Are you interested in research and/or want to learn more about scientific research in animal agriculture and biomedicine? If so, you may be interested in participating in the Utah State University (USU) Animal, Dairy and Veterinary Sciences (ADVS) Summer Undergraduate Research Internship Program. In this program, you will work under the guidance of a faculty member in the ADVS Department and his/her graduate students and other laboratory personnel.

**Areas of study include:**
- Animal Health and Disease
- Animal Models for Biomedical Research
- Animal Molecular Genetics
- Animal Nutrition and Growth Biology
- Biotechnology, Epigenetics and Stem Cells
- Reproduction and Development
- Toxicology
- Virology and Antiviral Research

**Eligibility:**
- We anticipate two positions will be available for ADVS students currently enrolled with a minimum GPA of 3.0 AND
- We anticipate two position will be available for students across USU or at other universities with a minimum GPA of 3.0.
- Student must be a continuing student in the fall.

**Program Dates:** Internship participation is 12 weeks between May through August 2022.

**Applications available at:** [https://usu.co1.qualtrics.com/jfe/form/SV_cMZ9R7tDoiA9VNC](https://usu.co1.qualtrics.com/jfe/form/SV_cMZ9R7tDoiA9VNC)
**Applications are due Friday, March 25, 2022 at 5:00 pm.** Selection will be made by April 6, 2022.

**Benefits:**
- $4,000 stipend for the summer.
- Valuable experience in a world-class university research environment.
- Hands-on laboratory and/or animal research experience.

**Selection of Interns** will be made by April 6, 2022 at 5:00pm. *For any inquiries please contact Cara Allen in the ADVS Office at 435-797-2162 or cara.allen@usu.edu*
Project title: **Dietary intervention with cocoa polyphenols to promote gut homeostasis and prevent colitis-associated colorectal cancer**

Principal investigator: **Dr. Abby Benninghoff**  [https://caas.usu.edu/directory/benninghoff-abby](https://caas.usu.edu/directory/benninghoff-abby)

Research area: diet, cancer and the gut microbiome

Background: Recent high-profile studies have established a link between our food system, the gut microbiome and chronic human diseases, and have suggested modification of the microbiome may improve health. In order to understand the mechanistic links between these factors, pre-clinical animal models are necessary for both discovery, and to guide human clinical studies. However, current animal models of chronic disease poorly emulate both the nutritional patterns and resulting gut microbiome of Americans, which decreases the applicability of such models to diseases related to diet and the gut microbiome, including colorectal cancer (CRC). In order to address these deficiencies, our group has developed two innovative approaches to pre-clinical animal model research: 1) a new mouse diet formulation that emulates an average American diet, called the total Western diet, and 2) a simplified method to humanize the mouse microbiome.

Project description: Dietary strategies to reduce colonic inflammation and promote gut homeostasis may reduce risk of colitis-associated colorectal cancer (CAC). Dark chocolate is rich in cocoa polyphenols that have demonstrated health benefits via their antioxidant and anti-inflammatory actions. However, there remains a substantial knowledge gap regarding the role of the gut microbiome in mediating the purported health benefits of cocoa polyphenols. The overall objective of this study is to determine the direct effects of dietary supplementation with cocoa powder that is enriched for cocoa polyphenols on gut health, including assessment of colitis and composition of the gut microbiome. We will employ an integrated, translational approach using the azoxymethane+dextran sodium sulfate model of CAC that incorporates a prudent diet and a Western diet as part of the experiment design and that considers the role of gut bacteria in health maintenance and/or disease development. Our goal is to determine the impact of dietary supplementation with cocoa polyphenols on symptoms of colitis, inflammation and mucosa injury in the colon. This project is supported by the USDA National Institute of Food and Agriculture and addresses a current USDA research priority, to investigate whole food approaches to promote gastrointestinal health.

Duties and responsibilities: This project will begin May 2022 in the laboratory of Dr. Benninghoff. The intern will work closely with Dr. Benninghoff’s graduate students. This schedule will allow for the intern to be involved in the routine animal care, colitis assessments, and sample processing. Students will also learn lab assays for isolating DNA from fecal samples for microbiome assessment. Interns may also provide assistance in other analyses of samples obtained from prior studies, including continued analysis of gut microbiome samples. Interns will be required to complete Lab Orientation (1 hour), Basic Lab Safety Training (4 hours), LARC Animal Training (1 hour), and Sexual Harassment Training (2 hours).
Project Title: Influence of Trace Minerals on Quantity and Quality of In Vitro Produced Embryos

Principal Investigator: Clay Isom https://caas.usu.edu/directory/isom-clay

Research Area: Reproduction & Development; Developmental Genetics and/or Epigenetics

Background: Early embryo mortality is a major source of reproductive inefficiency in agricultural and research animal settings around the world. In beef cattle, mice and humans, and swine as few as 50% of successfully in vivo-fertilized embryos survive pre- and peri-implantation development; in dairy cattle and horses, early embryonic losses can approach or even exceed 70%! In many circumstances, implementation of so-called assisted reproductive technologies (ART) are undertaken to enhance or supplement ‘natural’ reproductive processes. Unfortunately, embryo survival is generally even lower using in vitro techniques. While many causes of early embryonic failure have been documented in in vitro produced embryos – gross chromosomal abnormalities, immunological rejection of the conceptus, luteal insufficiency, and/or a compromised uterine environment, e.g. – the majority of preimplantation embryonic deaths remain unexplained. The research focus of the Isom lab is on fundamental aspects of oocyte maturation and early embryo development that relate to improving the efficiency of natural and assisted reproduction in domestic livestock animals. Specifically, we intend that this research will build on previous efforts to describe the development, maturation, and proper function of mammalian oocytes and embryos, using samples generated in vitro and in vivo. This work will strengthen the basic foundation of knowledge regarding early mammalian embryo development and hopefully result in very practical approaches to improving the efficiency of reproductive technologies in domestic livestock species.

Project Description: Production of embryos in a laboratory for research, agricultural, or human clinical purposes generally involves subjecting gametes and embryos to two prolonged culture periods (in vitro oocyte maturation [IVM] and in vitro embryo culture [IVC]) in highly artificial culture media. Both IVM and IVC media have negative effects on embryo developmental potential, probably because their incomplete and artificial nature does not exactly match the in vivo environment. We have preliminary data to suggest that the standard embryo culture media for pig and cattle embryos are significantly deficient in the following trace minerals: calcium (~60% of ‘normal’ biological levels), chromium (12% of ‘normal’), copper (18%), iron (26%), magnesium (32%), phosphorus (15%), selenium (<1%), and zinc (2%). And we have reason to believe that most (all?) other embryo culture medium formulations will be similarly deficient in many of these critical micronutrients. We therefore propose to study the impact of trace mineral supplementation on the performance of embryos cultured in vitro. The objectives for this experiment are two-fold: 1) provide a more thorough characterization of the trace mineral content of medium designed for in vitro embryo culture and how it compares to that of normal oviductal and/or uterine secretions that support embryo development in vivo; and 2) explore the role that trace minerals might play in dictating embryo developmental potential and quality.

Duties and Responsibilities: The student selected to work on this project will participate in making embryo culture medium, collecting biological samples from animals, culturing oocytes and embryos in the laboratory, recording developmental data on in vitro produced embryos, staining embryos to count cells, isolating mRNA from oocytes and embryos, performing quantitative gene expression analysis on harvested mRNA, and other tasks as necessary. There will be a good assortment of animal, cell culture, and molecular biology work. This will need to be an organized and exceptionally motivated student.
Project Title: Biology of Zika Virus Infection

Principal Investigator: Dr. Young-Min Lee [https://caas.usu.edu/directory/lee-youngmin]

Research Area: Molecular Virology

Background: Zika virus (ZIKV), a mosquito-borne flavivirus closely related to Japanese encephalitis virus (JEV), is causing an unprecedented ongoing epidemic in the Americas. Infection with ZIKV can lead to severe neurological diseases, including microcephaly in newborns and Guillain-Barré syndrome in adults. Despite the recent emergence and rapid spread of ZIKV in Latin America and its explosive pandemic potential, no vaccine or antiviral drug is available for ZIKV, and little is known about its life cycle, in vitro or in vivo. A key barrier to investigating ZIKV biology and to developing vaccines and therapeutics against ZIKV is the lack of a reverse genetics system (also known as “infectious cDNA technology”), a platform to rescue infectious ZIKV entirely from a cloned cDNA that allows for direct manipulation of the viral genomic RNA. In our previous work, we developed the first infectious cDNA clone for the live-attenuated JEV vaccine (SA14-14-2) approved for clinical use in humans. Recently, we also created a unique panel of three infectious ZIKV cDNA clones, for each of three spatiotemporally distinct and genetically divergent strains. Using the three molecularly cloned ZIKVs, together with a variety of newly established cell culture and mouse model systems for ZIKV infection, we have demonstrated cell type-dependent ZIKV replicability in vitro and mouse strain-specific ZIKV pathogenicity in vivo. Our research accomplishments with both JEV and ZIKV offer a unique opportunity for the rational design of a recombinant virus vaccine against ZIKV.

Project Description: Using newly developed, bacterial artificial chromosome-based reverse genetics systems of both ZIKV and JEV, the intern student will participate in generating and characterizing genetically modified viruses for the study of viral replication and pathogenesis.

Duties and Responsibilities: The intern student will learn a number of basic molecular biology techniques to create recombinant viruses entirely from a cloned cDNA and characterize their biological properties in the virus life cycle.
Project Title: **Identification of the ovary-dependent and germ cell-independent metabolic and physiologic mechanisms that regulate health span and life span in post-reproductive females.**

Principal Investigator: **Dr. Jeffrey Mason** [https://caas.usu.edu/directory/mason-jeffery](https://caas.usu.edu/directory/mason-jeffery)

Research Area: Physiology of Reproductive Senescence

Background: Young, reproductively-cycling women hold a significant health advantage over similarly aged men. As reproductive cycling continues, both ovarian germ and somatic cells are continually depleted until the time of menopause, when a large proportion of these cells are lost, along with the female health advantage. At the time of menopause, disease rates in women begin to exceed those of men. Current treatment in the form of hormone replacement therapy is often unpredictable and comes with several limitations and adverse effects, and is focused on replacing only a portion of the ovarian function lost at menopause.

Research from our lab shows that replacement of senescent ovaries in post-reproductive mice with young, cycling ovaries extends longevity and ameliorates age-associated dyslipidemia and chronic inflammation. In a pilot study, depletion of germ cells prior to transplantation enhanced the longevity-extending effects of the young, transplanted ovaries and, as with germ cell-containing ovaries, decreased the severity of inflammation, but did so independent of germ cells. In germ cell-depleted primitive species, longevity extension is dependent on the up-regulation of Foxo signaling. In mammals, Foxo suppresses the de novo methyltransferase Dnmt3b and reduces the age-associated erosion of methylation patterns and epigenetic reprogramming. Foxo signaling is also linked to gender-specific longevity in centenarians. Ovarian Foxo signaling is significantly reduced at menopause due to the loss of Foxo-producing ovarian tissue.

Project Description: Determine how young intact and germ cell-depleted ovaries affect age-related changes in health, DNA methylation, transcription, dyslipidemia and chronic inflammation in post-reproductive mice. Based on our preliminary data, we hypothesize that transplantation of young ovaries will improve health and slow/avert the age-related epigenetic reprogramming of metabolism- and immune-regulating genes in post-reproductive female mice. We expect to quantify differences in methylation and transcription profiles of metabolism and immune function genes in post-reproductive female mice and that these age-related differences will be mitigated by transplantation of young ovaries both with and without germ cells.

Duties and Responsibilities: The intern student will learn microsurgery and to assess health with in vivo health span assays, DNA methylation by reduced representation bisulfite sequencing, gene expression by RNA sequencing, immune function changes by T-cell, cytokine and pathological analyses and dyslipidemia by in vivo lipid tolerance and circulating lipoprotein levels in post-reproductive mice.
Cystic fibrosis (CF) is a progressive, genetic disease that causes long-lasting lung infections and limits the ability to breathe over time. It is caused by a mutation, in a gene called CFTR (cystic fibrosis transmembrane conductance regulator). This gene controls the flow of salt and fluids in and out of cells. If the CFTR gene doesn't work the way it should, a sticky mucus builds up mainly in the lungs and pancreas and blocks tubes, ducts, and passageways. Treatments may ease symptoms and reduce complications but there is currently no cure for CF. The sheep is a potentially ideal model to study CF as the development and function of the respiratory epithelium and the immune system of the sheep lung is similar to the human.

This project will examine how these CFTR mutations affect (a) lung anatomy; (b) pancreas anatomy and (c) the inflammation status of lung and pancreas of CF sheep at birth and 6 months of age to better understand the progression of this disease and identify possible therapy targets. We have generated cystic fibrosis sheep models using gene editing and animal cloning techniques. We will also examine lung anatomy, pancreas anatomy and the inflammation status of lung and pancreas of these

The student who conducts this project will be responsible for evaluating the presence of immune cell populations in the lung and pancreas tissue of the CF sheep models using quantitative PCR and immunohistochemistry analyses. Liver and proximal and lung tissue samples will be collected, and tissue sections will be acquired for immunohistochemical analyses to evaluate the presence of immune cell populations such as T cells, mast cells, macrophages and B cells as well as cytokines. This work should ultimately translate into novel therapies to fix or replace the defective CFTR gene.
Project Title: Understanding how trace minerals impact growth of cultured bovine satellite cells in the presence of anabolic hormones

Principal Investigator: Dr. Kara Thornton-Kurth  https://caas.usu.edu/directory/thornton-kurth-kara

Research Area: Growth and Nutrition

Background: Dr. Thornton’s research program aims to gain a deeper understanding of how different nutritional strategies alter molecular mechanisms within the skeletal muscle resulting in changes in growth and quality of end-products in production animals. One of the projects that is currently underway is investigating the interaction between trace minerals and anabolic implants in growth of skeletal muscle. Anabolic implants improve skeletal muscle growth in beef cattle. Approximately 90% of feedlot cattle in the US receive at least one anabolic implant in their life, which results in a 15-20% improvement in growth. Recent research demonstrates that cattle that receive an implant have increased requirements for trace minerals. As such, we will be conducting some cell culture studies to determine how anabolic implants and trace minerals impact growth of skeletal muscle in culture.

Project Description: In this project, our primary objective is to investigate the relationship between trace minerals and anabolic implants as they relate to growth of skeletal muscle. To do this, we are going to isolate primary satellite cells, muscle precursor cells, from cattle and grow them in culture in the presence of different concentrations of trace minerals with or without the hormones found in anabolic implants. This will allow us to specifically determine how these different molecules may interact to alter growth of skeletal muscle.

Duties and Responsibilities: The undergraduate research intern will work closely with Dr. Thornton, graduate student researchers and laboratory staff to help in completing the experiments associated with this project. The intern will need to learn primary cell culture and help with the other ongoing cell culture experiments. In addition, there are several live animal research projects that will be occurring in Dr. Thornton’s lab this summer. The undergraduate research intern is expected to help with the live animal trials as time allows.

Through this internship, the intern will be able to gain experience in culturing primary bovine satellite cells and assessing proliferation, differentiation and protein synthesis. In addition, the student will also learn several other laboratory techniques including: mRNA isolation and quantification, protein isolation and quantification, as well as various assays to measure different metabolites. In addition, the students will also be expected to help collect biological samples (weights, blood, liver, skeletal muscle) from cattle/lambs that will be used in other trials that are going on in the lab this summer. Interns are not required to have previous experience working in a laboratory setting, but must be willing to learn and receive training to complete this type of work. If a student is selected for this position, the student must complete the initial laboratory safety training class.
Project Title: Developing Syrian hamster models for studying SARS-CoV-2 infection

Principal Investigator: Dr. Zhongde Wang [https://caas.usu.edu/directory/wang-zhongde](https://caas.usu.edu/directory/wang-zhongde)

Research Area: Genome engineering, animal model and virology

**Background:** As of March 1, 2021, the unprecedented ongoing COVID-19 pandemic caused by SARS-CoV-2 infection has led to 2,520,550 deaths and 113,467,303 infected cases worldwide. While vaccines against SARS-CoV-2 have been developed and are being administered to eligible populations, no FDA-approved antiviral drug is available for treating SARS-CoV-2 infections. There is a wide spectrum in disease outcomes from SARS-CoV-2 infection, from asymptomatic to fatal disease. The identification of host factors involved in SARS-CoV-2 infection and understanding their roles in disease outcomes are essential for developing efficacious therapies against SARS-CoV-2 infection. The Syrian hamster, due to their susceptibility to SARS-CoV-2 and developing similar lung disease to what observed in COVID-19 patients, has emerged as an excellent animal model for studying SARS-CoV-2 infection. However, SARS-CoV-2 infection in wild type hamsters is a self-limiting disease with viruses being cleared in about 8 days post infection, which severely limits the use of hamster as a model to study severe COVID-19 conditions and as a fetal disease model. Supported by an over $2 million dollar grant from the NIH, working with the antiviral research institute at Utah state university, the Wang lab has developed a human ACE2 transgenic hamster model for studying SARS-CoV-2 infection. We have demonstrated that the hACE2 hamsters are highly susceptible to SARS-CoV-2 and develop fatal disease with severe lung pathology. In the meantime, through a research collaboration with Genentech Inc., the Wang lab also employed the CRISPR/Cas technology that they pioneered in the Syrian hamster (the Wang lab was the first in the world succeeded in establishing gene targeting techniques in the Syrian hamster) and has created three gene knockout (KO) hamster lines in which candidate genes implicated as host factors involved in SARS-CoV-2 infection (proprietary information) and disease progression are genetically inactivated. We will cross the hACE2 transgenic hamster line with each of the 3 KO hamster lines and use the resultant new hamster lines as models for studying the roles of each of these 3 genes in the pathogenesis of SARS-CoV-2 infection. This research project may not only lead to the understanding the roles of host factors in the pathogenesis of COVID-19 but also lead to the discovery of new drug targets for treating this disease. We also expect that the research project will lead to scientific publications with the intern sharing co-authorships. The intern may have the opportunities to continue the projects or work on other projects in the Wang lab, either as future intern or a graduate student (for those who are interested in pursuing MS or PhD degrees).

**Project Description:** The intern will closely work with postdoctoral researchers and a research technician on the development of these novel genetic hamster models and the genetic characterization of the models.

**Duties and Responsibilities:** The intern will learn a wide range of molecular and cellular biology techniques, including genomic DNA isolation, genomic PCR, PCR-RFLP genotyping analysis, mRNA isolation, real time RT-PCR, Western blotting, and cell culture, etc. The intern will also have the chance to learn CRISPR/Cas technologies in conducting genome engineering. In addition, the intern may also learn skills in hamster husbandry and breeding.
Project Title: **Investigating the non-classical virulence mechanisms of Enterotoxigenic *Escherichia coli***

Principal Investigator: Dr. Shawn Zimmerman [https://caas.usu.edu/directory/zimmerman-shawn](https://caas.usu.edu/directory/zimmerman-shawn)

Research area: Molecular Bacteriology, Infectious Diseases, Animal and Human health

Background: Worldwide 780 million individuals lack access to clean drinking water and 2.5 billion lack adequate sanitation. The lack of these preventable measures in developing countries has led to the continued transmission of infectious diarrheal disease (IDD), which is particularly detrimental to children. Globally, childhood IDD results in 1.7 billion cases each year and is the leading cause of death (~525,000 annually) and malnutrition in children under the age of 5 years. *Escherichia coli*, specifically the enterotoxigenic and enteropathogenic pathotypes, are the most common bacterial organisms associated with moderate to severe, debilitating IDD in low-income countries. Enterotoxigenic *Escherichia coli* (ETEC) is also the causative agent of traveler’s diarrhea, which routinely infects soldiers, non-governmental organization personnel, and Peace Corp volunteers. Furthermore, economically important livestock species (e.g. post-weaning calves and piglets) are highly susceptible to this pathogen, and when outbreaks occur they result in serious economic losses to producers. Unfortunately, ETEC strains are very diverse and have highly complex interactions within their various niches (e.g. host gastrointestinal tract and environmental reservoirs), and these complexities have hindered the development of effective vaccines and other therapeutics.

Project description: Historically, surface-exposed proteins on Gram-negative bacteria make excellent vaccine targets because they are readily-accessible to the host immune system and can elicit robust, protective, and durable immune responses. Likewise, targeting virulence factors that play key roles in the early pathogenesis of ETEC in the host (e.g. colonization, adherence, and biofilm formation) could have the added benefit of interfering with the ability of ETEC to establish itself in the mammalian GI tract and cause diarrhea. By mining an innovative dataset obtained from a combination of human and rhesus macaque ETEC infection studies, our laboratory has identified 16 putative virulence factors that may contribute to the colonization, adherence, and/or biofilm formation of ETEC in the mammalian GI tract. Our laboratory’s goal is to functionally characterize these potential virulence factors *in vitro* and screen them in mice to identify the best potential vaccine target(s). The selected student will work to characterize one or more of these virulence factors, as time permits.

Duties and responsibilities: This project will begin May 2022 in Dr. Zimmerman’s research laboratory in the Center for Integrated Biosystems. The intern will work closely with Drs. Zimmerman (PI) and Dyke (postdoc) and gain substantial experience with common microbiology and molecular biology techniques, including but not limited to bacterial propagation, cloning, mutagenesis, DNA isolation, PCR, electrophoresis, western blot, and tissue cell culture. The intern will also have the opportunity to assist with other on-going studies in the laboratory involving animal husbandry and infection studies with mice. Successful interns will need to be organized, motivated, and hard-working. Prior experience is not required, but if selected for this position the student must be willing to complete all required training.