dogs presented for elective sterilization will be randomly assigned to one of two possible anesthetic protocols and undergo laryngoscopy prior to intubation. Scoring for each dog will be based on ease of laryngeal visualization and assessment of laryngeal function.
Sponsors: OSU Center for Veterinary Health Sciences, Research Advisory Committee
PI/PDs: Marjorie Gross, Kelci McKeirnan, Mark Rochat

Effect of Ampicillin/Sulbactam and Enrofloxacin on the Arterial Blood Pressure of Healthy Anesthetized Dogs
Antibiotics are commonly administered medications during surgical procedures. In general, these medications have few side effects. The two antibiotics used in this study are ampicillin/sulbactam, and enrofloxacin. Ampicillin/sulbactam contains sulbactam sodium, a beta-lactamase inhibitor that is added to ampicillin sodium to extend its spectrum to include a wider range of gram-positive, gram-negative, and some anaerobic bacteria. Side effects of penicillins include hypersensitivity reactions, tachypnea, dyspnea, edema, and tachycardia. The second antibiotic to be used in this study, enrofloxacin, is one of the most common fluoroquinolones used in veterinary medicine. Side effects of fluoroquinolones that have been reported include CNS (seizures, possible with NSAID administration), gastrointestinal (vomiting, anorexia, diarrhea), chondrotoxicity (young growing dogs), cardiovascular (hypotension, bradycardia), and nephropathies (Takayama 1995). The goal of this experiment isto determine the effect of these commonly administered antibiotics on the blood pressure in anesthetized healthy dogs.
Sponsor: Cohn Family Chair for Small Animals
PI/PDs: Mark Rochat, Jeremiah Moorer, Meg Gross, Heather Towle
Statistics: Mark Payton

Evaluating the Feasibility of a Dual-modality Optical Sensing Approach in Assessing Hepatic Steatosis in a Rat Model for Fatty Liver
This research aims to develop and evaluate a technology for rapidly assessing the intensity of steatosis (fatty liver), and reliably discriminating the macro-steatosis (single large lipid droplet in a hepatocyte) from the micro-steatosis (numerous small lipid droplets in a hepatocyte). Such technologies are urgently needed for liver transplantation but do not exist clinically. Liver transplantation programs increasingly

use livers of “marginal” quality such as fatty livers. Steatosis, specifically macro-steatosis, in the donor organ represents a major risk to organ recipients. Micro-steatosis, on the other hand, is not associated with an increased risk of dysfunction. This research develops a photonic-needle sensing approach that integrates an optical spectroscopy technology and a depth-resolved optical imaging technology for the aim of quantifying the content and size-distribution of lipid droplets in liver tissue. Such a device may enable hepatic surgeons to determine if an available organ is within a safe steatosis range.
Sponsor: Oklahoma Center for the Advancement of Science & Technology Medical Research
PI/PDs: Kenneth E. Bartels, Reed Holyoak
Veterinary Pathobiology: Jerry W. Ritchey
Electrical and Computer Engineering: Daqing *Piao*

Comparison of Three Anticoagulants to Obtain Hematologic Values in Captive Bull Sharks (*Carcharhinus leucas*)
To date, there is no published data available for blood values in bull sharks. Since bull sharks have specific physiologic adaptation systems enabling them to inhabit marine, estuarine and fresh water systems, their blood data will not be comparable with other strict marine fish species. Blood was collected multiple times from five captive bullsharks. Samples were collected in three different anticoagulants, and compared with each other to evaluate the influence of the different anticoagulants on the blood cell morphology and differentiation.
Sponsor: Department of Veterinary Clinical Sciences
PI/PDs: Cornelia J. Ketz-Riley, T.A. MacNab

Regular Blood Collection from Captive Bull Sharks (*Carcharhinus leucas*) to Establish Hematological and Biochemical Normal Values for this Species Under Controlled Conditions
Only few reports exist on normal ranges of blood values in cartilaginous fish, also called elasmobranchs. To date, there is no published data available for blood values in bull sharks. Since bull sharks have specific physiologic adaptation systems enabling them to inhabit marine, estuarine and fresh water systems, their blood data will not be comparable with other strict marine elasmobranch species. Blood was collected multiple times from five captive bullsharks. The samples were collected in liquid Sodium Heparine. The values obtained were used to establish normal values for bull sharks.
Sponsor: Department of Veterinary Clinical Sciences
PI/PDs: Cornelia J. Ketz-Riley, T.A. MacNab

Comparison of Three Anticoagulants in Hemolysis and Plasma Biochemical Values in Captive Southern Stingray (*Dasyatis americana)* Blood
Only few reports exist on normal ranges of blood values in stingrays. Most of the values have been obtained opportunistically from single rays in aquariums or from wild rays under less controlled conditions. Blood was collected from 11 Southern stingrays (*Dasyatis americana)* kept in an Aquarium in the Mid Western US. Sample collection occurred under controlled conditions. Three different anticoagulation protocols were compared for their influence on hematologic and serum biochemistry values. The values obtained were used to establish normal values for Southern stingrays.
Sponsor: Department of Veterinary Clinical Sciences
PI/PDs: Cornelia J. Ketz-Riley, A. Hahn

The Effects of Low Level Laser Therapy on Distal Limb Full-thickness Skin Wounds in Horses
Cutaneous wound healing in the distal limbs of horses is an aspect of veterinary medicine that has made few advances in spite of our expanding knowledge and technological progress. In fact, treating

cutaneous distal leg wounds (DLWs) and the ensuing exuberant granulation tissue remains one the most frustrating clinical challenges. There have been countless topical preparations and medications that have been applied to DLWs over the millennia and even in recent times; but few have actually been scientifically shown to possess significant clinical efficacy. The goals of treating cutaneous DLWs include minimizing exuberant granulation tissue and facilitating wound contraction and epithelialization. Minimizing scar tissue and adhesion of underlying deep structures are also important considerations. Low level laser therapy (LLLT) has been shown to be beneficial in facilitating healing of slow or non- healing wounds in humans and research data has demonstrated beneficial effects in laboratory animals. This experiment will document the effects of LLLT on surgically created identical and symmetrical DLWs in a controlled environment.
Sponsor: Erchonia
PI/PDs: Henry W. Jann, Kenneth E. Bartels
Colorado State University: Ted Stashak
Auburn University: Steven Swaim

The Effects of Low Level Laser Therapy on Equine Tendon Healing
Although many treatments for overstrain injury of the equine superficial digital flexor tendon have been anecdotally shown to be effective, actual scientific data is lacking. It is also difficult to compare existing studies because experimental injury models differ. Currently the commonly used forms of therapy include stem cell, shock wave, platelet rich plasma (PRP), and immunoreactive antagonistic protein (IRAP). Experimental efficacy data are few and inconsistent for all these modalities. At present no one therapy is universally accepted as being effective. Low-level laser therapy (LLLT) has been shown to have positive effects on tendon and ligament healing in laboratory animals and humans. The purpose of this experiment is to evaluate the therapeutic efficacy of LLLT to augment tendon healing in equine superficial digital flexor window tenectomies.
Sponsor: Erchonia
PI/PDs: Henry W. Jann, Kenneth E. Bartels
Colorado State University: Ted Stashak
Auburn University: Steven Swaim

High-resolution Thermographic Perfusion Imaging for Wound Assessment
The specific aim of this research is to develop high-resolution perfusion imaging capability based on use of a high resolution thermo-camera. This Research will further evaluate if thermographic perfusion imaging is potentially more sensitive than laser Doppler (LDI) imaging in detecting small and slower perfusion, and is able to visualize transverse flow that cannot be detected with LDI.
Sponsors: Kerr Foundation, McCasland Foundation
PI/PDs: Kenneth Bartels
Electrical and Computer Engineering: Daqing Piao

***Bdellovibrio bacteriovorus* 109J: a Non-chemotherapeutic Treatment for Pinkeye and Preventative Measure for Bovine Respiratory Disease in Cattle**
Pinkeye and bovine respiratory disease (BRD) are two diseases associated with significant economic loss in the cattle industry. Although antibiotic therapy is the treatment of choice for both pinkeye and BRD, treatment failures are common and are associated with antibiotic residues. Vaccination is one of the most common practiced measures taken throughout the industry to protect against both diseases, however it is not considered optimally effective. As a result, our laboratory has been actively investigating the potential of *Bdellovibrio bacteriovorus* 109J as a new, “non-antibiotic” treatment for pinkeye and as a preventative measure for BRD. The main goals of this study are to identify and validate

the ophthalmic delivery system of *B. bacteriovorus in vitro* and *in vivo* (using healthy cattle), and to evaluate the killing efficiency of *B. bacteriovorus* against various BRD isolates *in vitro*.
Sponsors: Oklahoma State University Technology and Business Development Program
PI/PDs: Melanie J. Boileau
Veterinary Pathobiology: Kenneth D. Clinkenbeard, Rinosh Mani

***In Vitro* Assessment of *Bdellovibrio bacteriovorous* 109J as a Preventative Measure for Bovine Respiratory Disease**
Mannheimia haemolytica is one of the major causative agents of bovine respiratory disease (BRD), the largest cause of economic loss in the beef cattle industry. Current preventative measures rely on vaccination and the practice of metaphylaxis; however, vaccination is not 100% effective and the practice of metaphylaxis is associated with antibiotic residue. Consequently, our laboratory has been investigating the potential of *Bdellovibrio bacteriovorus* 109J as a preventative measure for BRD. The goal of this study is to evaluate the killing efficiency of *B. bacteriovorus* against various strains of *M. haemolytica* isolated from fatal bovine cases of fibrinous pneumonia in the state of Oklahoma *in vitro*.
Sponsors: Oklahoma State University's Veterinary Summer Research Training Program (supported by NIH, Merial Veterinary Scholars Program, OSU Center for Veterinary Health Sciences).
PI/PDs: Melanie J. Boileau
Veterinary Pathobiology: Kenneth D. Clinkenbeard, Rinosh Mani

Thermo-acoustically Trace and Thermally Mediate Magnetic Nanoparticles Targeting Breast Tumor Initiating Cells by Using Alternating Magnetic Field
This project is a collaboration between the School of Electrical and Computer Engineering and the Center for Veterinary Health Sciences at OSU. It involves the development of a nanoparticle mediated thermal therapy (NMTT) to target breast tumor initiating cells (BTIC), which are a type of cancer stem cell. Cancer stem cells, which are present in many tumors, are typically resistant to currently available therapies and their survival allows for tumor recurrence and metastasis. The goal of the proposed NMTT is to induce cell death in the BTIC. The success of this project has the potential to revolutionize clinical management of breast cancers that contain treatment-resistant BTICs.
Sponsor: Department of the Army (pending)
PI/PDs: Kimberly B. Reeds, Reed Holyoak
Electrical and Computer Engineering: Daqing Piao

Phase 3 Study to Compare Efficacy and Safety of Masitinib to Placebo in the Treatment of High Grade, Non-resectable Mast Cell Tumors in Dogs
This project is a prospective, multi-center, randomized, placebo controlled study. The objective of this study is to evaluate the efficacy and safety of masitinib, in comparison to placebo in dogs with grade 2 or 3 non-resectable mast cell tumors, not previously treated by chemotherapy (other than corticosteroids) or radiotherapy. Enrolled dogs will be monitored for clinical or tumor progression so that the overall time to progression can be determined.
Sponsors: AB Science
PI/PDs: Kimberly B. Reeds
Veterinary Oncology & Hematology Center, LLC in Norwalk: Gerald Post

Early Diagnosis of Lymphomas Using Magnetic Resonance Methods
This project is a collaboration between the Center for Veterinary Health Sciences at OSU at the Oklahoma Medical Research Foundation (OMRF). The goal of this study is to develop a method to detect non-Hodgkin's lymphomas early in pre-clinical models by evaluating tumor unsaturated lipid

metabolism (ULM) with magnetic resonance spectroscopic imaging. Early detection of lymphomas can result in earlier therapeutic intervention, which could increase patient survival and disease prognosis.
Sponsors: NIH (Pending), OMRF
PI/PDs: Kimberly B. Reed
Veterinary Pathobiology: Patricia Coutinho de Souza
OMRF: Rheal Towner

Geographic Response to a CHOP Based Chemotherapy Protocol in Dogs with Lymphoma
This project is a retrospective study involving many veterinary oncology centers across the United States. The goal of this study is to determine if geographical differences exist relative to disease free intervals and survival times in dogs with lymphoma in the United States receiving a standard chemotherapy protocol. It is a retrospective study to determine when dogs obtain remission, how long remission is maintained, and survival times.
Coordinating Investigator: Heather Wilson (Texas A & M University)
PI/PD: Kimberly B. Reeds

Low Level Laser to Treat Non-resectable Tumors in Dogs
This project is a collaboration between the Animal Medical Clinic (a private veterinary practice in Fayetteville, Arkansas), LiteCure LLC, and the Center for Veterinary Health Sciences at OSU. The aim of this project is to utilize a combination of treatments, including micro doses of chemotherapy, low level laser therapy, and photosensitizers to treat superficial, non-resectable tumors in dogs. The overall goal is to offer a novel treatment alternative to patients that are not good candidates for surgical intervention.
Sponsors: LiteCure LLC
PI/PDs: Kimberly B. Reeds, Kenneth E. Bartels
Animal Medical Clinic: Mike Mohler
LiteCure: Brian Pryor

Small Animal Physical Medicine Investigation
OSU Center for Veterinary Health Sciences is developing a robust program to complement current rehabilitation services and investigate innovative modalities in small animal physical medicine. These modalities include low level laser therapy, acupuncture, electro-acupuncture, ultrasound and transcutaneous electric nerve stimulation. In addition to clinical services, this program will provide didactic training for professional students, as well as, research opportunities to determine the effectiveness of these applications in veterinary medicine, further advancing the knowledge of complementary physical medicine.
Sponsors: Henthorne Foundation
PI/PD: Lara Sypniewski

Clinical Effectiveness of Low Level Laser Therapy in Reptilian Wounds
Reptiles have prolonged healing times relative to warm blooded species, with wounds taking as long as four to six weeks to heal; essentially twice as long as healing in a mammalian species. Rapid establishment of the skin's protective barrier is essential to decrease hospitalization time, lower the risk of infection, and reduce wound associated pain. Low level laser therapy has been extensively studied in many wound models, and this project will determine if this application will have similar clinical effects in a reptilian species. This research will advance our current knowledge of the effects of low level laser therapy on a novel wound model, allowing for continued investigation into its clinical applications for exotic species.

Sponsors: Henthorne Foundation, Kerr Foundation
PI/PDs: Lara Sypniewski, Connie Ketz-Riley, Kenneth Bartels
OADDL: Gregory Campbell
Statistics: Mark Payton

OKLAHOMA ANIMAL DISEASE DIAGNOSTICS LABORATORY

Veterinary Medical Diagnostic Program

The Veterinary Medical Diagnostic Program at the Oklahoma Animal Disease Diagnostic Laboratory (OADDL) serves to: 1) investigate and document injuries sustained by horses involved in racing and training on racetracks that fall under the jurisdiction of the Oklahoma Horse Racing Commission (OHRC); 2) monitor this population of migrating horses for the presence of any epizootic disease(s) that may pose a threat to the Oklahoma horse industry; and 3) evaluate the overall effects of all other aspects (including diet and stress) of racing and race training on the health and well being of Oklahoma's racehorses. This program is the result of an alliance formed between the OHRC and OADDL.
Sponsors: Oklahoma Horse Racing Commission, Oklahoma Bred Program.
PI/PD: Grant B. Rezabek

Equine Central Nervous System Disease Monitoring Program

Beginning in 2012, the Oklahoma Animal Disease Diagnostic Laboratory (OADDL) provides panel testing for equine central nervous system disease. The program is financially supported by the Oklahoma Department of Agriculture, Food and Forestry (ODAFF). Clinical cases identified by practitioners State-wide are eligible for funded screening of Equine Herpes Virus (1&4), West Nile Virus (WNV), Eastern Equine Encephalomyelitis (EEE), Western Equine Encephalomyelitis (WEE) and Venezuelan Equine Encephalomyelitis (VEE). Monitoring for these viral diseases is important to protect the valuable equine industry in Oklahoma. Reportable diseases are forwarded to the Federal Area Veterinarian in Charge (AVIC) and Oklahoma State Department of Health. The zoonotic potential of many of these arboviral diseases is also of concern to over-all Public Health.
Sponsor: Oklahoma Department of Agriculture, Food and Forestry (ODAFF)
PI/PDs: Grant B. Rezabek
ODAFF: Michael Herrin