Dr. Erik Hofmeister: Students may choose one of the following projects:
Surgical Knot Terminology Different names are applied to the same knots used in surgery. This would be a literature search to identify the names used in the literature and historically, as well as a survey to current surgeons to find out what they call certain knots.

ICU/IMC Patient Interactions Each time a care provider (student, technician, doctor) interacts with a patient is an opportunity for a problem to occur. Documenting the frequency of interaction and types of interactions will improve understanding of medical errors in a veterinary context. This would be an observational study where the student observes IMC and ICU for periods of time to quantify the patient interactions.

CV Accuracy Fifty-six percent of academic CVs in a recent study had one publication that was unverifiable or inaccurate. This would review all CVs submitted for internships to validate publications and verify the veracity of veterinary CVs.

Dr. Jeff Huang: *Lineage trace cells of gonadal origin in the adrenal gland.* The adrenal cortex can be divided into different zones based on its histological features and function. The current model of the adrenal cortex development is based on two lineage tracing mouse lines. Data from these two genetic models suggested that the adrenal cortex is composed of two distinct populations: the fetal zone and the adult zone. The fetal zone originates from the adrenaogonadal primordium, whereas the adult zone is developed from the stem/progenitor cells reside in the adrenal capsule. During development, cells in the fetal zone undergo regression and are replaced by the continuously renewing adult cortical cells from the capsule. AMHR2 (Anti-Müllerian Hormone Receptor Type 2) is mainly found in Müllerian duct, the primordial anlage of the female reproductive tract. It is also expressed in fetal ovary and testis. Surprisingly, by using the lineage tracing mouse model that labels *Amhr2*-positive cells, we found that the *Amhr2*-positive cell population contributes to both fetal zone and the adult zone. This is the first lineage tracing model that labels cells in both fetal zone and adult zone. The student will use double immunostaining to characterize the cell population originates from the *Amhr2*-positive cell population to further confirm this groundbreaking finding.

Dr. Constantinos Kyriakis: *Antigenic and genetic evolution of influenza A viruses in the presence of preexisting homologous or heterologous immunity in the porcine model.* Influenza A viruses (IAVs) infect a wide range of host species, including wild birds and poultry, humans, swine, horses and other mammals. Influenza is one of the leading causes of outbreaks of respiratory disease in humans, resulting in approximately half a million deaths every year world-wide. At the same time, it is the second most important viral disease in pigs, contributing to severe economic losses to the swine production industry. One important characteristic of IAVs is the fact that they escape immunity by antigenic drift, which is the result of the accumulation of point mutations, mainly in the gene segment expressing the hemagglutinin (HA) protein. This mechanism, which is not fully understood, is responsible for the annual outbreaks of disease in the human population despite previous exposures and preexisting immunity due to infection or vaccination. It is also the main reason why influenza vaccines in both humans and pigs are not highly efficient. In the proposed study we will use the porcine model to study this phenomenon. We will infect or vaccinate pigs with one of two strains of H1N1 IAVs: A/California/07/2009 or A/swine/North Carolina/154076/2015, generating a homologous or heterologous to challenge

immune response. We will then monitor both humoral and cell-mediated responses, and finally challenge pigs with A/California/07/2009. Following challenge, we will collect nasal swabs over a period of 10 days and deep-sequence them by Next Generation Sequencing (NGS). By analyzing the NGS data and combining them with our serology, we will identify patterns in virus evolution under different types of immune pressure, develop a model that could predict the trajectory of viral quasispecies and discover novel correlates of protection against infection and disease.

Dr. Amarjit Mishra: *Molecular mechanism of asthma pathogenesis*. The main goals of the laboratory is to identify novel pathways that regulate distinct feature of asthma pathogenesis in obesity, which then may inform us regarding the development of new treatment approaches. Obese asthmatics have a higher incidence of asthma complications and respond poorly to typical asthma medications, leading to greater healthcare utilization and a reduced quality of life. The major research theme of the laboratory centers on how obesity contributes to the proliferation and differentiation of dendritic cell (DCs) - restricted common DC progenitor cells (CDPs) and focused on understanding the imperative signals in progenitor cells involve in obesity-associated airway inflammation. The hypothesis is based on that obesity exacerbates airway inflammation in asthma by inducing the proliferation and differentiation of CDPs, which enhances the ability of DCs in the lung to promote adaptive immune responses. A specific objective of the research in the proposal is to identify novel endogenous signaling pathways and druggable targets in CDPs related to adaptive immunity that regulates airway inflammation in obesity. The proposal will utilize synergistic combination of murine models of experimental obesity induced airway inflammation and cellular investigations of immune and progenitor cell functions. The laboratory employs experimental techniques including airway hyperactivity measurements, multicolor flow cytometry, biochemical and immunological evaluation of the disease. Students may participate in both experimental procedures and laboratory research. This work is supported by the National Heart, Lung, and Blood Institute of the National Institutes of Health.

Dr. Haroldo Toro: *Viral diseases of commercial poultry.* Our laboratory seeks to understand infectious diseases affecting the poultry industry and develop strategies/tools to prevent outbreaks of disease.

Dr. Tommy Wheeler (SUMARC, USDA, ARS) ***Project 1:*** An experimental cattle vaccine to reduce colonization and shedding of E. coli O157:H7 will be evaluated in cattle during a feedlot experiment at USMARC. This will require repeated sampling of feedlot pen surface, cattle hides, and feces as well as extensive lab analyses of these samples to determine vaccine efficacy in simulated commercial conditions.
Project 2: A feedlot study will be conducted to understand if common treatments such as beta agonists and growth promoting implants are related to lameness in feedlot cattle. This study will use diverse genetic breeds of cattle to examine potential management by genetic interactions. Knee joint cartilage will be collected at slaughter for evaluation of health and function.

Location for both projects: US Meat Animal Research Center USDA, ARS
P.O. Box 166
Clay Center Nebraska 68933-0166

Drs. Melissa Singletary and Lucia Lazarowski: Post-whelping experiences of puppies is largely dependent on maternal behavior and has a significant impact on the subsequent physical and behavioral development of puppies. The Canine Performance Sciences (CPS) Program produces elite dogs that go on to serve high-profile roles in the United States in detection of explosives and other contraband/hazardous materials. To sustain the production of these leading canine athletes, CPS, in cooperation with the Small Animal Theriogenology Service at Bailey Small Animal Teaching Hospital, is investigating the influence of maternal behavior on the development and future outcome of offspring. Clinical management of the dam before, during, and after birth may influence maternal behavior. The student shall investigate literature regarding maternal behavior and its impact on puppy development, receive instruction in behavioral observation techniques, conduct systematic observations of dams and puppies, examine possible relationships between clinical management of dams and maternal behavior, evaluate potential predictors of maternal behavior and analyze and report findings. As a collaborative activity in association with the Theriogenology Service, the student will be exposed to clinical duties in the Bailey Small Animal Teaching Hospital under the guidance of Dr. Robyn Wilborn (e.g., canine breeding, management of pregnancies and C-sections, postpartum and neonatal care). Additionally, this person will assist in puppy development activities and observe training sessions with CPS staff to better understand what is required of these dogs and how performance is measured. Some weekend duties may be required (depending on due dates and C-sections), but schedules will be arranged with ample planning and weekend duties will be shared with the student from Dr. Wilborn's Summer Scholar project.

Dr. Bruce F. Smith: *Molecular Genetics of Cancer.* Several projects are available in the area of gene therapy for cancer. Projects include laboratory studies and pre-clinical and clinical trials for dogs with osteosarcoma, lymphoma, melanoma, mast cell tumor and breast cancer. These studies involve the creation, evaluation and administration of gene therapy vectors and novel biological molecules, and the assessment of patient progress, as well as detailed laboratory assessments of the impact of the therapy. The latest genetic approaches may be used to understand the basis of the disease. Projects involve the use of a wide variety of techniques including RNA and DNA isolation, quantitative PCR amplification, cell culture and flow cytometry as well as animal handling, phlebotomy, tissue biopsy and necropsy.

Manuel F. Chamorro. Respiratory disease is the leading cause of death of nursing beef calves older than 3 weeks of age. Economic losses to the United States (US) beef cow-calf industry associated with this condition are approximately $165 million/annually. Bovine respiratory viruses such as bovine viral diarrhea virus 1 and 2 (BVDV 1; BVDV 2); bovine herpesvirus 1 (BHV-1), and bovine respiratory syncytial virus (BRSV) play an important role in the pathogenesis and clinical presentation of respiratory disease in young calves. Maternal antibodies derived from colostrum provide clinical protection against BVDV, BHV-1, and BRSV infection in calves. The higher the initial antibody titer absorbed from maternal colostrum, the longer the duration of passive immunity. Calves that nurse colostrum from dams vaccinated during gestation may have greater initial serum antibody titers against respiratory viruses such as BVDV, BHV-1, and BRSV from maternal colostrum; however, it is unknown the amount of colostrum-derived virus-specific IgG (i.e. BVDV, BHV-1, BRSV-specific IgG) translocated to the calf's upper respiratory tract mucosa and its decay rate in nasal secretions. Additionally, it is unknown if vaccination of pregnant beef cows before calving with a multivalent inactivated-

virus vaccine results in grater concentrations and persistency of virus-specific IgG in nasal secretions of calves that nurse colostrum from vaccinated dams. If vaccination during gestation results in greater levels and persistency of virus-specific IgG in nasal secretions of beef calves, this will allow veterinarians and producers novel to modify current vaccination protocols in cow-calf beef operations to reduce the incidence of respiratory disease in young calves.

Dr. Douglas Martin: *Molecular Therapy of Neurodegenerative Disease.* The laboratory's model of neurodegenerative disease is feline gangliosidosis, similar to human Tay-Sachs disease, a disorder in which abnormal function of lysosomes causes progressive nervous system dysfunction and death. Though first reported in 1881, Tay-Sachs disease remains virtually untreatable, and affected children die by 5 years of age after spending several years in a semi-vegetative state. However, new gene therapy strategies have been tested in mouse models of gangliosidosis with excellent results. Before inclusion in human clinical trials, new therapies are tested in the feline model for safety and therapeutic benefit. The laboratory employs a variety of experimental techniques including intracranial injection of therapeutic agents, MRI-based analyses of disease progression, and biochemical and molecular biological evaluation of therapeutic benefit. Students may participate in both experimental procedures and laboratory research. This work is part of an international effort of collaborative scientists and physicians, the Tay-Sachs Gene Therapy Consortium, whose goal is to begin gene therapy clinical trials in humans.

Dr. Robyn Wilborn: For pregnant dogs, accurate prediction of whelping date is paramount to a successful delivery. The Small Animal Theriogenology service commonly monitors normal and abnormal canine pregnancies via ultrasonography and hormonal testing. Outside of client-owned dogs, the Theriogenology service is responsible for year-round reproductive management of the Canine Performance Sciences (CPS) detection dogs (adult breeding animals, neonates, and puppies). The student working in this position will help our lab investigate the prediction of accurate whelping dates based on available diagnostic tools and will compare data between CPS dogs and client-owned animals via a retrospective analysis of medical records. This student will be exposed to all aspects of clinical canine theriogenology including planned breedings, pregnancy diagnosis, C-sections, and neonatal care. Additionally, they will assist with puppy development and training alongside CPS staff to gain a better understanding of the CPS program and reproductive management goals. Study of patient breeding records and published literature will be expected as part of the data collection process. Student will become proficient in canine theriogenology techniques by the end of the program, as well as develop their clinical skill set with a great degree of hands-on canine experience. Some weekend duties will be required (depending on estrus cycles), but schedules will be arranged with ample planning and weekend duties will be shared with the student from Dr. Singletary and Lazarowski's project.

Maria Naskou, Peter Christopherson, Beth Spangler: *Laboratory evaluation of dogs with thrombocytopenia.* Laboratory evaluation of dogs with thrombocytopenia relies on performing complete blood cell count and a coagulation panel. However, specific values provided by the hematology analyzer such as plateletcrit, mean platelet component, and platelet volume distribution width might provide relevant information when evaluating patients with diseases such as immune-thrombocytopenia (ITP). Moreover, testing of platelet function and thromboelastography (TEG) might provide useful information to predict the bleeding risk in

patients with thrombocytopenia and possible guidance regarding the management of the disease. The main objective of this study is to compare platelet parameters provided from the hematology analyzer (Advia 120) in healthy dogs and dogs with marked thrombocytopenia to determine whether those could be used to predict risk of bleeding. Medical records and laboratory data from dogs with a platelet count <30,000/ul will be retrieved and platelet parameters will be compared to those from healthy dogs. Other variables such as treatment, evidence of hemorrhage and presence of infectious diseases will be evaluated. A minimum concentration of platelets is required for accurate performance of platelet function testing and TEG. Thus, whole blood from healthy patients will be obtained and samples containing variable platelet concentrations ranging from 20,000 to 100,000/ul will be prepared and used for platelet function testing (aggregation and activation) and TEG. Activation of platelets will be assessed following stimulation with an agonist and expression of P-selectin via flow cytometry. Aggregation of platelets will be assessed via flow cytometry following gating of the platelets for CD61 and CD45. This study will provide useful information regarding clinical and laboratory evaluation of patients with thrombocytopenia and data from this study will be used in subsequent studies to demonstrate the use of platelet function and TEG in evaluation of bleeding risk in dogs with ITP.

Dr. Maureen McMichael: *Working K9s: Optimizing Quality of Life.* Working dogs are essential to many facets of security, safety, rescue, and health. New uses are detection of cancer, bed bugs, pythons, mold, and a host of ecological conditions. They assist diabetics, the hearing and sight impaired, and for seizure alert. Security dogs as well as search and rescue dogs save lives every day and their numbers are increasing significantly. Our group focus is optimization of the quality of life for working dogs and there are several themes under that umbrella. Currently there are no data on how many working dogs are active in the U.S. and there is no mandatory reporting of deaths or illnesses among working dogs. There are no data on K9 team structure, training frequency, training venues, work schedules, rest cycles, night shifts, or emergency response. Gathering this data will help to inform guidelines for schedules, prevention for specific illnesses, considerations for night shift and optimization of emergency response. Working dogs suffer a battery of conditions unique to their specific work. PTSD is devastating to dogs and their handlers. The military identified canine PTSD (C-PTSD) and estimates that it occurs in up to 10% of military working dogs (MWD). C-PTSD occurs in non-military working dogs and in civilian dogs and it is usually from trauma, abuse, isolation (e.g., animal control), or hospitalization. There is no data on how many working and civilian dogs in the U.S. suffer from PTSD, though it is likely to be much higher in shelter populations. It is also very likely that PTSD makes shelter dogs unadoptable. Options for treatment, particularly in shelter dogs would need to be inexpensive, non-invasive, and easily administered. One research theme of our group is the health of working dogs and this includes estimating how many dogs suffer from PTSD in the U.S. This will set the stage for justification of future funding. Our group is also researching options for treatment of PTSD that include specific sound frequencies, probiotics, and some training techniques.

Dr. Dawn Boothe. *Impact of Cannabinoids on Drug Movement.* The Clinical Pharmacology Laboratory has oriented its Summer Scholars Research toward the study of cannabinoids in animals. This includes molecular studies that characterize cannabinoid receptors in the tissues of companion animals, pharmacokinetic studies that characterize the disposition of cannabidiol in

companion animals, therapeutic drug monitoring and survey-based studies that examine the clinical efficacy of cannabidiol, and molecular studies that are exploring the impact of various endogenous, phyto, and synthetic cannabinoids on cancer tissues. This summer, we would like to begin to explore the impact of phyto and possibly synthetic cannabinoids on proteins that influence drug disposition, and specifically transport proteins (eg, P-glycoprotein and other efflux pumps), drug metabolizing enzymes (cytochrome P450) and their regulators, using primarily canine cells. The successful applicant will work with both Dr. Boothe and Dr. Pondugula.

Drs. Lindsey Boone and Reid Hanson: *A Study of the Visco-elastic and Friction Profiles of Equine Cartilage Surfaces.* Our lab seeks to characterize and compare the material properties of cartilage located within various joints of the equine limb. Specifically, we will investigate the visco-elastic stiffness and friction coefficient of the biphasic cartilage structure. These biphasic properties affect the performance of the joint as it carries different loads and motions. We are investigating to determine if different types of joints with different ranges of motion possess similar or different material properties and which properties are best suited for the joint's individual conditions. Analyzing the various cartilage surfaces within each joint and between joints will lead to a better understanding of the mechanisms controlling the performance of healthy joints in horses and humans. This data will be used to translate onto the design of better human artificial joints. Articular samples will be extracted from horses and analyzed in the Multiscale Tribology Laboratory, a multidiscipline lab between the Samuel Ginn College of Engineering and the College of Veterinary Medicine. Cartilage surface geometries will be characterized using nano-scale surface profilometry, scanning and transmission electron microscopy and mathematical/numerical modeling techniques to analyze the structure of the surfaces over many scales. The key is to mesh the geometries at multiple different scales into one complete model.

A Study on the Co-culture of Equine Cartilage and Synovium. The student will also participate in our laboratory seeking to characterize an in vitro model of osteoarthritis that more accurately reflects the in vivo articular environment. The student will learn techniques for harvesting osteochondral explants as well as learn methods for establishing synoviocyte and chondrocyte cultures to be stored for later studies. A study investigating mitigation of the chondrotoxic effects of local anesthetics on articular cartilage and synovium. The student will learn cell culture techniques, ELISA, and PCR analysis.

Dr. Emily C. Graff: *Fibroblast growth factor 21 in feline health and disease.* One of the current projects in my lab, explores the physiological role of the metabolic regulator, fibroblast growth factor-21. Fibroblast growth factor 21 (FGF21) is a potent regulator of lipid homeostasis and targets both the liver and adipose tissue. As a member of the endocrine family of fibroblast growth factors, it acts primarily on the FGFR1c receptor in conjunction with the co-receptor β-klotho in multiple organs to improve glucose and lipid homeostasis. The use of FGF21 analogs and gene therapy is currently being explored as therapeutics for obesity and obesity-related syndromes like non-alcoholic fatty liver disease, dyslipidemia, and type 2 diabetes, in people. Treatment with FGF21 analogs improves circulating lipoprotein and triglyceride values, body weight, and increases serum adiponectin. There is evidence that the beneficial effects of FGF21 extend beyond the direct metabolic effects. Recent literature indicates that FGF21 can act as an exocrine

pancreatic secretagogue and in mice, and FGF21 can ameliorate experimentally induced pancreatitis. Diseases, including obesity, hepatic steatosis, and pancreatitis are relatively common in domesticated cats, and present with both therapeutic and diagnostic challenges. Despite the importance of FGF21 in metabolic health, the physiology of FGF21 in domestic cats is unknown and there are currently no available methods to evaluate endogenous FGF21 or to detect FGF21 in tissues. The summer scholar in our lab will join our lab group and work focus on this project to explore the physiology of FGF21 in domestic cats.