**Dr. 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 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 into the design of better human artificial joints. Articular cartilage 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.

**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.

**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 untreated, 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. 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. Jeff Huang: Lineage trace cells of gonadal origin in the adrenal gland. Testis, ovary and the adrenal gland share a common primordium. During development, a group of cells separates from this common primordium and forms the fetal adrenal cortex. However, the molecular events driving the cell differentiation of adrenal cortical cells from gonadal cells are poorly understood. AMHR2 (Anti-Mullerian Hormone Receptor Type 2) is found on the surface of Mullerian duct cells. In males, Mullerian duct regresses during development. In females, it becomes the uterus and fallopian tube. This gonad-specific gene, Amhr2, has not been reported to be expressed in the adrenal gland. In our lineage tracing mouse model, we found that a group of cells in the adult adrenal gland originates from the Amhr2-positive cell population. The student will learn how to characterize this cell population in the adrenal gland and also study its cell fate throughout development.

Dr. Maninder Sandey: Nanobody-based drug conjugate for targeted therapy of canine oral melanoma. Canine oral melanoma is a highly aggressive disease with a median survival time ranging from 3 to 18 months, depending on the stage at diagnosis. Surgery is used for the control of non-invasive tumors; however, treatment options are limited and ineffective for the cure of metastatic disease. Thus, it is vital to investigate novel therapeutic modalities for the treatment of cancers in pet animals. In recent years, antibody-drug conjugates (ADCs) have revolutionized the field of human cancer therapy. Antibody-drug conjugates (ADCs) target specific antigens overexpressed on tumor cells and deliver cytotoxic drugs specifically to tumor cells that are otherwise too toxic for normal cells. Although ADCs are very powerful in the treatment of human cancer, their production is very difficult and cost prohibitive to be an affordable treatment option for pet animals. The single domain antibodies also called as nanobodies can provide answers to several of these concerns. Thus, our primary goal is to identify nanobodies that bind specifically to canine chondroitin sulfate proteoglycan 4 (CSPG4), a tumor-specific antigen that is highly expressed on several hematological and solid cancers in humans and dogs. The identified anti-CSPG4 nanobody will be conjugated with monomethyl auristatin E (MMAE) to develop a nanobody-drug conjugate, which will selectively bind and deliver cytotoxic drug to CSPG4 expressing canine melanoma cells.
**Dr. Amol Suryawanshi:** *Cancer Immunotherapy & Anti-viral Immunity.* Our laboratory’s research mainly focuses on targeting immuno-regulatory signaling pathways in dendritic cells (DCs) to regulate CD4+ and cytotoxic CD8+ T cell responses during tumor progression and viral infections (Influenza A Virus and Herpes Simplex Virus). The long-term goal of our lab is to develop novel immunotherapies targeting DCs to suppress tumor progression and promote anti-viral immunity. We are using different *in vitro* and *in vivo* experimental approaches to identify DCs-specific molecular and cellular targets that play an important role in evasion of host tumor and anti-viral immunity. Summer scholar working in our lab will have an opportunity to learn different cellular & molecular immunology techniques such as cell surface, intra-cellular and intra-nuclear staining, flow cytometry, cell-sorting using magnetic beads, ELISA, Western-blot, mouse genotyping, PCR, RT-PCR, mammalian cell culture including various tumor cell lines, primary immune cell isolation and culture, bone marrow differentiation to DCs, T cell differentiation and proliferation assays, apoptosis assay, phenotypic and functional characterization of immune cells, virus culture, virus quantification by plaque assay, immunometabolism etc. Summer scholar will get an exposure to design hypotheses, experimental plan of study, conduct basic cellular immunology research, analyze and interpret data. Preliminary *in vitro* studies will be conducted using mouse bone marrow derive DCs (BMDCs) treated with tumor cell supernatants or co-cultured with various tumor cell lines (melanoma, lymphoma, breast cancer etc.) in the presence or absence of different agonist/antagonists of immunoregulatory signaling pathway/s to analyze the DCs immunogenicity. Further *in vitro* studies will be carried out using BMDCs generated from DCs-specific conditional knock-out mice followed by *in vivo* studies using mouse syngeneic tumor models.

**Dr. Paul Walz:** Infections with *Bovine viral diarrhea virus* (BVDV) are endemic worldwide and bovine viral diarrhea is recognized as one of the most important infectious diseases of cattle. Infection of pregnant cattle prior to day 125 of gestation can result in the birth of calves that are immunotolerant to and persistently infected with BVDV. This infection of the developing fetus and the subsequent generation of persistently infected calves delivers the most significant reservoir of BVDV. Control of BVDV relies upon eliminating this reservoir and limiting transmission from infected individuals to susceptible animals. Testing and removal of persistently infected calves often involves testing of calves after birth. Since these PI calves often are less than 0.5% of the population, testing of all calves becomes necessary to identify the few. Our BVDV research lab has recently begun exploring the possibility of testing dams, in order to identify those cows who may be harboring these persistently infected fetuses. If methods are established and validated, this will allow beef and dairy cattle producers to identify at risk cows and segregate them prior to calving in order to eliminate exposure to the entire herd. Students will participate in both on-farm and laboratory activities as part of this project.

**Dr. Vinicia Biancardi:** *Brain signaling mechanisms in cardiovascular diseases.* Dysregulation of Angiotensin II (AngII), a pivotal contributor to exacerbated sympathoexcitation during hypertension, has been associated with brain inflammation. Our first studies support the involvement of the blood-brain barrier (BBB) disruption within critical brain regions involved in cardiovascular function during hypertension. They reveal a novel AngII-mediated feed-forward mechanism, by which elevated circulating AngII is associated with increased BBB permeability during hypertension, facilitating its access to the hypothalamus and brainstem. In association with BBB disruption, we found AngII promoting microglia activation and consequent inflammation
within the hypothalamus, and we became interested in understanding its possible underlying mechanisms. We are currently investigating whether a functional interaction between AngII and innate immunity contributes to BBB disruption and redox dysregulation within CNS cardiovascular nuclei, ultimately contributing to sympathoexcitation in hypertension. Experimental techniques in the lab include survival and non-survival rodent surgeries, immunofluorescence, confocal image, real time-PCR, and in vivo measurements of cardiac function, among others.

**Dr. Katie Horzmann:** Investigating developmental toxicity using the zebrafish model. I work with emerging and legacy environmental toxicants and study the effects of developmental exposure to these chemicals using the zebrafish (*Danio rerio*) biomedical model. Exposure to environmental toxicants during embryogenesis has been associated with adverse health effects including immune system dysfunction; obesity and metabolic syndrome; altered neurodevelopment and neurological deficits; and cancer. Student scholars would be able to join in a project investigating the toxicodynamics (effect of the toxicant on the body) and toxicokinetics (effect of the body on the toxicant) of trichloroethylene in larval zebrafish. Trichloroethylene is a legacy industrial solvent and degreaser that contaminates over half of all Superfund sites, is a known carcinogen, and is linked to adverse health outcomes including congenital cardiac defects and neurotoxicity. In addition to learning zebrafish husbandry and handling skills, scholars could evaluate embryonic mortality and hatching, embryonic and larval physical development and behavior, and gene expression alterations after developmental trichloroethylene exposure.

**Drs. Lindsay Starkey and Sarah Zohdy:** Vector-borne pathogens in dogs and cats from the Southeast and Caribbean. Diseases caused by vector-borne pathogens continue to plague not only veterinary medicine, but human health as well. Collaboratively, our laboratories are interested in the types and prevalences of vector-borne pathogens present in dogs and cats from the local region. This project would involve preparation and evaluation of blood smears, interpretation of patient-side diagnostic tests, as well as gross and molecular identification of vectors and vector-borne pathogens.

**Dr. Paul Waggoner:** Pregnancy is a dynamic event in all species, with offspring influenced by the intrauterine environment, maternal stressors, and medical interventions. The Canine Performance Sciences (CPS) Program produces elite dogs that go on to serve high-profile roles in the United States in contraband detection and prevention. To sustain the production of these leading canine athletes, CPS, in cooperation with the Small Animal Theriogenology service at Bailey Small Animal clinic, is investigating the influence of clinical medicine on the development and future outcome of offspring. The student participating in this role will be exposed to clinical duties in the Bailey Veterinary Teaching Hospital under the guidance of the Small Animal Theriogenology Service (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 parameters are scored. Individual review of patient hospital records will be key to the data collection process, and this information will then be analyzed to better characterize how circumstances that occur during pregnancy, birth and neonatal life might be used to predict performance characteristics of offspring. 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. Robyn Wilborn’s project.

**Dr. Robyn Wilborn:** Optimal use of genetic resources is a central aspect of reproductive success. For valuable stud dogs, this involves the accurate assessment of semen quality prior to cooling or cryopreservation efforts. The Small Animal Theriogenology service commonly admits male dogs for semen collection, evaluation, and storage of spermatozoa for dog owners and dog breeders. 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 proper management of semen samples for analysis of male fertility parameters. 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 semen evaluation 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 may 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. Paul Waggoner’s project.

**Dr. Anne Wooldridge:** Deficient vascularization and subsequent ischemia are common components of multiple disease mechanisms affecting horses and treatment options are limited. Regenerative medicine provides exciting therapeutic options, but variability and lack of differentiation into the tissue of interest are common in clinical studies using stem and progenitor cells, and the cells are one source of variation. Endogenous endothelial progenitor cells (EPCs), specifically late outgrowth endothelial colony forming cells (ECFCs), are important in repair of vascular injury and in revascularization of ischemic tissues. Similarly to humans, horses of different ages, fitness, and health status are very likely to have different functional capability of endogenous (autologous) ECFCs. Biological scaffolds have a key role in stem cell therapy by mechanically ensuring that cells remain at the site they are administered and by regulation of the stem cell microenvironment, which are keys to cell survival and engraftment of the delivered therapeutic cells into the native, diseased tissue. Our group has demonstrated a safe and effective method of cell delivery using injectable, cell-laden hydrogel microspheres, and we have shown clinical improvement in a research model of equine distal limb wounds treated with ECFCs. Now our goals are to reduce some sources of clinical variability by developing optimized endothelial phenotype in lines of ECFCs for potential allogeneic use and to show evidence of cell engraftment and differentiation by demonstrating neovascularization in a more controlled setting. We have a system to produce highly uniform, injectable cell-laden microspheres with high cell viability after injection. We will use modified isolation procedures to gain a more homogeneous population of ECFCs from the peripheral blood of young adult, athletic horses and culture those cells with equine specific growth factors (platelet lysate and conditioned media from equine adipose derived mesenchymal stem cells (AdMSCs)) to produce highly functional
lines of ECFCs for allogeneic testing. The summer scholar student will be involved in ECFC isolation, cell culture, and growth in the different types of media.