

HSC IACUC Meeting Minutes for Thursday, September 3, 2020

Meeting time - 12:00 pm – 1:08 pm

***Due to COVID-19 restrictions, this meeting was conducted virtually via Zoom.**

Members Present

Attending Veterinarian
BHC Representative (NV)
Chair
Chemical Safety Rep (NV)
EOHS Representative (NV)
IACUC Administrator (NV)
Member #8
Member #11
Member #12
Member #20
Member #22 (Vice-Chair)
Member #23
Member #25
Member #26
Member #27
OACC Operations Manager, Recording Secretary (NV)
SRS Rep (NV)

Members Absent

ARF Representative (NV)
Member #18
Radiation Safety Representative (NV)

NV= non-voting members, consultant or staff

Per the request of the Chair, the Recording Secretary noted a quorum was present.

Voting members at meeting start time = 11

Item # 1: Approval of Agenda:

A motion for approval of the September 3, 2020 agenda was made and carried. The agenda was approved as presented.

Decision: Approved: Yes=11 No=0 Abstained=0 No=0 Recused=0

Item # 2: Approval of Minutes:

A motion for approval of the March 5, 2020 meeting minutes was made and carried. Several identifiers were removed from various pages. The minutes were approved as amended.

Decision: Approved: Yes=11 No=0 Abstained=0 No=0 Recused=0

Item # 3: Old Business:

200833 DMR Annual with Minor - "Role of neuron-specific gene family in behavior".

Reviewer: *Chair*

Summary: Add/remove staff.

Approved as a DMR by IACUC Chair on 4/7/2020.

200976 DMR - "Sin Nombre virus infection in deer mice."

Reviewers: *11, 24, AV, MC IACUC Rep, BHC Rep*

Summary: Sin Nombre virus is a hantavirus that causes disease in humans. Sin Nombre virus is carried by deer mice. The virus replicates in these mice but does not make the mice sick.

Humans can get infected when they breathe in aerosolized virus in the droppings of the mice.

There are no drugs available for treating Sin Nombre virus infection. Some new research has found that certain proteins called antibodies can protect against infection from different hantaviruses, but this has not been tested for Sin Nombre virus. In this protocol, we will test new antibodies against Sin Nombre virus by infecting deer mice and seeing if the antibodies block infection in the mice. To do this, we will construct an outdoor testing site at a National Wildlife Refuge where deer mice will be safely housed and infected with Sin Nombre virus. Antibodies will be tested to see if they can block infection in the deer mice. Also, different strains of Sin Nombre virus will be used to infect the deer mice in order to make virus stocks and to see if they replicate differently in the mice.

Approved as a DMR by Sub-Committee on 3/16/2020.

Item # 4 New Protocols:

201020 3-yr RW DMR - "Study of papillomavirus entry and infection in mouse models."

Reviewers: *11, 8, AV*

Summary: Human Papillomavirus (HPV) infections are the most common sexually transmitted disease (STD). Approximately 20 million Americans are currently infected with HPV and every year about 6 million people acquire new infection. One of the major difficulties limiting our understanding of how the virus infects and causes disease has been the lack of appropriate tissue-based model systems. The development of a genital model of HPV infection in laboratory mice by another PI's laboratory helps to overcome this hindrance, and permits study of HPV infection in live tissues. We intend to use the mouse challenge model to investigate the role of growth factor receptors in the infection of genital tract epithelium. This is a basic science question, which will improve our understanding of how some viruses infect cells. Although this work is not aimed to be translational, it could reveal new means of preventing HPV or other PV infections, or reducing transmission of the viruses. It is unlikely this work will lead directly to new therapies, however, through our finding that EGFR was involved in HPV infection (and many other studies of how HPV proteins alter cell functions), we posed a hypothesis that EGFR signaling is key to maintaining HPV infection. This hypothesis turns out to be supported by work in our lab, and is the focus of other grants we hold that aim to understand how HPV infections progress to malignancies. I would never have predicted we would reveal a therapeutic target by investigating HPV infection mechanisms in the past, but it seems we did! This underscores how important fundamental scientific research can give rise to translational efforts, and also underscores our poor ability to predict such occurrences that may come from basic science research. The infection of laboratory mice by MmuPV1 (a mouse papillomavirus) is a useful model for HPV infections, and MmuPV1 infections cause warts where questions regarding how

HPVs cause warts/tumors can be addressed. This is important as HPVs reporter viruses used for the studies outlined in the first paragraph do not cause disease in mice. Oral infections with HPVs cause oral cancers more often in men compared to women. We aim to study how the infected cells respond to virus infection using male and female mice infected with MmuPV1. We will also study the role that sex hormone (estrogen, progesterone, testosterone) influence MmuPV1 infection. The MmuPV1 infection model will also be used to study the role of growth factors in virus infection as described in the first paragraph.

Approved as a DMR by Sub-Committee on 5/26/2020.

201021 DMR - "VLP-based vaccines against dengue virus non-structural protein 1 in mice."

Reviewers: 18, 25, AV

Summary: Dengue virus is a mosquito borne virus that can result in potentially lethal hemorrhagic fever. There is only one vaccine licensed to prevent DENV and it was recently pulled from population-wide vaccination campaigns for safety concerns. The goal of this study is to make a new DENV vaccine by targeting a protein called non-structural protein 1 (NS1) with a bacteriophage virus-like particle platform. As part of this, we will be immunizing mice with our candidate vaccines and drawing blood to test for antibodies that block NS1 function. We will also test lead candidate vaccines in a mouse model of dengue virus infection. This involves immunizing the mice and then injecting DENV-2 in the skin and testing for increased bleeding time by a tail transection under anesthesia. The benefit of this study will be a potential vaccine against DENV that could protect some of the world's most vulnerable populations from this dangerous infectious disease.

Approved as a DMR by Sub-Committee on 4/7/2020.

201024 - "Glucocorticoid Resistance and Prenatal Alcohol Exposure in Mice."

Reviewers: 11, 27, AV

Summary: The goal of this research is to understand whether prenatal alcohol exposure causes a dysregulation of the hormonal response to stressors that are experienced throughout the lifespan, from early postnatal days to adulthood. The hormonal system that is well characterized to activate in response to stressors (i.e. fleeing from danger, fleeing from a predator) is referred to as the hypothalamic-pituitary-adrenal (HPA) axis. Activation of this axis can be measured in mouse models of stress by measuring the release of the glucocorticoid stress hormone in the blood. Key regions in the brain and body are highly responsive to glucocorticoids, which allow for one to appropriately respond to the stress. For example, deciding to flee or fight, and mobilizing energy stores so muscles can function quickly to allow one to run from a predator. However, we believe that prenatal alcohol exposure causes an insensitivity to glucocorticoids released by a stressor cue, such as when a neonatal pup (day 8, 10 or 12 after birth) is separated from its mom for a period of time, or when an adult animal must avoid a predator. This insensitivity is observed in people with prenatal alcohol exposure, as they typically have chronically elevated or blunted levels of glucocorticoids, and when a stressor occurs, these levels do not change in response to the stressor. Abnormal levels of glucocorticoids in people are associated with chronic diseases that range from lifelong depression to immune function dysregulation leading to diseases of chronic inflammation. This proposal aims to understand the mechanism(s) that cause prenatal alcohol insensitivity to glucocorticoids as it relates to stress responses in key brain regions and to immune function in the body and brain, with an examination of all aspects of the stress response (brain and peripheral tissue systems), such that

we can develop a novel target to catch this glucocorticoid insensitivity in early postnatal life, thereby mitigating the enduring effects of glucocorticoid resistance.

Returned for modification on 8/31/2020.

201025 3-yr RW DMR - "A mouse model to study inflammatory diseases."

Reviewers: 22, 27, *AV*

Summary: Inflammation is part of the immune response that helps combat against bacterial infection, but if it is not controlled it can contribute to various autoimmune and metabolic diseases. Therefore, my lab will investigate how components of the immune system maintain balance between healthy and disease states. Patients with inflammatory bowel disease have an abnormal immune response to gut bacteria which causes chronic inflammation in the gut. The studies proposed in this animal protocol seek to understand how the immune system contributes to disease and a healthy state of the gut. The work from these studies will be crucial in supporting and discovering new ways to control inflammation. My long-term goals are to identify the specific cells and pathways that balance immunity and inflammation. So we will use common laboratory mice to understand the biology of the immune system. The immune responses of mice are well characterized; reagents for manipulation of the immune system are readily available. Many of the immunological observations made in mice readily transfer to humans. These *in vivo* models are necessary in understanding the complex cellular interaction and regulation mechanisms in diseases and will benefit understanding and treatment of the diseases. Immune and inflammation responses require collaboration of the multiple types of cells in the organism, which can only be completed in intact animals but cannot be duplicated in cell culture or computer modeling. Also, to study the role of specific signaling molecules in intact immune cells, primary cells from knockout animals are required. Cell lines and computer modeling cannot replace this need.

Approved as a DMR by Sub-Committee on 5/21/2020.

201026 3-yr RW Breeding DMR by Vet - "A breeding protocol to understand inflammatory diseases in a mouse model."

Reviewer: *AV*

Summary: Inflammation is part of the immune response that helps combat against microbial infections but if it is not controlled it can contribute to numerous diseases. Therefore, my lab will investigate how components of the immune system maintain balance between healthy and disease states. The studies proposed in this animal protocol seek to understand how the immune system contributes to disease and a healthy state of the gut. Specifically, on understanding the role of macrophage and intestinal epithelial cell function in intestinal health and in diseases such as inflammatory bowel disease and metabolic syndrome. The immune responses of mice are well characterized; reagents for manipulation of the immune system are readily available. Many of the observations made in mice readily transfer to humans. These animal models are necessary in understanding the complex cellular interaction and regulation mechanisms in diseases and will benefit understanding and treatment of the diseases. We will utilize these mice to study the immune and metabolic functions of intestinal macrophages and epithelial cells to understand their contribution to disease and to potentially discover new therapeutic targets. Specifically, these mice will be used to study intestinal permeability, macrophage and epithelial biology, generation of organoids, and the microbiota. These mice will also be used in the acute and chronic DSS model of colitis as well as in our microplastic study where mice receive

microplastics in their drinking water to determine the effects of microplastics in health. Lastly, we will utilize these mice to study the therapeutic effects of 5-ASA, a common therapeutic used on mild to moderate IBD patients, to alleviate disease progression in these mice. Lastly, immune responses require collaboration of the multiple types of cells in the organism, which can only be completed in intact animals but cannot be duplicated in cell culture or computer modeling. Also, to study the role of specific signaling molecules in intact immune cells, primary cells from knockout animals are required. Cell lines and computer modeling cannot replace this need.

Approved as a DMR by Attending Vet on 5/6/2020.

201027 3-yr RW DMR - "A Novel Advanced Resuscitation Fluid for a Rat Model of Traumatic Brain Injury with Hemorrhagic Shock."

Reviewers: 20, 23, AV

Summary: Traumatic brain injury (TBI) causes ~30% of all injury related deaths and is especially frequent at battlefield. Severe bleeding due to multiple injuries occurring concurrently with TBI, results in blood loss and hemorrhagic shock (HS) which significantly drops arterial pressure (AP). Reduced AP restricts blood flow and delivery of oxygen to the brain which dramatically increases mortality. As a result, even mild TBI with HS became equal to severe TBI. Current treatments for TBI with HS are based on raising back AP by resuscitation fluids (battle field) followed by transfusion of blood (hospital). However, these fluids do not improve impaired capillaries flow (microcirculation) in brain that leads to neuronal death. We propose to improve microcirculation by adding drag reducing polymers (DRP) to the resuscitation fluid (DRP-RF). We hypothesize that DRP-RF, applied in rat with TBI/HS, will attenuate the severity of injury, increase survival, improve neurologic recovery and reduce the volume of resuscitation fluid required. DRP in animal blood increased microcirculation by modulation of blood flow properties in vessels by smoothing flow. We previously showed that DRP increased microvascular flow in the healthy and traumatized rat brain. We will evaluate DRP as additive to resuscitation fluids and define mechanisms in the acute and recovery phases. In Specific Aim 1 we will evaluate the effects of DRP-RF infused in the "pre-hospital" phase up to 6 hours after TBI/HS. In Specific Aim 2 we will evaluate the DRP-RF beneficial effects on long-term recovery. We will test colloid resuscitation fluid (6% Hetastarch), used in military, and crystalloid resuscitation fluid (Lactated Ringer), used in civilians, with and without DRP (5 mcg/ml of blood) prepared from polyethylene oxide. After TBI, we will induce HS for 60 minutes (AP = 40 mmHg) by blood withdrawal over 15 min - "hemorrhage phase". In the 2nd phase, "pre-hospital care" (60 min), resuscitation fluid will be slowly infused to AP = 50 mmHg. At the 3rd phase, "definitive hospital care", blood will be re-infused to get an AP of 70 mmHg. Over 6 hours after TBI/HS we will measure changes in brain blood flow, oxygenation and blood brain barrier, neuronal survival and oxidative stress using 2-photon laser scanning microscopy and laser speckle contrast imaging. In the long-term studies, magnetic resonance imaging will be used to quantitate brain edema, contusion and peri-contusion volumes at 24 and 48 hours and 1-4 weeks after TBI/HS. Neurologic recovery will be evaluated by behavioral tests. Injury severity and inflammation will be measured histologically at 6 hours and 4 weeks. DRP-RF will improve cerebral and systemic microcirculation reducing secondary brain injury from HS. This will reduce mortality and post-traumatic neurological disabilities. In addition, DRP-RF will significantly reduce the volume of fluid required for resuscitation which is an important factor at a battlefield. The major goal is to bring to pre-clinical trials a novel, highly efficient

resuscitation fluid for TBI/HS that can be easily administered in small-volume in the unique traumatic conditions of the battlefield and/or civilian trauma.

Approved as a DMR by Sub-Committee on 5/26/2020.

201029 Tissue - "Role of Gut Microbiome in Metal Immunotoxicity."

Reviewers: *Chair, AV*

Approved by IACUC Chair and Attending Vet on 5/1/2020.

201033 DMR - "Livestock Movement and Exposure to Abandoned Uranium Mine Waste in Cove Wash Watershed."

Reviewers: *11, 23, AV*

Summary: The presence of abandoned uranium mines in many Navajo communities has caused concern about human exposure to metals found in abandoned mine waste, soil, water, and vegetation on the Navajo Nation. The accumulation of uranium in meat and organs that are part of the traditional Navajo diet has also be observed in livestock that grazed in historic uranium mining areas. For members of the Navajo Nation there remain unanswered questions about human exposure to uranium by consuming organs and meat from animals that grazed in a watershed with 51 abandoned uranium mines and waste. In response to a request by the Navajo community, researchers are collaborating with researchers from other universities to investigate human exposure to uranium via consumption of animal meat and organs that are part of a traditional Navajo diet.

We propose to place global positioning system (GPS) tracking collars on 18 cattle, 5 sheep, and 5 goats to monitor their movements for approximately 6 months. Livestock owners and the grazing official will identify fully grown, non-pregnant female livestock to be tracked using a leather GPS collar. The collar and GPS device will weigh less than 1 pound and have been used successfully in other livestock tracking studies. The livestock owners will confine each animals using a squeeze chute long enough for a GPS collar to be fit around the neck. After fitting, the animals will be observed in their pens for signs of discomfort and collars will be removed at the request of the owner or grazing official. At the end of the grazing season the owners will collect their animals and the collars will be removed so that GPS data can be retrieved. These animals are already familiar with a squeeze chute and many animals have previously worn some type of collar. After the GPS collars are removed, the livestock owners will work with researchers from another university to identify animals for slaughter (by community members) so that tissue samples can be collected. Community needs will dictate which animals will be slaughtered for food or ceremonial practices. At the time of slaughter researchers will collect samples to determine accumulation of uranium in a variety animal tissue. Once tissue samples are analyzed for uranium, Statisticians will model the results to identify grazing patterns and animal behaviors that are associated with uranium accumulation in animal tissue. This study will use geospatial technology to determine the frequency of livestock grazing around abandoned mines and will identify the environmental and land cover factors that are associated with metal and radionuclide accumulation in animal tissue. This work enables us to better interpret inter-animal chemical uptake in animal tissue, calculate more accurate chemical transfer rates from animal tissue to humans, and inform community members about potential risk for human exposure to uranium from consumption of animal tissue as part of a traditional diet.

Withdrawn.

201035 Breeding DMR by Vet - "Breeding of hACE2 transgenic mice for coronavirus studies."

Reviewer: *AV*

Summary: SARS-CoV-2 coronavirus is causing millions of infections and hundreds of thousands of deaths worldwide. We propose to test vaccines and drugs against this virus (SARS-CoV-2) in a mouse model. Normal mice aren't infected with the virus, but mice that carry the human receptor for the virus (hACE2) are infected. This protocol will breed these mice to be used for vaccine and drug experiments against SARS-CoV-2

Approved as a DMR by Attending Vet on 5/12/2020.

201036 DMR - "Testing of vaccines and antivirals against SARS-CoV-2 in mice."

Reviewers: *18, 24, AV*

Summary: SARS-CoV-2 is a new coronavirus that has infected millions worldwide and caused hundreds of thousands of deaths in 2020. There are no approved therapeutics or vaccines to successfully treat or prevent infection. We have a number of drugs and vaccines that show promise in test tube experiments that we would like to test in a mouse model. Mice aren't usually infected with SARS-CoV-2, but mice that carry the human receptor for SARS-CoV-2 (ACE2) are infected with the virus and have weight loss and viral growth in their lungs. We will use this model to test vaccines and drugs for treatment and prevention of coronavirus infection.

Approved as a DMR by Sub-Committee on 6/11/2020.

201038 Breeding DMR by Vet - "Mouse models of gliomas."

Reviewer: *AV*

Summary: This is a breeding protocol to support an experimental protocol (yet to be submitted). Our overarching goal is to elucidate the origin of gliomas. In particular, we plan to: (i) identify all the mechanisms that contribute to glioma initiation; (ii) use this information to interrogate different brain cell populations in mice for the definitive identification of glioma cell of origin.

Approved as a DMR by Attending Vet on 6/16/2020.

201039 3-yr RW DMR - "A Mouse Model for Mechanisms of Immune Dysregulation Produced by Uranium, Arsenic, and Metal Mixtures (Biomedical Project (BP2), Superfund Center)."

Reviewers: *22, 8, AV*

Summary: A grant will support the continued work of the Metals Exposure and Toxicity Assessment on Tribal Lands in the Southwest team and Native American communities to ascertain exposures, health risks and remediation needs of the community as a result of more than 1100 abandoned uranium mine waste sites located on the Navajo Nation. The community is concerned as to the contribution of uranium and arsenic exposure to several health disparities associated with immune dysfunction. Biomonitoring of young adults and infants in this population demonstrate that the exposures to uranium and arsenic are substantially more than in the US population.

The abandoned uranium mine sites are unmarked and unfenced, and pose risks for transport through water, air, and food. Unregulated water sources are commonly used by area residents to water livestock and crops. Data from more than 500 unregulated water sources in the Navajo Nation identified 15% of these water sources exceed the uranium maximum contaminant level (MCL) and approximately 20% exceed the MCL for arsenic. The data also includes individual water sources that exceed MCL for both uranium and arsenic. These studies are important and relevant to both indigenous and rural communities throughout the Western US exposed to metal

mixtures from more than 4000 abandoned uranium mines and 161,000 abandoned hard rock mines.

Our lab currently studies the mechanisms associated with arsenic exposure and the effects on the immune system. Our studies have indicated that immature cells on the immune system, pre-T (thymus) and pre-B (bone marrow) are extremely sensitive to arsenic exposure; uranium toxicity has yet to be characterized. Although uranium may not have strong immunotoxicity on its own, we have identified a potentially important combined effect. The objectives of these animal studies are to investigate potential underlying mechanisms of immune toxicity of uranium, arsenic, and combinations of uranium and arsenic. These studies will also provide a framework for understanding how interventions, such as zinc supplementation, can be developed to prevent arsenic and uranium toxicity and in metal mixtures. Removal of the source material has been estimated to be decades away. Therefore, it is important to identify interventions that can reduce both exposure and risk.

The C57Bl/6 male mouse is a sensitive model to examine sodium arsenite immunosuppression; we have not yet examined female mice. The mouse model in general, is a much used and valuable model for immunotoxicity studies. Our own experiments have shown that they are valuable to predict risk in humans as well as to investigate mechanisms of action. In these studies we will compare males and females for arsenic, uranium, and combined arsenic and uranium, immunotoxicity. The C57Bl/6 mouse is not in short supply and transgenic and knockout mice that we might need to examine in the future are available on this genetic background. Mice will be exposed via drinking water, which imitates exposures in humans, will allow us to examine organs of the immune system such as the thymus, bone marrow and spleen. Procedures that we will conduct: treatment via drinking water, immunization with sheep red blood cells (SRB), CO2 euthanasia, blood collection (intracardiac), and tissue collection (spleen, thymus, and femurs and other bones for bone marrow). The immunization with SRB is part of the T-dependent antibody response assay (TDAR) to evaluate immune function.

Approved as a DMR by Sub-Committee on 6/22/2020.

201040 Tissue - "Cumulative Exposure models using GIS and Livestock Tracking."

Reviewers: *Chair, AV*

Summary: The presence of abandoned uranium mines in many Navajo communities has caused concern about human exposure to metals found in abandoned mine waste, soil, water, and vegetation on the Navajo Nation. The accumulation of uranium in meat and organs that are part of the traditional Navajo diet has also been observed in livestock that grazed in historic uranium mining areas. Our ability to interpret concentrations of uranium and other metals in animal tissue, and thereby to assess potential human exposure and risk, is limited however by our understanding of the source, mobility, and points of exposure for animals. To date there remains limited knowledge about how animal behavior patterns influence mine waste exposure.

To estimate potential exposure of animals grazing in proximity to mine waste, we will place global positioning system (GPS) tracking collars on 15 sheep, and 15 goats to monitor their movements for approximately 6 months. Livestock owners and the Chapter grazing official will identify fully grown, non-pregnant female livestock to be tracked using a leather GPS collar. The collar and GPS device will weigh less than 0.5 kilograms and have been used successfully in other livestock tracking studies. The livestock owners will restrain their animals long enough for a GPS collar to be fit around the neck. After fitting, the animals will be observed in their corrals for signs of discomfort and collars will be removed at the request of the owner or grazing

official. We also plan to attach a passive silicone sampler to the GPS collars for 2 one-month periods to measure chemical exposures such as pesticides or other organic chemicals from the environment. At the end of the grazing season the owners will collect their animals and the researcher will work with the livestock owners to remove the so that GPS data can be retrieved.
Approved by IACUC Chair and Attending Vet on 6/16/2020.

201045 DMR – “Bacteriophage virus-like particle vaccines for fentanyl and heroin overdose in mice and rats.”

Reviewers: 22, 27, *AV*

Summary: Currently, we have preliminary data that shows that an opioid displayed on our bacteriophage vaccine platform can elicit high-titer serum antibodies in as few as 7 days after a single intramuscular immunization. Our hope is to produce a vaccine platform targeting fentanyl, heroin, and morphine that will prevent a lethal overdose by binding drugs in the bloodstream and preventing them from crossing the blood-brain barrier.

We will continue to put new opioid drugs such as fentanyl, the metabolites of heroin, and morphine onto our vaccine platform. We will immunize mice with our vaccine and collect sera to test for antibodies. We will also perform pain tolerance assays and overdose challenge studies with immunized mice to see if they can be protected from the effects of the target drugs. We will also perform studies to see how long the protective antibodies stay in the blood stream of the mice. Using mice we will be able to do an assessment of respiratory function, which is a critical component to overdose in humans. We will be using rats following our mice studies to test inhalation and ingestion of our target drugs to test if the route of ingestion changes the vaccines ability to protect.

This is a two phased project (with the second phase only starting if the first phase results are approved by the funding agency), and we are currently submitting the IACUC protocol for Phase 1 (UG3).

Approved as a DMR by Sub-Committee on 8/18/2020.

201048 DMR - "Acceleration of Circulatory and Neurological Aging due to Wildfire Smoke Inhalation Exposures in Mice."

Reviewers: 20, 25, *AV*

Summary: Air pollution exposure during pregnancy is associated with adverse health effects to both the mother and child. In the present study, we propose to examine the linkages between inhaled pollutant exposure and how the mother may be vulnerable to pregnancy-related high blood pressure and heart failure. These studies will help us 1) confirm that there is a causal relationship between exposure and hypertension and 2) identify biological markers of exposure that may be valuable in confirming these studies in humans.

Approved as a DMR by Sub-Committee on 8/21/2020.

201049 Breeding DMR by Vet - "Breeding Protocol - Mouse models for studying the molecular mechanisms of gliogenesis and gliomagenesis."

Reviewer: *AV*

Summary: This is a breeding protocol to support an experimental protocol. Glial cells are the most abundant and proliferative cell types in the central nervous system. Abnormal development of glial is associated with a number of neurological diseases, fetal alcohol spectrum disorder, and cancers. The propose studies utilize advance genetic techniques to study how ethanol exposure

affects glial development and function, and to investigate the roles of regulatory proteins (ASCL1, OLIG2) in driving the development of glial and glioblastoma in the brains of mice. Results from these studies will help to demonstrate the process of glial cell generation, proliferation, and differentiation in the context of ethanol exposure or glioblastoma, or both since alcohol exposure has been shown to increase the disposition for brain tumor development.

Approved as a DMR by Attending Vet on 8/10/2020.

201052 3-yr RW DMR– “Role of non-coding RNAs in brain development and function and antipsychotic treatment in mice.”

Reviewers: 22, 25, AV

Summary: There is growing evidence that RNAs that do not encode for proteins (non-coding RNA) are highly abundant in the brain, regulate the expression of the vast majority of protein-coding genes, and can, thus, have a significant impact on numerous cellular functions. Our projects aim in deciphering the role of a subset of noncoding RNAs in neurodevelopmental disorders. Specifically, we will first use a mouse model of psychiatric drug treatment, which can reveal the effects of different psychiatric disease drugs on non-coding RNA expression. We aim to measure the expression of a subset of small evolutionary conserved non-coding RNAs known as microRNAs, and long non-coding RNAs such as circRNAs, both shown to be altered in the brain of subjects with psychiatric disorders and to potentially respond to treatment. In an additional project related to prenatal insults and neurodevelopmental disorders we will treat time-pregnant mice with valproic acid, a known animal model for studying autism, and examine the expression of another class of non-coding RNAs known as circular RNAs. In all cases time-pregnant mice will be subjected to intraperitoneal injections of the proper agents and pups will be euthanized at various developmental intervals so as to extract brain tissue and perform RNA quantifications. Collectively, our experiments will shed light to the role of non-coding RNAs in neurodevelopmental and psychiatric disorders. Treating pregnant dams with VPA at this specific developmental stage is very well established model to induce autism-like behavior in the offspring. This mouse model of autism has been used by a plethora of studies and has demonstrated that it recapitulates various neurodevelopmental, behavioral, and molecular abnormalities related to autism. However, our study will be the first to examine the effects of prenatal VPA treatment on circRNA expression. Data in our lab suggest that some of these circRNAs such as circHomer1 are upstream regulators of multiple autism-linked genes and are capable of affecting neuronal development, function, and cognition (paper under review).

Returned for modification on 9/3/2020. Original Expires 9/12/2020.

Item # 5 Major Amendments:

200640 DMR - "A Novel Advanced Resuscitation Fluid for a Rat Model of Traumatic Brain Injury with Hemorrhagic Shock."

Reviewers: 26, 24, AV

Summary: Please change the PI role on the protocol.

Approved as a DMR by Sub-Committee on 4/13/2020.

200678 DMR - "Research Protocol: Mouse Model for Glial and Glioma Development - Tamoxifen Administration, Electroporation, Tumor Transplantation & Alcohol Exposure."

Reviewers: 20, 23, AV

Summary: We are not requesting additional animal numbers for this protocol since we have plenty of animals left for our tumor studies, in which this amendment is an extension of. Additionally, this major amendment is for a pilot study. We will request additional numbers if the pilot study shows data supporting our hypothesis that alcohol binge drinking accelerates glioma formation and progression in the brain. The reason for this amendment is so that we can subject our established glioma tumor mouse model for alcohol binge drinking using a collaborator's alcohol drinking paradigm.

Sent for DMR by Sub-Committee on 8/31/2020.

200704 DMR - "Cellular and Molecular Mechanisms of Mild Traumatic Brain Injuries in Mice."

Reviewers: *II, 8, AV*

Summary: Add staff; we are requesting a major amendment to add a New Aim. Aim 5 will investigate the combinatorial effects of alcohol and mTBIs (mild Traumatic Brain Injuries). We will utilize our concussion model following alcohol injections of varying doses to achieve blood alcohol levels between 0.08 – 0.03 g/dL. These studies will use test if alcohol exacerbates the threshold for spreading depolarizations (SDs), acute behavior, cerebral blood responses, and long-term pathology of our mTBI model. Sub-Aim 5.1 will first test if alcohol alone alters cerebral blood flow (CBF) and/or our acute behavioral tasks. We will utilize our laser speckle contrast imaging system to monitor CBF following varying doses of ethanol. We will image the animals every 10 minutes for 2 hours to monitor CBF. We are currently using a battery of behavioral tasks that include: open field, escape task, gait analysis, inverted mesh, and beam walk to assess acute behavior following mTBIs. We will have to determine the extent to which alcohol of varying doses affects this behavior. In Aim 5.2 we will test if alcohol alters the threshold for light induced SDs. These studies will utilize the Thy-1/ChR mice (described in Aim 4). We will inject mice with varying doses of alcohol and then through fiber optic probes we will deliver light stimulus of varying intensities. We will monitor for SDs via intrinsic optical imaging or laser speckle contrast imaging. Aim 5.3 will test the hypothesis that alcohol alters the hemodynamic responses of mTBIs. Our current data demonstrates that our mTBI model induces an SD and the SD is associated with an immediate hemodynamic response and long-term reductions in CBF. We hypothesize that alcohol will exacerbate these changes in CBF. Given the results of Aim 5.1 Aim 5.4 will investigate the combinatorial effects of alcohol and mTBI on the acute behavior. These mice will then be sacrificed to assess for long-term pathology. Aim 5.5 will test the hypothesis that alcohol exacerbates the pathology of the mTBIs. All animals will be listed in Cat. D, with alleviated pain, because they will either be given injections of alcohol and/or undergo our mTBI model. I have included a new animal numbers table.

Amendment to Non-Survival Surgeries

#1 Animals will be injected I.P. with ethanol prior to laser speckle or intrinsic optical imaging.

#2 The Thy1/ChR mice will undergo fiberoptic implantation prior to laser speckle contrast or intrinsic optical imaging. A small burr hole will be drilled into the skull to thin the skull below the fiberoptic probe. The fiber probe will be placed in the burr hole and glued in place using cyanoacrylate glue. Once dry the fiber probe will be connected to a patch cord coming from LED light source.

Amendment to Imaging Description

Intrinsic optical imaging – Spreading depolarizations (SDs) are depolarizing waves that complete reverse ionic gradients. This massive change in ions results in significant swelling of the tissue. The increase in intracellular water alters the reflectance of the brain. These changes and those of

altered FADH and NADH levels can all be detected with white light and low magnification imaging. These intrinsic responses can be detected through the skull making it a nice non-invasive way to detect SDs.

Amendment to Behavioral

We would like to add forced swim. Also, under other we would like to add tail suspension. A full description will follow.

We want to add a transgenic strain B6.Cg-Tg (Thy1-COP4/YFP) 18fng/J (Jax # 007612 that expresses channel rhodopsin in glutamatergic neurons. We are currently breeding this animal and in the near future we plan to use this animal to initiate spreading depolarizations in the absence of an impact to the head. These studies will identify the contributions of spreading depolarization in the short and long term pathology, behavior, and cognitive that are associated with concussions. Because these transgenic animals will be run in parallel to our impacted animals we need to adjust our animal numbers more than 10%. I have attached a revised animal numbers sheet to the protocol.

Approved as a DMR by Sub-Committee on 7/27/2020.

200769 DMR - "Study of T cell responses in a mouse model of influenza infection."

Reviewers: 26, 25, AV

Summary: We have just received NIH funding to test how vaping with E-cigarettes containing Vitamin E Acetate will affect immune responses to lung infection including influenza. To do these studies, we will need to ask for an increase of 384 animals to accomplish the aims set out in the funded studies.

We will be testing how E-cigarette exposure, in particular, E-cigs with Vitamin E acetate has on susceptibility to influenza and immunity against influenza infection. To do this, we will treat animals in the following groups: 1-untreated 2-Electronic nicotine delivery system (ENDS) liquid without Vitamin E Acetate (VEAc); 3-ENDS+VEAc; and 4-VEAc only. After exposures, we will transfer animals to where we will treat half of each group with influenza and leave the other half without influenza.

Animals will be exposed in the vaping chamber for 4 weeks daily. Animals will be exposed to the conditions above using a customized, commercially-derived system for mouse inhalation of cigarette smoke. A flow-actuated electronic cigarette is connected in-line with an air pump to draw puffs of vaporized solution into the exposure chamber. The exposure chamber allows for free movement, albeit in a smaller footprint than in a standard shoebox cage. Mice will be exposed to puffs of vapor every 10 minutes for 4h/d.

E-cig droplet size can range from 180 nm (based on count distribution) to 3 μ m, depending on the conditions. We will utilize relatively freshly delivered (i.e., smaller particles) e-cigarette vapor as a "mainstream" delivery. The system is fully characterized and consistently delivers atmospheric air with no displacement of oxygen or build-up of CO₂.

Mice will be acclimated to the exposure chamber over three days prior to study initiation, with increasing acclimation periods (1h, 2h, 4h). Control mice will be placed in the same exposure chamber before or after e-cig exposures are conducted (randomized by day).

Animals will be exposed whole body to 1) air; 2) VEAc (100%), 3) ENDS liquid (50:50 v/v) or 4) a combination of both ENDS liquid and VEAc using a customized system built around an InExpose inhalation exposure platform (SciReq).

At the end of the 4 week treatment course, we will transfer animals from [REDACTED] for influenza infection as previously described in the protocol.

In addition to weight loss measurements, we plan to sacrifice animals at days 6, 8, and 10 post influenza infection to assess immune cell infiltration and function in lung to determine whether exposure to E-cigarettes changes immune responses to influenza.

For each group of animals in each treatment group, we will need 6 mice as previous published results show that we need at least 4-5 animals to see biological effects and each experiment needs to be done 3-4X. So for each experiment we will need 6X4 treatment groupsX4 times for a total of 96 animals to measure weight loss. To assess immune cell function, we will need 96X3 for 3 time points for a total of 384 animals. As animals will be exposed to vaping and influenza, all animals will be category D.

Approved as a DMR by Sub-Committee on 6/3/2020.

200795 DMR - "Targeting aberrant signaling pathways in mouse xenografts of human acute lymphoblastic leukemia."

Reviewers: 18, 23, AV

Summary: The goal of this amendment is to add a new procedure (intrafemoral injection) and related analgesia that will be used to inject leukemic cells into mice.

Sent for DMR by Sub-Committee on 8/31/2020.

200802 DMR - "Alcohol and developing neuronal circuits: characterization using mice."

Reviewers: 12, 27, AV

Summary: We request authorization to intracerebrally deliver retrobeads, to label specific neuronal populations that connect with the cerebral cortex, or channelrhodopsin-2 (or a related opsin) via commercially available adeno-associated virus in order to optogenetically stimulate specific afferent or efferent synaptic connections of the cortex in control mice and mice exposed to ethanol during the mouse-equivalent to the 3rd trimester of human pregnancy. Synaptic activity in regions of interest will be evoked with light in acute brain slices. Activity will be recorded ex vivo using patch-clamp electrophysiological techniques.

Approved as a DMR by Sub-Committee on 3/20/2020.

200860 DMR - "Metabolic Phenotype of the Cerebral Vascular Wall in a Rat Model of Hypertension."

Reviewers: 20, 27, AV

Summary: Add additional animals, add exposure to 48 hours of chronic hypoxia, and add additional animal strain.

Approved as a DMR by Sub-Committee on 6/19/2020.

200867 DMR – "Evaluation of Virus-like Particle based vaccines for Chlamydia."

Reviewers: 26, 23, AV

Summary: Up to 196 total female BALB/c mice will be utilized (up to 10 vaccine candidates, 1 naïve, and 1 unconjugated control, for both Q β and MS2). Groups of 8 mice will be immunized with 5 μ g of modified virus-like particles in a total volume of 50 μ L of PBS without exogenous adjuvant. Two immunizations will be administered intramuscularly in the hind leg, three weeks apart. Blood serum will be collected via retro-orbital bleed (collecting a maximum of 0.1 mL of blood) prior to immunization (pre-immune sera) and three weeks after each immunization. If necessary, a third immunization will be given. Immunizations and retro-orbital bleeds will be conducted under light (isoflurane) anesthesia. Three weeks after the final immunization, mice

will have their estrous cycles synced via Depo-Provera. At this point, mice will be challenged intravaginally with luciferase-expressing *Chlamydia muridarum* (Cm). For the Cm challenge, infection will be monitored by *in vivo* imaging system (IVIS) to determine clearance of infection and ascension of Cm to the upper genital tract multiple days post-infection. Mice will be sacrificed via euthanizing with a mixture of xylazine/ketamine and the upper genital tract (uterus and uterine horns) will be collected to score pathology and inflammation.

Approved as a DMR by Sub-Committee on 9/2/2020.

200870 DMR - "Assessment of the immune responses in mice and rabbits induced by VLP-based vaccines targeting self and foreign antigens."

Reviewers: 22, 23, AV

Summary: In this amendment, we are adding experiments to assess the immunogenicity of VLP-based vaccines delivered through a microneedle patch. This amendment involves a significant change to the protocol (a new administration technique) and additional numbers of animals.

Approved as a DMR by Sub-Committee on 3/18/2020.

200870 DMR #2 - "Assessment of the immune responses in mice and rabbits induced by VLP-based vaccines targeting self and foreign antigens."

Reviewers: 18, 25, AV

Summary: We are requesting an additional 8 animals in order to repeat atherosclerosis experiments (our previous major amendment).

Approved as a DMR by Sub-Committee on 7/6/2020.

200899 DMR - "Role of Acid Sensing Ion Channel in the Vasculature."

Reviewers: 18, 8, AV

Summary: I would like to request addition of two non-invasive protocols. Both these protocols are currently being performed in a collaborator's lab and she is going to train the PI on DEXA scanning and metabolic phenotyping analysis. Neither protocol will require additional animals or increase risk of pain or distress.

Sent for DMR by Sub-Committee on 9/1/2020.

200975 DMR - "Repeated Binge Alcohol Drinking and the Genetic Regulation of Neural Synchrony in Mice."

Reviewer: 26, 8, AV

Summary: Addition of behavioral procedures. Adding behavioral procedures will allow us to further analyze the effects of binge alcohol drinking on behavior, and study whether binge alcohol drinking affects different types of behaviors. All of the behavior procedures have been approved by the IACUC on training protocol.

Sent for DMR Review #2 by Sub-Committee on 9/2/2020.

Discussion: Although this protocol is a DMR and not up for a vote, the committee discussed whether or not the pain category classification for the swimming behavior was appropriate and they decided that it was.

200984 DMR - "Cargo of Exosomes and Microvesicles in Tuberous Sclerosis Complex Utilizing Mouse Models."

Reviewers: 20, 29, AV

Summary: This major amendment is to add imaging in the form of ultrasound and MRI to our protocol. There will be no additional number of animals for this protocol since imaging will only be performed on a few animals. They will be placed in Category D since they will have Isoflurane administered for the ultrasound and MRI procedures.

Approved as a DMR by Sub-Committee on 3/20/2020.

200996 DMR - "Noninvasive Vagus Nerve Stimulation for Treatment of Brain Injury (nVNS-TBI) in Rats."

Reviewers: *II, 24, AV*

Summary: Currently, we have proposed the use of lithotripsy TBI model. However, we like to add the control cortical impact (CCI) model to the protocol.

Approved as a DMR by Sub-Committee on 3/10/2020.

Item # 6 Minor Amendments:

200657 - "Role of non-coding RNAs in brain development and function and antipsychotic treatment in mice."

Reviewers: *Chair, AV*

Summary: We need to test the effects of one more additional psychiatric disease medication (lithium) in non-coding RNA expression and use valproic acid in non-pregnant mice as well.

Approved by IACUC Chair and Attending Vet on 3/9/2020.

200658 - "Trafficking of nanoparticles and synthetic RBC in murine breast and ovarian tumors."

Reviewers: *Chair, AV*

Summary: Increase the injection dose of all nanoparticles that include mesoporous silica and gold to enable dosing studies

Approved by IACUC Chair and Attending Vet on 3/16/2020.

200658 #2 - "Trafficking of nanoparticles and synthetic RBC in murine breast and ovarian tumors."

Reviewers: *Chair, AV*

Summary: Add LNCap cells, 10 nude mice and 68Ga-Dotatate to protocol.

Sent for IACUC Chair and Attending Vet Review on 7/28/2020. Waiting for Radiation permit approval.

200699 - "Elucidating the role of micronutrient metabolism in gastrointestinal diseases using mouse models."

Reviewer: *Chair*

Summary: Add staff.

Approved administratively per IACUC Chair on 3/27/2020.

200701 Breeding - "Breeding Protocol for 200699 "The role of micronutrient metabolism in gastrointestinal disease".

Reviewer: *AV*

Summary: IRP2 is a critical gene in cellular iron regulation. The purpose for this revision is to get the mouse line IRP2 KO (n=918) from NIH for breeding

Approved by Attending Vet on 3/2/2020.

200701 Breeding #2 - "Breeding Protocol for 200699 "The role of micronutrient metabolism in gastrointestinal disease"."

Reviewer: *AV*

Summary: Add staff.

Approved administratively per Attending Vet on 3/27/2020.

200701 Breeding #3 - "Breeding Protocol for 200699 "The role of micronutrient metabolism in gastrointestinal disease"."

Reviewer: *AV*

Summary: Due to expansion of the research project, I would like to look at the role of macrophage in iron metabolism. Thus, LysM-Cre mice were acquired. n=918.

Approved by Attending Vet on 6/25/2020.

200714 - "Chemokine receptors in MRI contrast-induced organ fibrosis [a mouse model]."

Reviewers: *Chair, AV*

Summary: Serpin B13 has an established and critical role in the skin. Cathepsin (Cat) L, is a crucial lysosomal proteinase involved in a variety of cellular functions; including intracellular protein turnover, epidermal homeostasis, and hair development. Hursin (serpinB13) is a cross-class specific serine protease inhibitor of cat L. Additionally, our gadolinium-induced systemic fibrosis studies of afflicted skin show the presence of gadolinium clusters in the skin, increased dermal cellularity and skin fibrosis. For this reason, we would like to study our mice colony, strain Serpin 13 ko animals (N= 80) injected with Gadolinium, 2.5mmol/kg for 4 weeks Our Aim is to clarify if the Serpin b13 ko condition will play any role on presence of gadolinium and find if this deposition increases the fibrosis risk on these animals.

Approved by IACUC Chair and Attending Vet on 7/2/2020.

200717 - "A mouse model of *Mycobacterium abscessus* lung infection that mimics human infection."

Reviewers: *22 (VC), AV*

Summary: This minor amendment is for a collaborative project with another PI. We plan to do a pilot study examining whether the mice subject to hypoxic conditions under the approved IACUC protocol, # 19-200848-HSC, have altered susceptibility to *Mycobacterium abscessus* lung infection.

The rationale for this study is that mice subjected to hypoxic conditions undergo pulmonary vascular remodeling which has been found to promote a pro-inflammatory lung phenotype which could predispose to chronic lung infection *M. abscessus*.

This is a pilot study for an invited proposal submission for a project which will be submitted on September 3, 2020. For this study, C57/BL6J mice will be obtained from a major vendor. A total of 12 mice will be used. Six mice will be subjected to hypoxic conditions under 19-200848-HSC and 6 mice will serve as control mice. Mice will then be transferred to my protocol and will be intratracheally inoculated with *M. abscessus*. Two mice from the treatment and two mice from the control group will be euthanized shortly after inoculation to determine time 0 deposition of bacteria in the lungs. The remaining treatment (4) and control mice (4) will be followed for 30 days and then euthanized. A portion of lung tissue will be plated for lung CFU and a portion will be fixed for histopathology studies to be done by my collaborator's laboratory.

Approved by Vice-Chair and Attending Vet on 7/21/2020.

200745 - "Spinal neuroimmune mechanisms underlying pain control: the role of prenatal alcohol exposure and identification novel or repurposed therapeutic targets to minimize peripheral neuropathy in rats and mice."

Reviewer: *Chair*

Summary: Add staff.

Approved administratively per IACUC Chair on 8/20/2020.

200769 - "Study of T cell responses in a mouse model of influenza infection."

Reviewer: *Chair*

Summary: Add staff.

Approved administratively per IACUC Chair on 8/28/2020.

200790 Breeding - "Breeding Protocol for Autophagy Science Core (ASC)."

Reviewer: *AV*

Summary: B6.Cg-Tg(K18-ACE2)2PrImn/J; stock# 034860; 630 mice.

Approved by Attending Vet on 4/10/2020.

200795 - "Targeting aberrant signaling pathways in mouse xenografts of human acute lymphoblastic leukemia."

Reviewers: *Chair, AV*

Summary: We would like to add a new strain (CB57BL6) that will be used to test the inhibitors in syngeneic model of leukemia induced by MLL gene rearrangements (MLL-R). This will allow for testing the inhibitors of interests in immunocompetent mice as opposed to SCID or NSG mice that are immunocompromised. The increase in 10% is required to account for mice that will serve as bone marrow donors for MLL-R transformation. Typically one donor mouse is sufficient for transplantation into 3-4 recipients.

Approved by IACUC Chair and Attending Vet on 6/25/2020.

200802 - "Alcohol and developing neuronal circuits: characterization using mice."

Reviewer: *Chair*

Summary: Add staff.

Approved administratively per IACUC Chair on 4/24/2020.

200803 - "A murine model of Staphylococcus aureus host-pathogen interaction."

Reviewer: *Chair*

Summary: Remove staff.

Approved administratively per IACUC Chair on 7/31/2020.

200806 Breeding – "Mouse Models of Obesity and Diabetes."

Reviewer: *AV*

Summary: We are going to housing AdipoP-rtTA and delta-gly adiponectin mice shipped from outside lab. Increasing animal numbers less than 10%.

Approved by Attending Vet on 3/9/2020.

200806 Breeding #2 – “Mouse Models of Obesity and Diabetes.”

Reviewer: *AV*

Summary: We are going to purchase 1 male B6-EP4 flox/J from a major vendor then cross with the B6-Foxp3 cre female mouse which is from another lab. We will get the final experimental B6-EP4 Foxp3 KO mice. Increasing animal numbers less than 10%.

Approved by Attending Vet on 3/13/2020.

200806 Breeding #3 - "Mouse Models of Obesity and Diabetes."

Reviewer: *AV*

Summary: We are going to house 1 male and 2 females B6-CaMKII KO mice which given by another research institute. Then we will build up a breeder cage get the final experimental mice. Increasing animal numbers less than 10%.

Approved by Attending Vet on 3/19/2020.

200806 Breeding #4 - "Mouse Models of Obesity and Diabetes."

Reviewer: *AV*

Summary: We are going to generate JUNB and UCP1 dko mice by JUNB KO mice (available in another PI's lab) cross with UCP1 KO mice (from a major vendor).

Approved by Attending Vet on 8/4/2020.

200809 Breeding - "Breeding Protocol for Molecular Regulation of Hematopoietic Stem Cell Homing."

Reviewer: *AV*

Summary: We would like to add a new strain of mice to our protocol. The a-catulin GFP Knock in mice from a major vendor express GFP in the hematopoietic stem cell population. The addition of these mice will increase the animals in our breeding protocol by less than 10%.

Approved by Attending Vet on 6/25/2020.

200822 - "Alcohol Research Center Scientific Core Breeding and Drug Exposure Protocol for Mice and Rats."

Reviewers: *Chair, AV*

Summary: We request authorization to collect blood from ethanol intoxicated pregnant mice (gestational day 17) from the retro-orbital sinus without general anesthesia. This will be performed in dams from which pups will be used in subsequent experiments. Ethanol will be administered via intragastric gavage and blood collected 30 min later (peak of ethanol levels in blood). Mice will be heavily intoxicated (expected blood ethanol levels will be between 100-200 mg/dl), which will significantly mitigate pain and distress. The procedure will take 30 seconds per mouse. Retro-orbital blood collection was chosen over other collection methods because it has been shown to be the least stressful method compared to other methods in mice. We cannot use general anesthetics in the dams because these agents will have complex interactions with ethanol on brain development, complicating the interpretation of the results of our experiments.

Approved by IACUC Chair and Attending Vet on 3/13/2020.

200822 Vet Review #2 - "Alcohol Research Center Scientific Core Breeding and Drug Exposure Protocol for Mice and Rats."

Reviewer: *AV*

Summary: Adding [REDACTED] to agent administration location.
Approved by Attending Vet Review on 7/10/2020.

200823 - "Murine Models to study the impact of the peritoneal immune environment on ovarian cancer progression and response to treatment - COMBINED PROTOCOL."

Reviewers: *Chair, AV*

Summary: > Foxp3-GFP mice for regulatory T cell study

We have been using murine ovarian cancer models by inoculating ovarian cancer cell line to the naive recipient mice which are the same strain background with cell line (FVB or C57/Bl6 strains). To start the study about the contribution of regulatory T cells during cancer development as well as the responses against our treatment, recently we have started to breed Foxp3-GFP strain at ARF. In this amendment, we request to add this strain to our experimental protocol to apply our described experimental procedures. By utilizing the FoxP3 mice as donors of the source of regulatory T cells for adoptive transfer, or as recipients of tumor inoculation, we can identify and track Tregs at the tumor microenvironment (tumor mass or peritoneal washes) at the time point of analysis. For the adoptive transfer of "green"-regulatory T cells into C57/Bl6 recipients, we request to increase the number of mice for Pain Category C for donor mice (150 mice in Pain Category C).

> Antigen presentation functional assays

Additionally, we request to add a modification of procedure to examine antigen-uptake and processing assay in vivo. This is for further analysis to address how the whole-cancer cell vaccination can achieve the enhanced anti-tumor T cell responses. In addition to elevated activation of DC after vaccination, it is important to examine if their function (antigen uptake, antigen processing and presentation on the cell surface) is enhanced to induce the consequences of T cell activation. By modifying our regular we vaccination procedure approved in the original protocol, we will co-inject prepared whole cancer cells with fluorochrome-conjugated OVA peptide reagents (OVA-AlexaFluor 647 as a traceable antigen and DQ-OVA;obtaining from a major vendor. We will adopt the protocols provided by the vendor for animal use and the published papers. We plan to mix 10 ug of OVA reagent in the 100ul of sterile PBS for sc injection. All reagents will be handled with sterile technique and stored at the recommended storage condition. The experiments will be under Project III-C3 and we will not need to request an additional number of mice.

Approved by IACUC Chair and Attending Vet Review on 6/1/2020.

200839 - "Role of brain specific tyrosine phosphatase, STEP, in neuroprotection and death in rodents."

Reviewer: *Chair*

Summary: Add/remove staff.

Approved administratively per IACUC Chair on 5/13/2020.

200841 Breeding - "Breeding protocol for the Role of Neuroinflammation in Tauopathies."

Reviewer: *AV*

Summary: MyD88-f/f (008888) TMEM119-creERT-2 (031820). Add 311 animals.

Approved by Attending Vet on 8/13/2020.

200841 Breeding #2 - "Breeding protocol for the Role of Neuroinflammation in Tauopathies."

Reviewer: *AV*

Summary: Add staff.

Approved administratively per Attending Vet on 8/28/2020.

200848 Chair - "Mechanisms of hypoxic pulmonary hypertension in a mouse model."

Reviewers: *22 (VC), AV*

Summary: We would like to replace the 2 weeks administration of tamoxifen containing diet to 5 days of tamoxifen/corn oil ip injections. The reason is that lately a few mice were morbid or died because they refuse to eat the tamoxifen diet. Other investigators use tamoxifen/corn oil successfully and is recommended by one of the major vendors.

In addition, I'd like to remove the study Role of G protein-coupled estrogen receptor (GPER) in CH-induced PH and use those animal numbers for a collaboration with a UNM PI under another protocol. We have been invited to submit a collaborative project and we need to generate preliminary data. We will supply C57B6 mice exposed to 5 days of CH to my collaborator. CH exposure is already approved in this protocol.

Approved by Vice-Chair and Attending Vet on 7/24/2020.

200855 - "The role of mTORC1 in regulating browning of fat tissue in mice."

Reviewers: *Chair, AV*

Summary: We are going to add 30 Foxp3 GFP animals, which will be donated by another PI, to do Treg cell transfer assay as the donors.

Approved by IACUC Chair and Attending Vet on 6/25/2020.

200855 #2 - "The role of mTORC1 in regulating browning of fat tissue in mice."

Reviewers: *Chair, AV*

Summary: To address the role of Bradykinin signaling in adipose tissue, we will perform B2R antagonist (HOE140) administration (200ug/kg body weight) by IP injection every 2 days for 2 Weeks in JunB flox and KO with High fat diet challenge. Mice will be perform study as described in Aim. 4. At the end of study, the mice will be euthanized, and the tissue samples will be collected for further analysis.

Approved by IACUC Chair and Attending Vet on 7/7/2020.

200870 - "Assessment of the immune responses in mice and rabbits induced by VLP-based vaccines targeting self and foreign antigens."

Reviewers: *Chair, AV*

Summary: We are requesting 60 additional balb/c mice in order to perform experiments testing the immunogenicity of VLPs displaying peptides derived from SARS-CoV-2.

Approved by IACUC Chair and Attending Vet on 4/6/2020.

200872 - "Molecular Regulation of T cell migration."

Reviewer: *Chair*

Summary: Add/remove staff

Approved administratively per IACUC Chair on 8/12/2020.

200873 - "VLP-based vaccines targeting Staphylococcus aureus virulence in Mice."

Reviewer: *Chair*

Summary: Remove staff.

Approved administratively per IACUC Chair on 7/31/2020.

200878 Vet Review - "Regulation of vascular tone by hydrogen sulfide in rats."

Reviewer: *AV*

Summary: Update on using 2 additional compounds added to the protocol to test impact on gut bacteria. These substances will be used in a similar manner to the approved protocol being tested. As per the approved protocol, Bismuth subsalicylate was used to test the impact on hydrogen sulfide produced in the intestine by chelating to produce H₂S. The two added compounds magnesium oxide (frequently used for digestive diseases to treat constipation) and cobinamide (a vitamin B12 analog) will be tested one at a time. As per the protocol, these compounds will be added to the food supply of the animals being tested. Remainder of the protocol will not change.

Approved by Attending Vet on 7/8/2020.

200889 - "Mechanisms of Vascular Toxicity from Inhaled Toxicants in Pregnant Rodents."

Reviewer: *Chair*

Summary: Add staff.

Approved administratively per IACUC Chair on 8/3/2020.

200925 - "Molecular Regulation of Stem Cell and Cancer Cell Mobilization, Homing and Engraftment with the Bone Marrow using Mouse Models."

Reviewer: *Chair*

Summary: Add staff.

Approved administratively per IACUC Chair on 8/25/2020.

200932 - "Neurochemical, electrophysiological and behavioral studies of a rat model of prenatal ethanol exposure."

Reviewer: *Chair*

Summary: Remove staff.

Approved administratively per IACUC Chair on 4/15/2020.

200932 #2 - "Neurochemical, electrophysiological and behavioral studies of a rat model of prenatal ethanol exposure."

Reviewers: *Chair, AV*

Summary: We are requesting a minor amendment for the purpose of examining the impact of a different rodent diet on ethanol consumption and serum ethanol levels in female Long-Evans rats. We are currently approved to use the Teklad 2920 diet. However, another PI has recently observed that mice consuming the 5001 diet consume nearly twice as much alcohol and produce higher blood ethanol concentration using his drinking paradigm. We would like to conduct a preliminary study to examine whether our adult female Long-Evan rats would consume greater amounts of alcohol producing higher blood alcohol levels than we have observed in recent years using a specific diet from a major vendor.

We have identified 12 five-month-old female Long-Evans rats for this preliminary study. Once approved, we would immediately place these females on the special diet for the duration of the preliminary study. After one week of acclimation to the new diet, we would begin our standard

voluntary drinking paradigm, titrating the rats up to a 5% ethanol in 0.066% saccharin water solution over a five-day period. Thereafter, we would track their daily four-hour consumption of ethanol for two weeks. Subsequently, during a third week, we would draw tail blood samples, 45 minutes after the introduction of the drinking tubes, on alternating mornings over five days, for a total of three tail-vein bleedings.

If, based on this preliminary study, the mean ethanol consumption on the 5001 diet exceeds 2.5 g/kg/day and the resultant mean peak serum ethanol levels exceed 80 mg/dL, we will move forward with the prospect of converting our standard rat chow diet to the special diet.

Approved by IACUC Chair and Attending Vet on 8/13/2020.

200932 #3 - "Neurochemical, electrophysiological and behavioral studies of a rat model of prenatal ethanol exposure."

Reviewer: *Chair*

Summary: Add staff.

Approved administratively per IACUC Chair on 8/19/2020.

200938 - "Preclinical development of subunit tularemia vaccines in F344 rat model."

Reviewers: *Chair, AV*

Summary: Due to the COVID-19 pandemic, there is a shortage of PPE required to work safely in the select agent ABSL-3 laboratory. We would like to temporarily limit daily observations to once-a-day to conserve PPE until additional supply can be secured.

Approved by IACUC Chair and Attending Vet on 5/15/2020.

200950 - "Neurovascular Consequences of Inhaled Uranium Minesite-Derived Dusts in Mice."

Reviewer: *Chair*

Summary: Add staff.

Approved administratively per IACUC Chair on 7/2/2020.

200950 #2 - "Neurovascular Consequences of Inhaled Uranium Minesite-Derived Dusts in Mice."

Reviewers: *Chair, AV*

Summary: I would like to re-arrange the C57BL/6J group to allocate 48 mice of these mice to B6J-Albino "white mice" instead of C57BL/6J. (So now we're left with 336 C57BL/6J and 48 B6J-Albino mice which are easier for tail-vein injections than black mice. These mice will also be subjected to behavioral /neurological outcomes (behavioral tasks). No increase in overall animal numbers.

Approved by IACUC Chair and Attending Vet on 7/10/2020.

200950 #3 - "Neurovascular Consequences of Inhaled Uranium Minesite-Derived Dusts in Mice."

Reviewers: *Chair, AV*

Summary: I am transferring 60 FVB/N-Tg (Kdr-mCherry) 1Medi/2 mice (30 male and 30 female) from my collaborator's protocol to my "neurovascular consequences of inhaled uranium mine-site derived dust in mice" for lab experiments in Aim 3. My collaborator will no longer be needing these mice, and I will be using them for experiments outlined in my protocol.

Approved by IACUC Chair and Attending Vet on 7/20/2020.

200960 Breeding - "Mouse Breeding Protocol - Cargo Of Exosomes and Microvesicles In Tuberos Sclerosis Complex."

Reviewer: *AV*

Summary: Addition of B6.129S1-ATP6v1b1 Global KO mice (H⁺-ATPase KO).

Approved by Attending Vet on 7/8/2020.

200970 - "Molecular Determinants of Brain Invasion and Metastasis in Mice Models."

Reviewer: *Chair*

Summary: Add staff.

Approved administratively per IACUC Chair on 4/22/2020.

200970 Vet Review #2 - "Molecular Determinants of Brain Invasion and Metastasis in Mice Models

Reviewer: *AV*

Summary: We would like to add retro-orbital blood collections in mice to this protocol.

Approved by Attending Vet on 7/2/2020.

200970 #3 - "Molecular Determinants of Brain Invasion and Metastasis in Mice Models."

Reviewers: *Chair, AV*

Summary: We would like to add MRI imaging to the protocol.

Approved by IACUC Chair and Attending Vet on 8/26/2020.

200973 - "Spreading Depolarizations and Post-Ischemic Injury in Mice."

Reviewer: *Chair*

Summary: Add staff.

Approved administratively per IACUC Chair on 6/22/2020.

200973 #2 - "Spreading Depolarizations and Post-Ischemic Injury in Mice."

Reviewer: *Chair*

Summary: Add staff.

Administratively approved per IACUC Chair on 8/7/2020.

200975 - "Repeated Binge Alcohol Drinking and the Genetic Regulation of Neural Synchrony in Mice."

Reviewer: *Chair*

Summary: Add staff.

Approved administratively per IACUC Chair on 5/7/2020.

200975 #2 - "Repeated Binge Alcohol Drinking and the Genetic Regulation of Neural Synchrony in Mice."

Reviewer: *Chair*

Summary: Add staff.

Administratively approved per IACUC Chair on 8/6/2020.

200987 - "FosTRAP mice for neural circuit identification in chronic pain models - Breeding Protocol."

Reviewer: *Chair, AV*

Summary: The funding agency has requested this breeding protocol be changed to Category D. (Due to genotyping procedure)

Approved by IACUC Chair and Attending Vet on 6/22/2020.

201002 - "Oncolytic Treatment of cancer in mice."

Reviewer: *Chair, AV*

Summary: We would like to add a new drug treatment onto our protocol (ruxolitinib). It is FDA approved for use in humans and frequently used in mice as a JAK inhibitor or inhibitor of interferon. We therefore don't feel that it increases the chances of animal pain or distress.

Approved by IACUC Chair and Attending Vet on 3/13/2020.

201002 #2 - "Oncolytic Treatment of cancer in mice."

Reviewer: *Chair*

Summary: Add staff.

Approved administratively per IACUC Chair on 3/20/2020.

201002 #3 – "Oncolytic Treatment of cancer in mice."

Reviewers: *Chair, AV*

Summary: We would like to test the efficacy of one of our viruses (vPD1/IL12) in mice lacking IL15Ra. We are therefore adding IL15Ra knockout mice to the protocol. These mice lack mature NK cells, but should not display any significantly altered risk following treatment.

Approved by IACUC Chair and Attending Vet on 5/7/2020.

201002 #4 - "Oncolytic Treatment of cancer in mice."

Reviewer: *Chair*

Summary: Add staff.

Approved administratively per IACUC Chair on 6/18/2020.

201002 #5 - "Oncolytic Treatment of cancer in mice."

Reviewers: *Chair, AV*

Summary: We would like to add a new drug for testing in combination with our recombinant myxoma viruses. The drug is Nor-NOHA. It's a fairly well studied arginase inhibitor that has been used in animals numerous times and demonstrated preclinical anti-tumor efficacy in multiple models. I'm also adding a new member of the lab to the protocol.

Approved by IACUC Chair and Attending Vet on 7/10/2020.

201013 - "Mouse and Rat Models of Orofacial Nerve Injury, Back Pain and Visceral Pain for Preclinical Studies of Pain Mechanisms and Potential Therapeutics."

Reviewers: *Chair, AV*

Summary: We are requesting approval to add two new rat strains to our protocol in order to reflect our future collaboration with another PI's Alzheimer's project. (This collaboration will also be reflected in the protocol.) We are also submitting updates to our TIC (Now FRICT-ION) protocol in conjunction with our newly published protocol, which will be referenced in the

protocol procedure. We will not be requesting any additional animals; we will be receiving animals via transfer from another PI's protocol. We will not be requesting any changes to the previously approved models that would increase pain or distress to the animals.

Approved by IACUC Chair and Attending Vet on 4/21/2020.

201013 #2 - "Mouse and Rat Models of Orofacial Nerve Injury, Back Pain and Visceral Pain for Preclinical Studies of Pain Mechanisms and Potential Therapeutics."

Reviewers: *Chair, AV*

Summary: We are requesting approval for the addition of a cisplatin-based model of chronic pain in mice. The model involves daily injections of the compound cisplatin, and the model will last for many weeks after the injections are completed. This model will be used in conjunction with our other pain models as a comparative to help understand the mechanisms underlying chronic pain. We will not be requesting any additional animals; we will repurpose numbers from initially proposed experiments that were not performed due to changes in research objectives. We will not be requesting any changes to the previously approved models that would increase pain or distress to the animals.

Approved by IACUC Chair and Attending Vet on 5/12/2020.

201013 - "Mouse and Rat Models of Orofacial Nerve Injury, Back Pain and Visceral Pain for Preclinical Studies of Pain Mechanisms and Potential Therapeutics."

Reviewers: *Chair, AV*

Summary: We are requesting approval to add two additional compounds for testing in our previously approved mouse models of chronic orofacial pain and spared nerve injury: KYT-0353 and the TAT-C3P peptide. KYT-0353 is a selective inhibitor of LAT1. LAT1 expression is upregulated following spinal cord injury; thus, we plan on studying the effectiveness of this inhibitor on our chronic models. TAT-C3P is a combination peptide with a Cav3.3 blocking component as well as a transactivator of transcription component that has strong membrane-penetrating properties. Alteration of the Cav3.3 channel has been associated with a number of human neuronal disorders, and we plan on studying the effects blocking that channel has on our chronic model. We will not be requesting any additional animals; we will repurpose numbers from initially proposed experiments that were not performed due to changes in research objectives. We will not be requesting any changes to the previously approved models that would increase pain or distress to the animals. It is our hope that these drugs will prove to be therapeutic and relieve pain.

Approved by IACUC Chair and Attending Vet on 8/13/2020.

201020 Vet Review - "Study of papillomavirus entry and infection in mouse models."

Reviewer: *AV*

Summary: While performing a pilot MmuPV1 treatment experiment we are finding that MEK inhibitor treatments can successfully reduce tumor volume. Currently, we have approval to treat the animals with MEK inhibitors for two weeks but we would like to extend treatment for 2 or more weeks to determine if MEK treatment is able to cause further regression of the tumor. We have another protocol for tumor xenografts where we treat with the same drugs and similar concentrations for 6-8 weeks. And many other studies treat for longer. Thus there is precedent that the drugs are safe for longer periods.

Approved by Attending Vet on 8/27/2020.

201025 - "A mouse model to study inflammatory diseases."

Reviewer: *Chair*

Summary: Add staff.

Approved administratively per IACUC Chair on 8/17/2020.

Item # 7 Annual Renewals:

200369 Closure - "Repetitive Concussive Mild and Severe Traumatic Brain Injury Mechanisms and Treatment in Rats."

Reviewer: *Chair*

Summary: Study has concluded.

Closed administratively per IACUC Chair on 3/19/2020.

200654 Closure - "Breakthrough Threshold of Intracranial Pressure Autoregulation."

Reviewer: *Chair*

Summary: Study has concluded.

Closed administratively per IACUC Chair on 3/19/2020.

200657 DMR with Minor - "Role of non-coding RNAs in brain development and function and antipsychotic treatment in mice."

Reviewer: *Chair*

Summary: Remove staff.

Approved as a DMR by IACUC Chair on 8/21/2020.

200671 Closure - "Acquired Post-Hemorrhagic Hydrocephalus from Intraventricular Hemorrhage in Rats."

Reviewer: *Chair*

Closed administratively per IACUC Chair on 8/7/2020.

200707 DMR - "Mechanisms of melanoma metastasis in mouse models."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 4/9/2020.

200710 DMR - "Nasal Administration of Epinephrine/Phentolamine in a Rat Model - A Proof of Concept Study."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 6/22/2020.

200714 DMR - "Chemokine receptors in MRI contrast-induced organ fibrosis [a mouse model]."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 3/9/2020.

200717 DMR - "A mouse model of *Mycobacterium abscessus* lung infection that mimics human infection."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 5/1/2020.

200720 Breeding DMR by Vet - "Breeding protocol for chemokine receptors in magnetic resonance imaging contrast-induced systemic fibrosis."

Reviewer: *AV*

Approved as a DMR by Attending Vet on 7/27/2020.

200722 DMR - "Targeting ErbB Receptors in Mouse Models of Cancer."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 8/3/2020.

200723 DMR - "Imaging of the immune response in a murine ovarian cancer model after checkpoint inhibition."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 7/10/2020.

200724 Tissue - "Blood- and tissue-related Discrimination of Infectious Disease Patterns."

Reviewers: *Chair, AV*

Approved by IACUC Chair and Attending Vet on 8/21/2020.

200728 Breeding DMR - "Rodent models of pulmonary hypertension, intermittent hypoxia induced systemic hypertension and asthma."

Reviewer: *AV*

Approved as a DMR by Attending Vet on 5/5/2020.

200730 Breeding DMR - "Breeding protocol for a mouse model of *Mycobacterium abscessus* lung infection using mice with abnormal lung airways."

Reviewer: *AV*

Approved as a DMR by Attending Vet on 7/20/2020.

200734 DMR - "A Rat Model for Microsurgery Training."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 8/21/2020.

200758 Baca DMR - "Characterization of the exosome and microRNA content of interstitial fluid in rats."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 8/7/2020.

200767 Nemoto DMR - "Treatment of the rat malignant brain tumor."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 6/30/2020.

200769 DMR - "Study of T cell responses in a mouse model of influenza infection."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 8/21/2020.

200822 DMR - "Alcohol Research Center Scientific Core Breeding and Drug Exposure Protocol for Mice and Rats."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 5/13/2020.

200832 Closure - "Ferroptosis in the EAE mouse model of Multiple Sclerosis".

Reviewer: *Chair*

Closed administratively per IACUC Chair on 3/10/2020.

200834 Breeding DMR by Vet - "Mouse lines for studies of the role of RNA-binding proteins in neural development".

Reviewer: *AV*

Approved as a DMR by Attending Vet on 3/9/2020.

200838 DMR - "Establishing Humanized Mice for Immuno-Oncology Xenograft Models."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 6/9/2020.

200839 DMR- "Role of brain specific tyrosine phosphatase, STEP, in neuroprotection and death in rodents."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 5/26/2020.

200841 Breeding DMR by Vet - "Breeding protocol for the Role of Neuroinflammation in Tauopathies."

Reviewer: *AV*

Approved as a DMR by Attending Vet on 3/19/2020.

200842 DMR - "Microbiome-driven mouse models for Candida commensalism and gut-derived candidiasis."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 3/31/2020.

200843 DMR - "Molecular Regulators of T-Acute Lymphoblastic Leukemia (T-ALL) cell migration."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 3/31/2020.

200846 Closure - "Growing primary human ovarian cancer cells in mice."

Reviewers: *Chair*

Summary: Over the course of the year we have only received 2 ovarian cancer samples. With this protocol we proposed to inject mice with the ovarian tissue we received but with so few samples we were unable to use the mice that were ordered. We have decided to terminate this study due to the lack of an appropriate sample size.

Closed administratively per IACUC Chair on 3/16/2020.

200848 DMR - "Mechanisms of hypoxic pulmonary hypertension in a mouse model."

Reviewer: *12 (VC)*

Approved as a DMR by Vice Chair on 3/16/2020.

200849 DMR - "Animal Procedures and Techniques Training – HSC."

Reviewer: *12 (VC)*

Approved as a DMR by Vice Chair on 3/18/2020.

200852 DMR - "Neurophysiological biomarkers of behavioral dimensions from cross-species paradigms in mice."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 5/13/2020.

200855 DMR - "The role of mTORC1 in regulating browning of fat tissue in mice."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 4/20/2020.

200856 DMR - "Regulation of T helper cell effector function - Mouse models"

Reviewers: *Chair, AV*

Summary: 1) In Experiment 2 Cell or tissue transfer, we request to replace lymphopenic Rag1KO mice with non-lymphopenic CD4KO as recipients and the resulting mice will be used in experiments 3 Asthma induction and 4 Experimental autoimmune encephalomyelitis (EAE) induction. 2) In immunization, we request to add IL-23 or vehicle (PBS) for intranasal administration with inactivated *Candida albicans*. No increase in stress/pain.

Approved as a DMR by IACUC Chair and Attending Vet on 3/31/2020.

200857 Closure - "Regeneration after stroke and brain trauma in mice".

Reviewer: *Chair*

Closed administratively per IACUC Chair on 3/2/20.

200858 Breeding DMR by Vet - "Laboratory Mouse Breeding Protocol."

Reviewer: *AV*

Approved as a DMR by Attending Vet on 3/9/2020.

200859 DMR - "Evaluation of Virus-like Particle based vaccines for HPV in mice."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 4/20/2020.

200864 DMR - "Arsenic-enhanced skin carcinogenesis by UV radiation in mice."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 3/9/2020.

200867 DMR - "Evaluation of Virus-like Particle based vaccines for Chlamydia."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 3/25/2020.

200868 Tissue - "Immunohistochemical analysis of Mammalian Brain Tissue".

Reviewers: *Chair, AV*

Approved by IACUC Chair and Attending Vet on 3/9/2020.

200869 DMR - "zinc chemoprevention of arsenic co-carcinogenesis in mice."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 3/16/2020.

200870 DMR with Minor - "Assessment of the immune responses in mice and rabbits induced by VLP-based vaccines targeting self and foreign antigens."

Reviewer: *Chair*

Summary: Add staff.

Approved as a DMR by IACUC Chair on 4/20/2020.

200872 DMR - "Molecular Regulation of T cell migration."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 3/31/2020.

200873 DMR - "VLP-based vaccines targeting Staphylococcus aureus virulence in Mice."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 3/25/2020.

200874 Holding DMR - "Animal Holding Protocol Laboratory Mice and Rats, Rabbits & Frogs-HSC."

Reviewer: *Chair*

Summary: Add staff.

Approved as a DMR by IACUC Chair on 4/22/2020.

200875 DMR - "Quality Assurance Sentinel Rodent and Rabbit Testing Program." H

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 3/31/2020.

200878 DMR - "Regulation of vascular tone by hydrogen sulfide in rats."

Reviewer: *AV*

Approved as a DMR by Attending Vet on 4/29/2020.

200880 DMR - "Effects of passive immunization on immunogenicity of filovirus vaccines in mice."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 3/9/2020.

200881 with minor Tissue - "Live Imaging of Brain Circuitry in Mouse Models of PTSD."

Reviewers: *Chair, AV*

Approved by IACUC Chair and Attending Vet on 6/16/2020.

200882 with minor Tissue - "Imaging Brain anatomy and Function in mice using MRI."

Reviewers: *Chair, AV*

Summary: Add/remove staff. My main collaborator moved universities. His approved animal protocols have been submitted with my live animal experimental protocols and will be updated when those UNM protocols come up for renewal, necessitating a minor modification of the procedures. We have existing MTAs for these exchanges.

Approved by IACUC Chair and Attending Vet on 6/16/2020.

200883 DMR - "Control of allergic airway inflammation - Mouse models."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 4/21/2020.

200884 with Minor DMR - "Breeding protocol for ovarian cancer mouse models."

Reviewer: *AV*

Summary: Remove staff.

Approved as a DMR by Attending Vet on 5/11/2020.

200886 Breeding DMR by Vet - "Mouse Breeding Protocol for Studies on the Effect of Alcohol Exposure on Brain Development."

Reviewer: *AV*

Approved as a DMR by Attending Vet on 4/7/2020.

200889 DMR - "Mechanisms of Vascular Toxicity from Inhaled Toxicants in Pregnant Rodents."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 6/22/2020.

200893 DMR with Minor - "A Rat Model for Neuroinflammation in Intracerebral Hemorrhage."

Reviewer: *Chair*

Summary: Remove staff.

Approved as a DMR by IACUC Chair on 5/26/2020.

200894 Closure - "Effect of intermittent hypoxia on renal function in rats."

Reviewer: *I2 (VC)*

Closed administratively per IACUC Vice-Chair on 5/4/2020.

200899 DMR with Minor - "Role of Acid Sensing Ion Channel in the Vasculature."

Reviewer: *Chair*

Summary: Add/remove staff; I am adding previously approved methods (measure respiration in mice) back into protocol so that I can finish data collection. This is a non-invasive technique and will not require additional animals. The methods have been added back to the updated "mouse description 050520" file.

Approved as a DMR by IACUC Chair and Attending Vet on 5/20/2020.

200901 DMR - "SerpinB13 knockout mouse strain characterization."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 6/9/2020.

200902 DMR - "Xenograft leukemia mouse models to test the in vivo efficacy of drug reducing polymers (DRPs) for prevention of leukemia metastasis."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 6/30/2020.

200903 Breeding DMR by Vet - "Breeding protocol for experimental animals on 18-200773-HSC."

Reviewer: *AV*

Summary: Add/remove staff.

Approved as a DMR by Attending Vet on 6/16/2020.

200907 DMR with Minor - "Investigating how different tungsten routes of exposure affect breast cancer progression in Mice."

Reviewer: *Chair*

Summary: Remove staff.

Approved as a DMR by IACUC Chair on 5/27/2020.

200909 Breeding DMR by Vet - "Breeding protocol for Hyper-IgE (B6-Tg mut-Stat3/J 027952) mice."

Reviewer: *AV*

Approved as a DMR by Attending Vet on 5/12/2020.

200910 DMR - "Inhalation of Contaminated Mine Waste Dusts in Mice as a Route for Systemic Metal Toxicity."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 6/16/2020.

200914 DMR - "██████-Preclinical MRI/PET Core for method development, instrument quality control, and diagnostic procedure protocol."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 8/13/2020.

200916 DMR – "Using In vivo model of mice and rats to study Mechanisms of Increased Vascular Permeability in Diabetic Retinopathy."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 5/15/2020.

200918 DMR - "Testing novel vaccines for Zika virus infection in mice."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 6/9/2020.

200919 DMR - "Remodeling of blood-brain barrier & cell death after stroke in Rats."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 6/9/2020.

200921 DMR - "The effect of pulsed electromagnetic field on synaptic transmission and calcium signaling in rat hippocampal slices."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 6/30/2020.

200922 DMR - "Murine models of neoplastic development and therapeutics."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 8/4/2020.

200923 Breeding DMR by Vet - "Lab Mouse Breeding Colony."

Reviewer: *AV*

Approved as a DMR by Attending Vet on 7/27/2020.

200925 DMR with minor - "Molecular Regulation of Stem Cell and Cancer Cell Mobilization, Homing and Engraftment with the Bone Marrow using Mouse Models."

Reviewer: *Chair*

Summary: Remove staff.

Approved as a DMR by IACUC Chair on 6/9/2020.

200928 DMR - "A Frog Model for Rhodopsin Trafficking and Photoreceptor Membrane Renewal."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 6/16/2020.

200931 Closure - "Nanoparticle Delivery of Cas9 Editing Machinery in Mice."

Reviewer: *Chair*

Summary: We have completed the contracted studies to determine the biodistribution of nanoparticles carrying the cas9 gene editing machinery.

Closed administratively per IACUC Chair on 6/25/2020.

200932 DMR - "Neurochemical, electrophysiological and behavioral studies of a rat model of prenatal ethanol exposure."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 5/13/2020.

200933 DMR - "Post-transcriptional control of neuronal mRNAs in normal conditions and mouse models of psychiatric illnesses/addiction"

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 8/4/2020.

200945 Closure - "Role of TRPV4 in obesity-induced vascular dysfunction in mice."

Reviewer: 22 (*VC*)

Closed administratively per by Vice-Chair on 7/24/2020.

200950 DMR - "Neurovascular Consequences of Inhaled Uranium Minesite-Derived Dusts in Mice."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 8/10/2020.

200955 DMR - "Assessment of pulmonary edema using a breath gas sensor in rats."

Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 7/10/2020.

200959 DMR – "Rapid Alcohol Detection and Monitoring in Dermal Interstitial Fluid (ISF) in Rats." Reviewer: *Chair*

Approved as a DMR by IACUC Chair on 8/7/2020.

200960 Breeding DMR by Vet - "Mouse Breeding Protocol - Cargo Of Exosomes and Microvesicles In Tuberous Sclerosis Complex."

Reviewer: *AV*

Approved as a DMR by Attending Vet on 8/25/2020.

General Business:

- 1) IACUC Concerns – Due to ongoing COVID-19 restrictions, the ARF is managing entry into the various animal rooms via a sign in sheet for users. The committee discussed whether or not using QR codes for contact tracing would be a more efficient method. The AV, who is the ARF Director will consider this request. The AV gave a brief update on animal census and staff operations. The AV also gave an update on a new animal facility and research space that will begin construction next year (2021).
- 2) 2020 Fall HSC IACUC Semi-annual Inspections will be completed virtually in September. Review of the final inspection report to the IO and Program Review will be carried out via Zoom meeting in October.
- 3) IPRA requests from NEAVS continue.

The meeting was adjourned at 1:08 PM.

Respectfully submitted by the Recording Secretary _____