PHI ZETA RESEARCH EMPHASIS DAY ABSTRACTS

Category: Basic Research, DVM, Non-DVM Students

142. MB0DSNDU

Role of Osteocalcin in Glucose Homeostasis During Diabetes Mellitus

H. Guidry, W. Grazian, W. Rong, Y. Yuan, S. Yao, M. Yoshimura, H. Cheng

Osteocalcin is a peptide hormone produced by bone osteoblast cells that contributes to bone mineralization. In addition to bone function, osteocalcin can stimulate insulin secretion from pancreatic ß-cells. Furthermore, diabetic patients develop osteoporosis at a higher rate than healthy ones suggesting a role for osteocalcin in the etiology of these two diseases. Nevertheless, how pancreatic ß-cells respond to osteocalcin under hyperglycemia remains unclear. The goal of the study was to quantify insulin secretion from ß-cells in response to osteocalcin under elevated glucose conditions. We also obtained insight into its mechanism of action by performing real-time intracellular calcium recordings in single cells and RT-qPCR analysis to examine the expression of genes involved in the insulin secretion pathway. We hypothesized that insulin secretion will be decreased/or absent in the presence of osteocalcin under elevated glucose conditions, along with downregulation of one or more genes involved in the insulin secretion pathway. The results showed that 1000pg/mL osteocalcin stimulated intracellular calcium increases in INS-1 and RINm5F cells and under hyperglycemic conditions, insulin secretion was decreased. It was also shown that under low concentrations of osteocalcin, gene expression decreased during hyperglycemic conditions, while under high concentrations of osteocalcin gene expression decreased during both normoglycemic and hyperglycemic conditions. Overall, our results show that osteocalcin plays a vital role in glucose homeostasis and our lab will work further to deduce the mechanism of action.

143. MB1DSNDU

Porcine Model of Costochondral Graft for Temporomandibular Joint Replacement

A. Fang, C. Takawira, T. Taguchi, J. Lopez, G. Mundinger, M. Lopez

An adult large animal model of costochondral graft for temporomandibular joint reconstruction is necessary to support preclinical trials. The hypothesis tested in this study was that costochondral graft promotes better mandibular condyle microstructure, morphology, and articular cartilage characteristics than no treatment. The left mandibular condyle and caudal ramus were replaced with either the 7th rib and costochondral junction (n=5) or no treatment (n=2) in adult Yucatan boars. Mandibular morphology, microstructure, and condyle articular cartilage were assessed up to 6 months after implantation using computed tomography, micro-computed tomography, and articular cartilage-specific gene expression, respectively. In both groups, the ostectomized tissue was replaced with new tissue. Overall bone volume in the treatment group (124±5.264%:115% at 12wk; 122% at 24wk) tended to be higher than no treatment (106.8±3.258%:111% at 12wk, 100% at 24wk). With no treatment, Col3 and SOX5 were upregulated and Col1 and 2, SOX6 and 9, TGFß3, Runx1, aggrecan, and BMP2 were downregulated. Preliminary gene expression suggests that scar-like fibrous tissue forms with no treatment. The graft led to slight overgrowth of the mandibular condyle, a common complication in humans. Results of this adult porcine model for costochondral graft mandibular condyle reconstruction suggests that the model is appropriate for human preclinical trials.

145. MB2DSNDU

Elucidating the Mechanisms of Polyunsaturated Fatty Acid Killing of S. aureus Small Colony Variants

K. E. Rico, W. N. Beavers

Staphylococcus aureus is a Gram-positive pathogen that causes 900,000 infections in the United States annually. It is the leading cause of Gram-positive sepsis and can infect every niche of the vertebrate host, emphasizing the need to develop more effective treatments. S. aureus grows by aerobic respiration, anaerobic respiration, or fermentation. Small colony variants (SCV) are obligate fermenters, extremely persistent in the host, and tolerate antibiotics. Arachidonic acid (AA) is an abundant host-derived polyunsaturated fatty acid (PUFA) at the host-pathogen interface. AA kills respiring S. aureus through a lipid peroxidation mechanism where electrophiles adduct proteins killing S. aureus. We tested the hypothesis that SCVs are differentially susceptible to PUFA killing due to their metabolism using NE1345, an SCV strain with disrupted menaquinone biosynthesis. AA kills NE1345 more than its parental strain, JE2. Exogenous menadione chemically complements the NE1345 phenotype, restoring respiration and growth to JE2 levels both with and without AA. Alpha tocopherol (aTOH), an antioxidant that halts lipid peroxidation, protects NE1345 and JE2 from AA killing, indicating that lipid peroxidation is involved in PUFA killing of SCVs. I hypothesize that the cellular machinery used during fermentation may increase SCV susceptibility to PUFAs. My future aims for this project include identifying lipid electrophiles, defining the protein targets of the electrophiles in S. aureus SCVs, and to uncover the pathways in SCVs that are affected by PUFA. These experiments will elucidate and validate targets for future antimicrobial therapies to treat S. aureus infections.

149. MB3DSNDU

Analyzing Baseline and Post-Restraint Plasma Corticosterone Levels in Hispaniolan Amazon Parrots (Amazona ventralis)

S. Parks, T. Tully, A. Settle, C. Lattin

Rationale: The purpose of this study was to measure baseline plasma corticosterone levels in 22 Hispaniolan Amazon parrots and assess the effects of handling and restraint on corticosterone levels over 1 hr, reflective of what parrots might experience during veterinary care.
Methods: Each parrot was removed from its cage and wrapped in a towel for restraint, similar to that performed in a clinical setting. An initial baseline blood sample was collected in < 3 min, after which blood samples were taken every 15 min for one hour (a total of five blood samples). To determine concentrations of plasma corticosterone, an enzyme-linked immunoassay was used.
Results: Parrots showed a significant increase in corticosterone between baseline samples and all subsequent post-restraint time points (average baseline corticosterone ± SD: 0.51 ± 0.65 ng/ml). Females, on average, displayed significantly higher corticosterone levels than males after 30, 45, and 60 min of restraint ($P = .016$, $P = .0099$, and $P = .015$, respectively). Birds with feather destructive behavior (FDB) did not have significantly higher corticosterone levels than birds without the condition ($P = .38$).
Conclusions/Significance: The results show that pscittacines experience stress in response to handling, and that stress response varies based on the sex but not necessarily underlying conditions (e.g. FDB). Understanding this response during routine handling will allow clinicians to better evaluate how stress may affect patient conditions and diagnostic test results. Assessing how corticosterone correlates to behavioral conditions such as FDB gives the potential to develop treatment options for these conditions.

150. MB4DSNDU

Behavioral Response to Auditory Cues Following Manipulation of Midbrain Projection Systems

C. Raymond, T. Adeyelu, O. Ogundele, and C. Lee

Hearing impairments are a major health issue that can have a considerable impact on quality of life. Central neural auditory circuits are critical to the processing of sound or auditory information. There have been many studies on the extraction of sound location. However, these studies rarely use mice because they are considered to have very little ability to detect auditory special cues. This ability in mice may be improved from the extraction of spectral information in higher auditory centers; notably, between the inferior colliculus (IC) and medial geniculate body. These pathways connect bilateral auditory structures, namely the projections of the tectum and thalamus. Manipulating these commissural pathways using chemogenetic techniques, may improve the ability of the mice to localize sound. This chemogenetic approach involves injecting a double-floxed virus into the IC and DREADD, or compound 21, peritoneally. This research will first assess the behavioral response of inhibitory VGAT-Cre, excitatory VGLUT2-CRE and wildtype mice by utilizing the acoustic startle response using a modified pre-pulse inhibition with and without DREADD; followed by a physiological assessment using the same stimuli. Research is on-going but we expect to see evidence of the impact of the (IC) on auditory processing.

Category: Basic Research, DVM, House Officers, Residents

151. MB5MHR

No evidence of FHV-1 mutation and development of antiviral resistance in feline hosts treated with antiviral medication

E.P. Mills, A.C. Lewin, N.E. Ineck, M.A. Mironovich, M. Marino, C.C. Liu, U. Emelogu, P. Camacho, R.T. Carter

Rationale: Feline herpes virus (FHV-1) is a common cause of ocular disease in cats. Multiple antiviral medications which target the UL23, UL30, and UL42 viral genome regions have been used as treatment for this disease. Compared to other herpes viruses such as herpes simplex virus (HSV1/2), FHV-1 is highly conserved. Antiviral resistance has been previously documented in HSV 1/2 but has not been documented following short term antiviral treatment in FHV-1 positive cats.
Methods: Fourteen immunocompetent cats positive for FHV-1 from shelters in Louisiana, USA were assigned to one of four treatment groups: placebo (n=3), cidofovir 0.5% ophthalmic solution (n=3), famciclovir oral solution (90mg/kg; n=5), or ganciclovir 0.15% ophthalmic solution (n=3). Conjunctival swabs were collected on Day 1 and Day 8 after receiving twice daily treatment. DNA was extracted for sequencing using Illumina MiSeq with variant detection between each viral pair (Day 1/8). In-vitro half-maximal inhibitory concentration testing (IC50) for each non-synonymous viral pair was completed to assess for development of antiviral resistance.
Results: 171 synonymous and 3 non-synonymous variants were identified between viral pairs. There were no variants in the UL23, UL30, or UL42 genes. A viral pair from each antiviral treatment group had one non-synonymous variant in the ICP4 region. The 3 non-synonymous variants were not associated with antiviral resistance when IC50 was evaluated.

Conclusions: This data suggests that short-term, low frequency use of various antiviral medications in immunocompetent cats with FHV-1 is unlikely to lead to viral mutation and development of antiviral resistance.

152. MB6MHR

Calibration of the Tono-Vera® Vet in rabbit and porcine eyes

E.P. Mills, C.C. Liu, U. Emelogu, R.T. Carter, P. Camacho, A.C. Lewin

Rationale: Both pigs and rabbits are commonly used as translational models. The Tono-Vera® Vet has not yet been validated in rabbit and pig eyes. The goal of this study was to determine which setting is the most appropriate for use in these species.
Methods: Six freshly enucleated rabbit eyes and five freshly enucleated pig eyes were cannulated and connected to a fluid reservoir and physiologic monitor. Triplicate measurements were obtained at various intraocular pressures (IOP) ranging from 5-80mmHg on each of the four species specific settings: dog, cat, horse, and rabbit. Linear regression and Bland-Altman analysis were utilized.
Results: In both rabbit and pig eyes, all settings demonstrated strong positive linear trends. In pig eyes, all settings demonstrated proportional bias except for the dog setting, which had an average bias of -2.00mmHg. The dog setting also had the smallest 95% limits of agreement compared to the other settings (-7.52, 3.53 mmHg) in pig eyes. This indicates that the dog setting is most accurate and precise setting in pig eyes. In rabbit eyes, all settings demonstrated proportional bias, however the average bias (-2.73 mmHg) and 95% limits of agreement (-12.21, 6.76 mmHg) were the smallest for the rabbit setting. This confirmed that the rabbit setting is the most precise and accurate in rabbit eyes.
Conclusions: This data suggests that when using the Tono-Vera® Vet, the dog setting is the most appropriate setting for use in pig eyes, and the rabbit setting is the most appropriate for use in rabbit eyes.

153. MB7MHR

Effect of Hyperbaric Oxygen Therapy on In Vitro Growth of a Novel Oomycete

M. Sachse, S. Dehghanpir, L. Hale-Mitchell, C. Liu, A. Johnston

Rationale:
Infections caused by oomycetes result in gastrointestinal and cutaneous disease in dogs. Canine oomycosis occurs in tropical and subtropical environments worldwide, and commonly along the US Gulf coast. Because management is challenging, adjunctive treatments are needed. Hyperbaric oxygen therapy (HBOT), which delivers 100% oxygen at high pressure, has been proposed as a secondary line of therapy. Benefits are due in part to the effects of hyperoxygenation of tissue. Hyperoxia generates reactive oxygen species which lead to cellular damage in organisms lacking an effective antioxidant response.
Methods:
Cultures of an unidentified Lagenidium species were subjected to HBOT. Two experiments, each consisting of one control and one treatment plate, were performed: 1) group A underwent 1 HBOT exposure and 2) group B underwent HBOT treatment daily for 3 consecutive days. Colony size was measured and examined microscopically to assess morphologic changes. A paired two-tailed t-test was used for statistical analysis.
Results:

In group A, there was no statistically significant size difference between the treated colony versus the untreated control. In group B, growth was significantly attenuated in the treated oomycetes compared to the control (delta diameter = 1.27mm, p = 0.002). No microscopic morphologic differences were observed in either experiment.
Conclusions:
HBOT had variable effects on in vitro growth of oomycete cultures. While 3 HBOT treatments significantly attenuated oomycetes growth, the change was minimal and unlikely to be clinically relevant. Additional in vitro and in vivo studies are needed to determine the value of HBOT as a treatment for oomycosis.

163. MB8MHR

Detailing Canine Aging-Related Immunoscenesence Using Single-Cell RNA Sequencing

C. Moeller, C. Quick, A. Lewin, W. Huang, B. Stanfield, E. Sparger, S. Withers

Rationale: Our primary objective was to explore the effect of aging on canine lymphocytes using single-cell RNA sequencing (scRNAseq). We hypothesized that a) naïve and memory canine lymphocyte subsets could be identified using scRNAseq, b) the ratio of naïve:memory lymphocytes will decrease with age, and c) genes associated with inflammation will be upregulated in aged dogs.
Methods: Peripheral blood mononuclear cells (PBMCs) were isolated from two young (2-3 y/o) and two aged (12-13 y/o) dogs. CD3+ lymphocytes were sorted using FACS, and 10,000 cells from each sample were input into the 10x Genomics pipeline for 3' scRNAseq. Sequencing was performed on an Illumina NextSeq 500 according to 10x guidelines. PBMCs from an additional six dogs were collected to validate key findings with RT-qPCR.
Results: Four basic cell subsets were defined by their gene expression as B cells, or naïve, effector memory, or cytotoxic T cells. Re-clustering of each basic subset elucidated more defined subsets such as CD4+ and CD8+ naïve T cells, and ?dT cells. Naïve T cells decreased from 44.8% to 19.8%, while effector memory T cells increased from 25.7% to 42.8% in young vs, aged dogs. Notably, we observed increased expression of proinflammatory transcripts (S100A5, S100A8 and vimentin) in aged dogs, which was confirmed by RT-qPCR.
Conclusions: We observed similar indicators of aging-related immunoscensence in dog lymphocytes compared to data in mice and humans.
Significance/Impact/Implications: Species-specific reagent limitations are often stated as downsides to utilizing immune-related canine diseases as comparative models. Our data demonstrate the ability of scRNAseq to overcome this limitation.

172. MB11MHR

Evaluation of the bovine bacterial ocular surface microbiome in the context of ocular squamous cell carcinoma

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Rationale: Ocular squamous cell carcinoma (OSCC) is common in cattle. The ocular surface microbiome may be altered in the context of disease. The purpose of this study was to characterize the bovine bacterial ocular surface microbiome (BBOSM) in eyes with and without OSCC, hypothesizing that there would be significant differences between groups.

Methods: Hereford (n=18) and Hereford-Red Angus cross (n=1) cows aged 2-13 years from Louisiana (n=1) and Wyoming (n=18) with normal eyes (n=28) and OSCC eyes (n=10) were sampled via swab of the conjunctival fornix. A unique quantitative polymerase chain reaction (qPCR) panel and 16S ribosomal ribonucleic acid (rRNA) gene high-throughput sequencing were performed using extracted DNA. Statistical analysis utilized JMP Pro 16.2.0 software and R scripts via the DADA2 workflow and phyloseq. Quadratic discriminant analyses (QDA) and linear discriminant analyses (LDA) were used to categorize qPCR data by disease status and geographic location, respectively.
Results: Euryarchaeota abundance was significantly lower in OSCC (median= 0.40% (0.00-3.81%)) compared to normal eyes (median=1.26% (0.02-6.90%)) (p=0.0372). Geographic differences in the relative abundance of three phyla were identified. QDA used to separate by disease status showed high sensitivity (100%) and specificity (83.3-100%). Pasteurellaceae and Mycoplasma were most highly associated with the canonical variable in QDA and LDA analyses, respectively.
Conclusions/significance: Few differences were identified using 16s rRNA sequencing. Discriminant analysis based on a unique qPCR panel allowed classification based on disease status and location. The BBOSM is altered in bovine OSCC. Bacterial QDA may have diagnostic potential for early detection of OSCC.

Category: Basic Research, DVM, Non-DVM Students

167. MB9DSNDU

High-Throughput Screening of Tyrosine Kinase Inhibitor Activity in Human and Canine Osteosarcoma Cells

K. Perkins, C. Moeller, K. Kousoulas, J. Francis, S. Withers

In both dogs and humans, osteosarcoma (OSA) exhibits an aggressive clinical progression and a modest anti-tumor immune response. Promising novel therapeutic targets include tyrosine kinase receptors such as Ret, Kit, PDGFRs, VEGFRs, and EGFRs. Our objective was to use a comparative approach to establish a shortlist of tyrosine kinase inhibitors (TKIs) that show a) growth inhibition in adherent and 3D OSA cell cultures, b) inhibition of OSA cell migration, and c) induction of immunogenic cell death.
Four canine, four human, and one human osteoblast cell line were utilized. Fifteen promising compounds were selected from a screen of 80 TKIs based on their inhibition of OSA cell proliferation. IC50s were determined for each of the 15 selected compounds. Viability was measured in adherent cells with an MTS assay, and in spheroids via live4-cell imaging using a fluorescent DNA-binding dye. Cell migration was measured with a scratch assay, and immunogenic cell death was detected with an HMGB1 immunoassay.
Preliminary findings revealed the inhibitors PHA-665752 (c-Met inhibitor), afatinib (EGFR/HER2 inhibitor), and ponatinib (Bcr-Abl/FGFR/PDGFR/VEGFR inhibitor) to be amongst the most cytotoxic compounds on both adherent and spheroid cultures of OSA cell lines. Additional data collection is ongoing.
TKIs targeting VEGFR, PDGFR, EGFR, HER2, and cMet were overrepresented amongst the compounds with efficacy against OSA cells, suggesting these receptors may be the most promising therapeutic targets. These findings will ultimately be translated into in vivo studies evaluating the synergistic activity of select TKIs in combination with established chemotherapy protocols and immunotherapeutics in OSA.

173. MB9DSNDU

Validation of Significant X-Linked Genes in Sexual Dimorphism of the BPH/5 Preeclamptic Mouse Model

K. Crissman, V. Gomes, K. Beckers, J. Sones

Rationale: Pre-conception maternal obesity is a risk factor for preeclampsia (PE), a hypertensive disorder of pregnancy with adverse offspring outcomes. The blood pressure high subline 5 (BPH/5) female mouse mimics PE risk factors, including obesity, while BPH/5 males are lean. Amelioration of the obese condition in dams has demonstrated improved offspring outcomes. Genome wide association studies performed on BPH/5 females revealed genetic mutations in the X chromosome that may potentially contribute to the dimorphic phenotype. We hypothesized that correlation exists between BPH/5 adiposity and cardiometabolic risk in offspring through epigenetic programming.
Methods: Reproductive white adipose tissue (rWAT) was collected from adult female and male BPH/5 littermates (n=6) for whole genome bisulfite sequencing (WGBS). qPCR measured Xist and Androgen Receptor (AR) mRNA in rWAT and compared using statistical tests.
Results: Methylation levels were identified and quantified with 10% in the promoter and 7% within the exonic region. WGBS analysis pinpoint key differentially methylated regions (DMRs) mapping to obesity-associated genes. Xist was 5-fold higher in BPH/5 females versus males (n=3-4; $p < 0.05$). AR was 2-fold lower in BPH/5 females versus males (n=3-4; $p < 0.05$).
Conclusions: qPCR results validate methylation directionality obtained via WGBS and suggest the X chromosome in BPH/5 females is silenced. However, x-linked AR is decreased in BPH/5 females despite high circulating testosterone. Future comparisons to lean female mice are needed to determine epigenetic origins of obesity. Genetic methylation signatures have potential as future biomarkers of disease risk, specifically genetic predisposition to obesity in offspring born to preeclamptic mothers.

176. MB13DSNDU

Leptospirosis in Domestic Animals in Louisiana: A 10 Year Retrospective Analysis

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Background and Rationale: Leptospirosis is an infectious disease that can threaten both humans and animals. The purpose of this study was to determine the occurrence of leptospirosis in domestic animals over the past 10 years in Louisiana based on submissions to the Louisiana Animal Disease Diagnostic Laboratory (LADDL), Louisiana State University School of Veterinary Medicine, and to establish possible associations with other epidemiological variables.
Methods: The laboratory information system at LADDL was used to gain data on submissions for Leptospira interrogans testing between 2012-2022. The number of positive and negative cases (based on serological or molecular confirmation) were recorded along with the time of year, species, age, sex, and antibody titer of affected animals.
Results: 194 positive/843 submissions were diagnosed at LADDL from January 2012 to May 2022. The species predominately affected were horses (46%). Positive cases were diagnosed mostly during the winter and fall. Leptospira interrogans serovar Pomona was the most detected serovar across species. Most positive submissions were from the southern regions of Louisiana. More than 50% of the submissions possessed titers ? 1:800 while 17 animals possessed titers ? 1:1600.

Conclusions: Our study identified more positive cases during the fall and winter months, with most submissions derived from southern regions of Louisiana. The high seroprevalence indicates that most of the animals in our study were previously exposed to L. interrogans. Determination of the relationship between case occurrence and other variables (e.g. rainfall) is still under analysis. Enhancing the education of the public is warranted to improve surveillance.

183. MB14DSNDU

Survey for Prevalence of Batrachochytrium dendrobatidis in the LSU Lakes

John Tuminello, Lindsay Newton, Shelby Parks, Jason Ray, DVM Javier Nevarez

Fungal infections such as Batrachochytrium dendrobatidis are becoming more prevalent in ecosystems and are causing amphibian die offs. (Galt et al.,2021; Searle et al., 2011). One of the qualities that make this disease so dangerous is its ability to inhibit the necessary gas exchanges that occur on the skin of amphibians. (Pare,2021). Although Batrachochytrium dendrobatidis has been documented around the world in a variety of ecosystems, little literature exists on how prevalent it is in native Louisiana frog populations. In recent years, Batrachochytrium dendrobatidis has been found in Louisiana infecting the Gulf Coast Water Dog (Necturus beyeri) as well as crayfish (Procambarus spp). (Brannelly et al.,2015; Glorioso et al., 2017). Because of the documented presence of Batrachochytrium dendrobatidis in Necturus beyeri and Procabarus spp in southeast Louisiana, anuran populations in the LSU lakes should be surveyed to portray the prevalence of this disease more accurately in Louisiana. Of the population sampled (N=100), two anurans tested positive for Batrachochytrium dendrobatids.

187. MB15DSNDU

Louisiana Surveillance of Bovine Parasite Resistance and Comparison of Fecal Diagnostic Tests

M. Davis, A. Vatta, C. Navarre

Rationale: Reports of cattle dying from Ostertagia ostertagi infections in Louisiana prompted investigations into anthelmintic efficacy.
Methods: Sixty-six calves were fecal-sampled on Farm 1 (SE LA) and Farm 2 (N LA) prior to administration of ivermectin (macrocyclic lactone), albendazole (benzimidazole), both drugs, or no drug (controls). Repeat sampling occurred on day 20 (Farm 1) or day 13 (Farm 2). The Modified McMaster (McM) and Mini FLOTAC (FLO) methods were used to determine fecal egg count pre and post treatment.
Results: The mean pre-administration fecal egg count was 60.00 eggs per gram of feces (EPG; 0-350 EPG; n=30; McM), and 74.33 EPG (0-405 EPG; n=30; FLO) for Farm 1, and 117.11 EPG (0-550 EPG; n=34; McM) and 126.97 EPG (0-580 EPG; n=34; FLO) for Farm 2. Compared with the McM, the FLO detected more positive samples ($P<0.05$; test for equal proportions) and the proportion of samples with higher EPGs was significantly greater for the FLO than the McM ($P<0.05$); test for equal proportions). Hence the FLO method was used to calculate the FECRs; animals with EPG ? 65 pre-treatment were included in FECR calculations. The ivermectin-treated groups had FECRs of 9.68% (Farm 1) and 39.44% (Farm 2). The albendazole-treated groups had FECRs of 69.66% (Farm 1) and 99.51% (Farm 2). The group treated with the combination (Farm 2) had a FECR of 98.48%.
Conclusions: Low efficacy of ivermectin and moderate to high efficacy of albendazole were detected.
Significance: Using albendazole in combination with a macrocyclic lactone would be recommended.

192. PhD12PHD

Nrf2 regulates host protection against pnemonia caused by Carbapenem-resistant Klebsiella pneumoniae

MK. Lee, T. Rangasamy, A. T. Brown, L. J. Le, and S. Jeyaseelan

Nrf2 regulates host protection against pneumonia caused by Carbapenem-resistant Klebsiella pneumoniae
Authors: MK. Lee1, T. Rangasamy1,2, A. T. Brown2, L. J. Le2, and S. Jeyaseelan1,2 Address: 1Center for Lung Biology and Disease and 2Department of Pathobiological Sciences; School of Veterinary Medicine, Louisiana State University, Baton Rouge.
Rationale: Physical, chemical, and biological factors can induce oxidative stress in pulmonary tissues following bacterial infection. The transcription factor Nrf2 is a critical regulator of cellular response to oxidative stress. The carbapenem-resistant Klebsiella pneumoniae (CRKP) strain is quickly spreading across the nation, and there are no vaccines available to prevent CRKP infection. The role of Nrf2 in pneumonia caused by carbapenem-resistant CRKP is not known.
Methods: We infected Nrf2 wild-type (Nrf2 WT), Nrf2 whole-body knockout (Nrf2 KO), Nrf2fl/fl, mice and alveolar type II epithelial-specific Nrf2-deficient (Nrf2fl/fl - mT/mG/SpC-deficient) mice with CRKP and sacrificed at 48 h post-infection. Mice were monitored for survival, and bacterial burden was examined in organs. The level of inflammatory cytokines in the lungs from infected mice was also quantified. In addition, H&E-stained lung sections from the infected mice were examined.

Results: Nrf2 ablation increased the bacterial burden in the lung, bronchoalveolar lavage fluid, spleen, and liver following infection when compared to their controls. At an inoculum of 1 X 109 CFUs, >75% of the Nrf2-deficient mice succumbed to CRKP-infection at 96 h compared to WT mice (15% mortality). Higher levels of TNF-a and IL-1? in lung supernatants were observed as compared to WT counterparts. Stained lung sections revealed enhanced leukocyte.

196. MB17DSNDU

Breaking the Cycle of Preeclampsia: Gestational Pair-Feeding Attenuates Sex Steroid Hormone Dysregulation in Preeclamptic-like BPH/5 Mice

J. Flanagan, K. Beckers, R. Awad, V. Gomes, C. Liu, J. Sones

Rationale: Preeclampsia (PE) is a hypertensive disorder of pregnancy and a leading cause of maternal mortality. Both PE mothers and offspring have increased risk for cardiometabolic disease as they age; however, the mechanism is unknown. Blood Pressure High (BPH)/5 mice are an inbred genetic model of PE, and adult offspring display adverse cardiometabolic outcomes in a sex-dependent manner. We hypothesized that maternal weight loss of BPH/5 dams via pair-feeding (PF) would attenuate previously characterized perturbed estrous cycles and sex steroid hormonal imbalances in female offspring.
Methods: Food intake of BPH/5 dams was restricted to the average daily intake of age- and gestation-matched C57 dams throughout pregnancy. Uterine wet weights and serum were collected from adult female BPH/5 ad libitum-fed dams/ad libitum-fed offspring (AL/AL) and BPH/5 PF dams/ad libitum-fed offspring (PF/AL). Estrous cycles were staged using vaginal cytology. Circulating 17B-estradiol concentrations were measured using liquid-chromatography mass spectrometry.
Results: Pair-feeding BPH/5 dams during gestation prevents maternal and fetal PE clinical signs. AL/AL BPH5 female mice are obese, hyperphagic, and have elevated circulating testosterone, decreased estradiol, and abnormal estrous cycles compared to control C57 mice. PF/AL females

have increased serum 17B-estradiol ($p<0.01$; n=4-17) and uterine wet weights ($p<0.01$; n=12-27) compared to AL/AL.
Conclusion: Increased uterine wet weights with higher estradiol suggest more appropriate sex steroid signaling in PF/AL offspring via in utero programming. Our results in BPH/5 mice indicate gestational pair-feeding improves sex steroid hormone signaling in offspring, which may contribute to our finding that PF/AL have attenuation of hypertension.

202. MB18DSNDU

Assessment of equine fibroblastic wound healing in vitro after exposure to stimulated adipose-derived mesenchymal stem cell supernatant.

F. Scott, C. Culbertson, B. Leise

Equine cutaneous lesions or wounds can have life-threatening implications for horses. Mesenchymal stem cells (MSC) have been shown to advance tissue regeneration, but limited information exist in the ability for MSC to improve healing rates. The objective of this study was to determine if supernatant from stimulated adipose-derived MSC (Ad-MSC) would enhance fibroblast migration and proliferation; thereby, leading to more rapid wound closure. Equine Ad- MSCs were stimulated in vitro with various mediators (lipopolysaccharide, transforming growth factor-beta 1, or interleukin-1b) followed by collection of the supernatant. Scratch wounds were created in cultured equine fibroblast using the Woundmaker tool. Stimulated Ad-MSC supernatant or the respective control media were added to the wounded fibroblasts. Wound gap area over time will be measured using Incucyte live cell imager and compared between groups. We anticipate that stimulated Ad-MSC supernatant will enhance closure of the wound gap compared to controls. Results from this study could be further used to develop in vivo therapies to improve wound healing in the horse.

203. MB19DSNDU

Effect of Ventral Tegmental Area Glutamate Neuron Excitation and Inhibition on Habituation Behavior in a Schizophrenia Mouse Model

J. Lazo, O. Ogundele

Rationale: Schizophrenia and related developmental neuropsychiatric disorders affect about 1.1% of the world’s population. Understanding the neural circuit mechanism for specific behavioral phenotypes, and targeting these circuits to rescue cognitive performance, will advance our understanding of disease mechanisms and approaches to intervention. The aim of this study is to assess the effect of ventral tegmental area (VTA) glutamate neuron excitation and inhibition on habituation behavior in a schizophrenia mouse model compared with a wild type strain.
Methods: Mice were injected with an excitatory or inhibitory adeno-associated virus (AAV) into the VTA to target glutamate neurons. An olfactory habituation test was performed, and movements of the mice were recorded to assess frequency and duration of visits to novel odors as a measure of their rate of habituation. Baseline results were collected from each mouse followed by treatment results after virus expression.
Results: The wild type and mutant strain did not consistently habituate to the odors during baseline or treatment. A lack of significance was observed between excitatory and inhibitory groups within strains. Significant differences in the olfactory habituation test results were observed between wild

type and mutant strains that received the same AAV, suggesting that the VTA may respond differently to the excitation and inhibition of glutamate neurons across strains.
Conclusions: The mutant mouse strain did not have a strong response to the scents. For future studies, an alternative behavior test may be indicated to better study the effects of the excitation and inhibition of glutamate neurons.

Category: Clinical Research, DVM Students

146. MC0DS

EHV-1 Specific Immune Response to EHV Vaccines in Horses

J. Windham, J. Miller, N. Moreau, M. Keowen, A. Chapman, D. Diel, R. Lemcke, U. Balasuriya, R. Keene, S. Grubbs, F. Andrews

EHV-1 infection is ubiquitous in horse populations and causes disease and economic loss with outbreaks of respiratory disease, abortion, neonatal death, and myeloencephalopathy. Prevention requires an effective immune response including mucosal (IgA), systemic humoral antibody (IgG), and cell-mediated immune responses. Commercially available vaccines produce serum viral neutralizing(SVN) antibodies; however, data is lacking on SVN antibody titers in horses administered EHV-1 vaccines. The purpose of the study was to determine EHV-1 SVN antibody titers to 3 commercially available vaccines: Vetera2XP, Calvenza03 EIV/EHV and Rhinomune. Hypotheses include: EHV-1 vaccinated horses will have higher EHV-1 antibody titers, and Rhinomune (MLV) vaccinated horses will have the highest antibody titers. From 52 horses in the LSU Equine Health Studies Program herd, whole blood was drawn and serum collected on day -14 for baseline serum antibody titers. Horses were randomized into groups 1-4 based on antibody titer and housed on pasture (16/pasture) with 4 horses from Group 4 (controls) with each of the EHV-1 vaccinated groups. Whole blood was drawn and serum IgG antibody titers to EHV-1 were measured in each of the horses on days 0, 21, 42, 63, 84 prior to administration of the vaccine. Preliminary results showed significant increases in antibody titers for EHV-1 vaccinated horses from day 0-21, and a significant increase in antibodies for horses receiving Calvenza and Rhinomune, with the greatest increase for Calvenza. Antibody titers did not increase in Group 4 horses, suggesting a lack of exposure to EHV-1 in the pastures. Data collection remains ongoing.

157. MC3DS

Assessment of the healing times of bone fractures when using photobiomodulation as an adjunct to traditional treatment in avian wildlife

M.J. Criscione, M.A. Mitchell, L.K. Hale-Mitchell

Rationale: Limb fractures are among the most common types of injuries that avian wildlife present to a veterinary hospital. Current average for hardware removal time is 37 days. Increased hospitalization time can lead to negative consequences such as contracture of wings or erroneous imprinting. Photobiomodulation (PBM) can decrease fracture healing times in mammals. We hypothesized it would do the same in avian species as well.
Methods: Avian species that presented to the Wildlife Hospital of Louisiana with surgically repairable limb fractures were included in the study. Photobiomodulation was applied to and around the fracture site three times a week. A pre-set for fracture repair was used on the class IV laser system. Pain

assessment, photographs, and visualization of the repair site occurred prior to PBM. Radiographs were taken weekly to assess bone remodeling and healing. Hardware was removed when radiographs and palpation indicated healing. An independent t-test was used to compare historical data to surgery + PBM the days to orthopedic hardware removal.
Results: Eight birds completed the study at the time (we now have 12 birds). Three birds died during treatment of complications unrelated to the fracture or the PBM. Birds with PBM had their hardware removed on average at 21 days compared to surgery alone at 37 days. (p=0.027).
Conclusion: Adding PBM to fracture repair three times a week, increases healing rates and decreases the number of days held in hospital before moving bird to a pre-release program, thereby decreasing the negative consequences of captivity.

179. MC10DS

Determining the Effects of Short Term Artificial UVB Lighting on Plasma 25-OHD3 Concentrations in Leopard Geckos (Eublepharis macularius)

A. Bitter, A. Settle, J. Tuminello, M. Mitchell

Leopard geckos (Eublepharis macularius) are on of the most common reptiles kept in captivity, but there remains much we don't know about their basic husbandry. One of the most common diseases reported in captive leopard geckos is nutritional secondary hyperparathyroidism. This disease is preventable but is typically attributed to diets with low calcium/vitamin D or a lack of ultraviolet B (UVB) exposure. Because these lizards are crepuscular, it was long believed that they didn't require UVB lighting; however, recent work has confirmed that UVB does increase plasma 25-hydroxyvitamin D3 (25-OHD3) concentrations in this species. Unfortunately, too much UVB exposure can lead to cancer and cataracts. The purpose of this study was to determine the duration of UVB exposure required to increase 25-OHD3 concentrations in leopard geckos. Twenty-four leopard geckos were used for this study and randomly assigned to three different UVB exposure groups: 15, 30, and 60 minutes/day. Each gecko served as its own control, and the geckos were exposed to the UVB for 28 days. There was a significant difference in 25-OHD3 over time ($P<0.001$) with 25-OHD3 concentration being higher in all geckos at 28 days compared to baseline. No significant difference in 25-OHD3 was found between groups.

181. MC11DS

A Retrospective Study on the Detrimental Effects of Fasciola hepatica (Liver Flukes) on Small Ruminants

B. Freeman, C.M. Scully, C. Liu, A. J.T. Muir

Rationale: Fasciola hepatica is known as the common liver fluke. Infection in small ruminants and cattle is a known source of chronic liver wasting, economic losses, and decreases in animal welfare. This study aims to determine common clinical signs, pursued diagnostics, outcomes of treatments, and autopsy findings of small ruminants with confirmed F. hepatica infection. We hypothesize there will be an increasing trend of F. hepatica mortality in herds during seasons of optimal temperatures for completion of the parasite life cycle, more noticeable initial symptoms, and a correlation between histories of prior infection and disease prevalence.
Methods: Medical records of cases of small ruminants that presented to the Louisiana State University Veterinary Teaching Hospital between 2012-2022 were assessed for confirmed infection. Out of 2,049 records, 15 confirmed cases were evaluated.

Results: The majority of F. hepatica infections (67%) occurred during the optimal period of February-July, with a mortality rate of 80%. Lethargy (64%), anorexia/emaciation (57%), dehydration (50%), and anemia (43%) were common exam findings. Euthanasia was the most common treatment (60%), along with flunixin meglumine (47%), thiamine (33%), and albendazole (33%). Frequent necropsy findings included bile duct hyperplasia (92%), concurrent parasite infection (75%), and grossly observed trematodes (67%).
Conclusions: F. hepatica is an extremely detrimental parasite to small ruminants. Its negative impact on animal welfare and economics warrants additional research of improved diagnostics, preventative methods, and treatments.

198. MC17DS

Pulmonary Health Impacts of Golden Tobacco Flavored Vuse Alto Aerosols in Vulnerable Populations of Young mice.

N. Black-Ocken, A. Noel

Rationale: Vuse Alto is a popular fourth-generation electronic nicotine delivery system (ENDS), also known as “e-cigarette”, that uses nicotine salt-based formulas to deliver high doses of nicotine. With over 2 million American youth using ENDS and the paucity of data regarding their health effects, serious public health concerns are being raised. Hence, the goal of this study was to investigate the pulmonary effects of golden tobacco-flavored Vuse aerosol exposures in juvenile mice.
Methods: 4-week-old male BALB/c mice were exposed to either air or golden tobacco flavored Vuse Alto aerosols via whole-body exposures for 1-hr/day, 5 days/week, for 3 months. At the end of the study, lung function testing was assessed and serum, broncho-alveolar lavage fluid (BALF), and lung tissue were collected.
Results: Nicotine exposure was confirmed by significantly elevated serum cotinine levels (>33.2 ng/mL) in exposed mice compared to controls (<2.1 ng/mL). Also, Vuse exposure significantly decreased the body weight of mice, suggesting an effect on weight gain. While Vuse exposure significantly increased the mean linear intercept values on the lung tissue, indicating enlarging airspaces, this exposure significantly decreased the inspiratory capacity of the lung, demonstrating impaired lung function. Additionally, significantly elevated levels of BALF 8-isoprostane, a biomarker of oxidative stress, were found in exposed mice (9.1 pg/mL) compared to controls (3.6 pg/mL).
Conclusion: Exposures to golden tobacco-flavored Vuse Alto aerosols in young mice result in lung structural, functional, and biochemical alterations.
Significance/Impact: This study provides laboratory-based evidence for future regulation of Vuse Alto products often used by American youth.

200. MC18DS

Effects of Prokinetic Drugs on Liquid Phase Gastric Emptying in Dogs with Clonidine-delayed Gastric Emptying

N. Akers, A. Harmon, T. Dugas, F. Gaschen

Rationale: Delayed gastric emptying (GE) commonly occurs following abdominal surgery or abdominal inflammation in dogs. There are no clinically applicable methods to document its occurrence. Orally administered acetaminophen (AAP) can be used to assess GE in dogs. Our objective was to evaluate the effects of gastric prokinetics on GE of liquids in dogs treated with clonidine, an alpha-adrenergic agonist that delays GE, using AAP as a plasma tracer.

Methods: Prospective cross-over study with 8 healthy purpose-bred dogs. Each dog served as its own control and received either no treatment, clonidine SC (0.03 mg/kg SC), azithromycin (2 mg/kg IV) and clonidine, or metoclopramide (0.5 mg/kg SC) and clonidine 1h prior to a liquid meal containing acetaminophen (20 mg/kg) over a 6-week period. Blood samples were collected 0, 15, 30, 45, 60, 75, 90, and 120 minutes postprandially. Plasma AAP concentrations were obtained using reverse phase HPLC. Repeated-measures 2-way ANOVA with Tukey-Kramer-adjusted multiple comparisons was performed to compare plasma AAP concentrations between treatments.
Results: Clonidine treatment significantly decreased plasma AAP concentrations at all time points after 15 minutes postprandially ($p<0.05$). Treatment with metoclopramide or azithromycin did not have any effect on the changes caused by clonidine.
Conclusions: Clonidine decreased absorption of AAP administered with a liquid meal, presumably due to its delaying effect on GE. Gastric prokinetic drugs had no effect on dogs treated with clonidine up until 2h postprandially. Further research using a longer observation period is required for a comprehensive assessment of the effect of gastric prokinetics in this model.

Category: Clinical Research, Master (MS), House Officers, Residents, Non-DVM Undergraduates

147. MC1MHRN

Factors Associated with Corneal Conjunctival Graft Repair Failure at Four Veterinary Specialty Centers: 2015-2021

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Rationale: Corneal conjunctival grafting is a commonly utilized surgical technique to repair deep corneal ulcerations in dogs. No recent multi-center review has been performed assessing factors associated with conjunctival graft failure in this species.
Methods: Medical records of 203 dogs (229 eyes) that underwent conjunctival graft repair for ulcerative keratitis from 2015 to 2021 were reviewed. A successful outcome was defined as graft integration with globe retention at final post-operative examination; vision was reported separately. Factors evaluated included: patient signalment, ophthalmic exam findings, surgical factors, and follow-up information.
Results: Conjunctival graft failure occurred in 11% (25/229) of eyes. Graft failure was significantly associated with ulcer depth with an odds ratio of 2.24 higher ($p<0.01$) with each increased depth level (superficial stromal < deep stromal < descemetocele < perforation). Brachycephalics had a significantly higher graft failure rate (odds ratio 4.13, $p<0.01$). Surgery on the opposite eye relative to surgeon handedness was significantly associated with an increased rate of graft failure (odds ratio 3.08, $p<0.01$). Graft failure was significantly associated with use of biosynthetic material and an increased frequency of topical medications post-operatively; however, this is likely due to overrepresentation of perforations within this subset of dogs. At last follow-up, 87% of dogs had vision. No other factors were associated with graft failure.
Conclusions/Significance: Depth of ulceration, brachycephalic conformation, and surgery on the opposite eye relative to surgeon handedness were significantly associated with increased risk of graft failure. These factors should be considered when determining prognosis for corneal ulcerations requiring surgical intervention.

158. MC4MHRN

Management of Benign Esophageal Strictures in Dogs and Cats – Long-Term Follow-Up of 32 cases.

M.K. Bollman, F.P. Gaschen

Background: Benign esophageal strictures (BES) may compromise quality of life (QoL) and survival in dogs and cats. Little data is available on long-term survival after management.
Hypothesis/Objectives: To describe the outcome of BES in dogs and cats treated with esophagoscopy-guided balloon dilation and identify factors influencing the outcome.
Animals: 28 dogs and 4 cats.
Methods: Retrospective analysis (2006-2022). Signalment, BES number and etiology, submucosal injection and triamcinolone acetate dose, PEG-tube placement, and number of dilations were recorded. The animals' owners were contacted to obtain survival data and diet information. Effects of recorded variables on survival were evaluated with Cox proportional hazards regression.
Results: Median [range] values were as follows: age, 6.5 years [0.3-14]; body weight, 5.45 kg [1-37]; number of BES present at initial visit 1 [1-5]. Identified causes for BES were peri-anesthetic regurgitation (17), esophageal foreign body (8), and vomiting (7). Twenty-two animals received submucosal injections of triamcinolone (median dose 0.5 mg/kg [0.22-0.76]). A PEG-tube was placed in 11 animals. A median of 2 dilations [1-6] was performed. Follow-up data were obtained for 26 animals. Ten could eat kibbles and 16 required a soft diet. Most animals had good QoL. Median survival time was 2,746 days [11-4,191]. Increased age at the time of diagnosis negatively impacted outcome (HR 1.39, 95% CI 1.11-1.85, p=.009).
Conclusions and clinical importance: Balloon dilation afforded prolonged survival with good QoL in dogs and cats with BES. More than one procedure was required in most cases. Increased age at presentation had a negative prognostic value.

171. MB10MHR

Ophthalmic parameters of the Whooping crane (Grus americana) and Mississippi Sandhill crane (Grus canadensis pulla)

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Rationale: Baseline ophthalmic parameters have not been reported for the endangered Whooping cranes (WC) and Mississippi Sandhill cranes (MSC). Vision is critically important to avian survival. The purpose of this study was to report ocular examination findings and to obtain species-specific ophthalmic diagnostic parameters for a cohort of WC and MSC.
Methods: Adult WC and MSC (0.25-32.5 years) were evaluated opportunistically during pre-scheduled examinations. Complete ophthalmic examination and diagnostic testing was collected based on patient tolerance including tonometry (TONOVET Plus, "canine" mode, head above [AH] and below heart [BH] level) and ocular biometric measurements by ultrasound.
Results: Ocular abnormalities included keratitis (n=2, WC), uveal cysts (n=1, MSC), and incipient cataracts (n=1, WC; n=4, MSC). Intraocular pressure in 21 adult MSC (mean±SD: 18.91±2.71 mmHg AH, 23.91±2.28 mmHg BH) and 18 adult WC (22.23±2.87 mmHg AH, 27.62±4.06 mmHg BH), was significantly correlated with head position (BH-AH = 4.8±0.31 mmHg, $p < 0.0001$ (MSC); 5.50±0.58, $p < 0.0001$ (WC)). Globe length ($p=0.001$) and vitreous chamber depth ($p<0.001$) were significantly greater in male (globe: 2.27±0.09 cm, vitreous: 1.44±0.04 cm) than female (globe: 2.12±0.13 cm, vitreous: 1.34±0.08 cm) adult WC (n=17); no difference was identified in MSC (n=19).

Conclusions/significance: WC and MSC are amenable to conscious ophthalmic examination, including ocular ultrasound. Significant differences in tonometry values based on head position were identified in both species. Sexual dimorphism was identified in ocular biometric measurements of WC. This study established baseline ophthalmic parameters for the future assessment and management of the critically endangered WC and MSC.

175. MC7MHRN

Treating Hypotension in Isoflurane-Anesthetized New Zealand White Rabbits: An Evaluation Study Among Dopamine, Dobutamine, and Norepinephrine

A. James, J. Cremer, T. Booke, G. Castro-Cuellar, N. Diaz-Falcon, Chin-Chi Liu, P. Queiroz-Williams

Background and Rationale: Rabbits carry a high peri-anesthetic risk of death which is partially attributed to cardiopulmonary depression and hypotension. Previously investigated dosages of positive inotrope drugs are not reliable in treating hypotension in anesthetized rabbits. The purpose of this study was to establish effective dosages of dopamine, dobutamine, and norepinephrine to treat hypotension in isoflurane-anesthetized rabbits.
Methods: Ten female (2-4-month-old), healthy New Zealand White rabbits were anesthetized in a randomized cross-over study. Baseline values (T0) for invasive blood pressures (systolic, mean, and diastolic pressures), heart rate (HR), and end-tidal isoflurane (ETiso) were measured after isoflurane anesthetic plane was established, and then every 3 minutes. Hypotension was defined as mean arterial blood pressure (MAP) below 60 mmHg. Rabbits were allowed to become hypotensive, and two of five treatments were administered separately for 15 minutes with a 10-minute washout period in-between. Treatments were: dopamine 10-20 mcg/kg/min (LDOP), dobutamine 10-20 mcg/kg/min (LDOB), dopamine 60-80 mcg/kg/min (HDOP), dobutamine 60-80 mcg/kg/min (HDOB) and norepinephrine 0.5-1 mcg/kg/min with dobutamine 60-80 mcg/kg/min (NOR-DOB). Statistical analysis was done with counts of MAP above 60mmHg and all continuous parameters were compared against 5 treatments via chi-squared test and mixed ANOVA.
Results: Treatment NOR-DOB significantly ($p < 0.001$) increased MAP with an average of 64 ± 1.4 mmHg. Treatment HDOB significantly ($p < 0.0001$) increased HR. Treatments LDOP, LDOB, HDOP and HDOB did not effectively treat hypotension.
Conclusions/Significance: Norepinephrine at 0.5-1 mcg/kg/min combined with dobutamine at 60-80 mcg/kg/min effectively treated hypotension in healthy, isoflurane-anesthetized New Zealand White rabbits.

177. MC8MHRN

Exploring the Immunomodulatory Effects of Localized Radiation Therapy in Dogs with Nasal Tumors

C. Goodermuth, C. Moeller, J. Merkle, J. Looper, S. Withers

Radiation therapy (RT) delivers ionizing radiation to cancer with the goal of halting localized cancer progression. There is increasing evidence that RT can trigger immune activation via the release of damage-associated molecular patterns (DAMPs), type-I interferon, and tumor antigens from dying cells. Together, these signals induce immune cell activation and chemotaxis. Our goal was to measure changes in cytotoxic T cells and immunosuppressive cell types such as T-regulatory cells (Tregs) and myeloid-derived suppressor cells (MDSCs) that occur both regionally and systemically in dogs with nasal tumors receiving localized radiation therapy.

Nine dogs with nasal tumors treated with stereotactic radiation therapy (3x10 Gy) were included. Flow cytometry was performed on peripheral blood mononuclear cells (PBMCs) collected at three timepoints (day 0, 7, and 16). Samples were stained with viability dye and two panels of fluorochrome-conjugated antibodies targeting lymphocyte subsets (CD3, CD4, CD8, CD25, FoxP3, Granzyme B) and myeloid cell subsets (CD5, CD11b, CD14, MHCII, CADO48A). Proportions of cell subsets were compared between timepoints. ANOVA and post-hoc multiple comparisons was performed for statistical analysis.
We observed trends towards increased CD8+Granzyme B+ T lymphocytes within lymph nodes at day 16 ($P = 0.060$), and increased CD4+FoxP3+CD25- T lymphocytes (Tregs) in peripheral blood at day 16 ($P = 0.082$), compared to day 0. Additional data collection is ongoing.
RT may trigger immune modulation in regional lymph nodes and peripheral blood 16 days after treatment. Significance/Impact/Implications: These data may be used to formulate additional hypotheses regarding the optimal timing of radiation therapy and immunotherapy combinations.

188. MC12MHRN

No Loop of Henle? No Problem! Furosemide Diuresis in Red Eared Sliders (Trachemys scripta elegans)

K. Metcalf, M. G. Aguilar, J. Tuminello, S. Dehghanpir, M. Acierno, M. Mitchell

Rationale: Furosemide is a commonly used loop diuretic in mammals. Because reptiles lack a loop of Henle, furosemide is often assumed to be of little value. However, previous studies involving reptiles suggest that diuresis could be induced via furosemide and proposed a possible passive effect. The purpose of this study was to determine if furosemide could induce diuresis in red-eared sliders (Trachemys scipta elegans) and determine objective methods to better assess dehydration.
Methods: Ten adult, male, red-eared slider turtles were used for this study. Turtles were randomly assigned to three different treatment groups in a complete-crossover study: 10 mg/kg furosemide q 12-hours, 4 doses; 5 mg/kg furosemide q 12-hours, 4 doses; and a control group. Baseline blood and urine samples were collected, and water and food were withheld for 48-hours. Blood and urine samples were re-collected, and they were replaced into water and weighed over the next 48-hours.
Results: Regardless of treatment, significant weight loss ($p<0.001$) was observed in all turtles after the 48-hour treatment. Upon returning to water, all turtles returned to their baseline weight within 48-hours. Diuresis was significantly ($p<0.001$) more likely to occur in furosemide treated turtles compared with non-treated controls. For the hematologic parameters, there was a significant elevation in the blood urea nitrogen and total protein post-dehydration. Total protein also revealed a significant, dose-dependent difference due to furosemide.
Conclusions/Significance: These results confirm red-eared sliders can be diuresed with furosemide, which may prove useful to treat states of fluid overload (e.g., congestive heart failure) in chelonians.

193. MC13MHRN

Evaluation of Fibroblast Growth Factor 19 (FGF19) in Healthy Dogs and in Dogs with Gallbladder Mucoceles

V. Truong, C. Liu, N.D. Welborn, A.N. Johnston

Rationale: Fibroblast growth factor 19 (FGF19) is a hormone produced in the canine ileum. Bile acids stimulate FGF19 protein translation and release into the portal circulation. The objective of this study was to test the hypothesis that serum FGF19 values will be significantly higher in healthy dogs than dogs with gallbladder mucoceles. The long-term goal of this project is to establish a reference interval for FGF19 in healthy dogs and to determine if FGF19 can be used as a biomarker of cholestatic hepatobiliary disease.
Methods: FGF19 serum levels were measured in 88 healthy dogs and 21 dogs with gallbladder mucoceles. FGF19 expression was quantified using a commercially available canine FGF19 ELISA kit, previously validated in our laboratory. CBC and serum biochemical data was recorded and compared between groups, when available. The 90% FGF19 reference interval was calculated using the non-parametric percentile method. Comparisons between normal and abnormal groups were made using the Mann-Whitney U test.
Results: Healthy dogs had a significantly higher median FGF19 value (104.1pg/ml, range:11.3 - 313.09pg/ml) than dogs with gallbladder mucoceles (37.0pg/ml, range: 7.5 – 163.6pg/ml; $p<0.0001$). Dogs with gallbladder mucoceles had significantly higher white blood cell counts, ALT, AST, ALP, GGT, cholesterol, and total bilirubin than normal dogs ($p<0.05$).
Conclusion: Dogs with gallbladder mucoceles have lower serum levels of FGF19, which may be caused by reduced bile acid stimulated synthesis and secretion of FGF19. Thirty-two additional healthy dogs are required to determine a canine serum FGF19 reference interval.

205. MC19MHRN

Evaluation of Anti-inflammatory Properties and Growth Factor Release After Repeated Intra-Articular Injections of Leukocyte-Poor, Platelet Rich Plasma in Horses with osteoarthritis

C. Manuel, A. Miranda, C. Aguilar-Miranda, C. Liu, C. McCauley, B. Leise, L. Riggs

Platelet-Rich plasma (PRP) has the potential benefit for osteoarthritis (OA) in horses. However, knowledge gaps exist over its cytokines influence after intra-articular injection. Our objective is to evaluate the long-term effect of repeated intra-articular injections of Leukocyte-Poor PRP (LP-PRP) in carpal joints with radiographic signs of OA. Eight healthy horses with bilateral grade 1 OA in both carpi were selected. In each horse, one radio-carpal joint was used as control (0.9% Sodium Chloride) and the contra-lateral joint treated (LP-PRP). At days 1, 7, and 21 synovial fluid (SF) were collected in both carpal joints, followed by their respective treatment. At days 51 and 81 only SF fluid was collected. At each time point, lameness was assessed, SF analyzed for hematology parameters and cytokine detection of IL-10, IL-13, IL-4, IL-1ß, IL-6, TNF-a, and PDGF-ßß. Repeated injections of LP-PRP do not cause an increase in any inflammatory SF parameter. Similarly, no significance in lameness was observed from day 1 to day 51 ($p=0.625$). Neither a significant difference was detected in IL-10 ($p=0.155$), IL-13 ($p=0.511$), IL-4 ($p=0.659$), IL-1ß ($p=0.387$). IL-6, TNF-a and PDGF-ßß were not detected in any time point. Repeated intra-articular injections with LP-PRP do not cause a long-term inflammation either improvement in lameness score. Our study provides further confirmation that PDGF- ßß cannot be detected after 7 days of LP-PRP injection. A naturally occurring OA model in the horse is not a suitable model to compare the difference between treatments.

210. MC20MHRN

Changes in the Antiviral Response by Tobacco Smoke

A. Mitchell, I. Martinez-Espinoza, and M. Antonieta Guerrero-Plata

Rationale:
Exposure to environmental tobacco smoke or secondhand tobacco smoke is a significant cause of mortality and morbidity among children. Exposure of infants to cigarette smoke is associated with several adverse health effects in childhood, including human respiratory syncytial virus (HRSV)-bronchiolitis and higher susceptibility to HSRV infection. This research project will be an attempt to determine the effects of secondhand tobacco smoke on the functionality of immune system macrophages (in phagocytosis) when infected with Human Respiratory Syncytial Virus (HRSV).
Methods:
Cell culture: Monocytes and epithelial cells will be grown in culture medium under sterile conditions and incubated at 37°C.
Cell infection: Cells will be infected at different multiplicities of infection during 24h.
Quantification of infectious virus: Cells will be exposed to cigarette smoke extract before viral infection. After 24 h of infection, cell-free supernatants will be collected. Viral titers were determined by methylcellulose plaque assay.
Results:
Our results show that there is a decrease in phagocytosis in macrophages between healthy cells and cells infected with HRSV. Additionally, that decrease was even more pronounced when the cells were exposed to smoke before infection.
Conclusions:
Exposure to smoke leads to a more severe impairment of the immune response. The decreased phagocytosis by macrophages could lead to a less efficient system of protection of epithelial cells to HRSV infection in the respiratory tract.
Significance:
This data is significant because, it could further demonstrate the serious risks being taken by pregnant mothers smoking while pregnant and parents exposing their infants to secondhand smoke.

Category: Clinical Research, Clinical Case Reports by House Officers and DVM Students

148. MC2CCRHOD

Lethal Blunt Force Trauma in a Kitten and a Hamster Thrown Against Firm Surfaces

D. Badamo, N. Wenzlow

Signalment and History: A hamster and a kitten were submitted as unrelated cases under criminal investigation to the Louisiana Animal Disease Diagnostic Laboratory (LSU) for forensic necropsy. The hamster had forcefully been thrown to the floor by a teenager during an episode of anger. The kitten was thrown against a wall by a man with a history of domestic violence during an episode of abuse of his female companion.
Gross Findings: Hamster- Gross findings were severe subdural hemorrhages; complete, non-displaced, mildly comminuted fractures of both nasal bones; fractures of both lower incisors; left eye exopthalmos and hyphema; and a focal area of abdominal wall hemorrhage. Kitten- Gross findings were acute full thickness fracture of the spine at the T2- T3 junction, severe hemorrhages over the head, neck, and scapulae.
Conclusions: The hamster likely impacted the ground with nose and head, where it sustained the lethal subdural hemorrhage. The abdominal wall hemorrhage likely resulted from the grip of the offender. The kitten’s spinal fracture represents the deadly impact point, and likely caused a

neurogenic shock. Death of both animals resulted from the direct action of a human and the manner of death was non-accidental killing, which is the animal equivalent to “homicide”.
Significance: These two cases confirm again, that acts of animal cruelty result from deviant behaviors of humans, also known to be linked to domestic abuse. Here, the victims were small enough to be held in one hand, even by a young individual, and propelled in a single movement with

160. MC5CCRHOD

Evaluating Agreement Between Invasive and Oscillometric Arterial Blood Pressure Measurement in Normotensive and Hypotensive New Zealand White Rabbits Under General Anesthesia

T. Booke, P. Queiroz, N. Diaz, G. Castro, A. James, C. Liu, J. Cremer

Rationale:
Rabbits have a higher mortality rate under anesthesia than cats or dogs. The objective of this study was to evaluate the agreement between invasive blood pressure (IBP) and noninvasive oscillometric blood pressure (OBP) measured at two anatomical sites. Good agreement was defined as a bias of less than 10mmHg and a standard deviation (SD) of less than 15mmHg.
Methods:
On three different occasions ten New Zealand White Rabbits were anesthetized with isoflurane. OBP was measured from the front and hind limb, and IBP was recorded simultaneously from the auricular artery. Hypotension was treated with dobutamine, dopamine or the combination of dobutamine with norepinephrine.
The Bland-Altman method was used to assess agreement between OBP and IBP for the front and hindlimb separately.
Results:
At the forelimb, the oscillometric mean bias for systolic arterial pressure (SAP) was 16mmHg (95% limits of agreement (LOA), -29 to 61mmHg), 1.6 mmHg for diastolic arterial pressure (DAP) (LOA, -40 to 42mmHg), and 4mmHg (LOA, -37 to 45mmHg) for mean arterial pressure (MAP).
At the hindlimb mean bias was 42 mmHg (LOA, -19mmHg to 102mmHg) for SAP, 14mmHg (LOA, -37 to 63mmHg) for DAP and 19mmHg (LOA, -32 to 69mmHg) for MAP.
Conclusions and Significance:
Agreement between OBP and IBP results was poor for both the hindlimb and the forelimb. However, agreement was worse for the hindlimb than the forelimb. The clinical use of this oscillometric device cannot be recommended based on these results and the invasive method is preferred.

169. MC6CCRHOD

Fatal Gastric Amoebiasis in a Linnaeus's Two-toed Sloth (Choloepus didactylus)

J. Lee 1, M. Braden2, A. Armien3, F. A. Uzal3, D. Paulsen1, and M. Carossino1

Rationale: Gastric amoebiasis has been reported in macropods and in leaf-eating monkeys which have a sacculated stomach. Gastric amoebiasis has not been reported in sloths, which also have a sacculated stomach.
Method: An 11-month-old Linnaeus's two-toed sloth (Choloepus didactylus) was submitted for necropsy with a history of weight loss and intermittent diarrhea for 18 days. Postmortem examination, histopathology, transmission electron microscopy (TEM), immunohistochemistry (IHC) on stomach

tissue using anti-Acanthamoeba spp., Balamuthia spp., and Naegleria spp. antibodies and PCR for Acanthamoeba spp. on stomach tissue were performed.
Results: The sloth was emaciated and had mild hydrothorax and ascites. The stomach was distended with fluid and had severe multifocal necrotizing gastritis in the glandular region, with intralesional amoebic trophozoites and cysts. TEM and IHC demonstrated that the organisms were most consistent with Acanthamoeba sp. The presence of mitochondria ruled out Amoebozoa of the family Entamoebidae. However, PCR for Acanthamoeba spp. was negative, and we were unable to characterize the amoeboid organism with a pan-free-living amoeba (FLA) PCR and sequencing.
Conclusions: This is a new presentation of FLA infection affecting the stomach of a two-toed sloth. While TEM and IHC suggested Acanthamoeba spp., the organism could not be further characterized by PCR and sequencing.
Significance/Impact/Implications: Gastric amoebiasis in other species is caused by Entamoeba histolytica, which also causes necrotizing colitis in human and non-human primates. FLAs are not primarily associated with gastrointestinal diseases. To our knowledge, this is the first report of gastric amoebiasis caused by a pathogenic FLA in a sloth.

178. MB12DSNDU

Phaeohyphomycosis in the Central Nervous System of Cats

B.S. de Cecco, C.E. Walsh, J. Lee, N. Falconnier, M.S. Mitchell, F. Del Piero, E. Sasaki

Rationale: Phaeohyphomycosis designates uncommon, opportunistic infections caused by dematiaceous fungi that are defined by their melanin-containing cell walls. This research aims to characterize the lesions caused by these fungi and their distribution in the central nervous system of cats.
Methods: A retrospective study was conducted at the Louisiana Animal Disease Diagnostic Laboratory archives searching for cases of central nervous system phaeohyphomycosis in domestic cats from January 2012 to December 2022.
Results: Six cases of central nervous system (CNS) phaeohyphomycosis in cats were retrieved. The ages of the cats ranged from 8 months old to 12 years old. The clinical signs depended on the location of the lesions in the CNS and included ataxia and seizures. All cats were submitted for postmortem evaluation. All cats had similar gross lesions in the CNS characterized by dark-green, gray-to-black soft areas in various locations of the CNS: right ventral medial cerebrum (1/6), left cerebellum and/or brainstem (2/6), left cerebrum (2/6), and spinal cord and brainstem (1/6). Microscopically, severe pyogranulomatous meningoencephalitis, rhombencephalitis, and myelitis with intralesional septate pigmented hyphae were observed. In one case, Cladophialophora bantiana was cultured from the CNS lesion.
Conclusions: Phaeohyphomycosis is an uncommon infection that affects the CNS of cats, and its complete documentation is scarce in the veterinary literature. CNS infections are thought to occur via the respiratory route; however, ocular and aural routes have also been suggested. This study provides an in-depth clinical and pathological characterization of CNS phaeohyphomycosis in cats.

194. MC14CCRHOD

Sepsis and Necrotizing Hepatitis, Splenitis and Myositis in a Domestic Goat (Capra hircus) Caused by Bacillus cereus

L. P. Guarneri 1, 2, A. Kuehr 3, C. M. Scully 3, M. Carossino 1, 2, and F. Del Piero 1, 2

Rationale: Bacillus cereus is a rod-shaped bacterium with a Gram-positive cell envelope and may be anaerobic or facultatively anaerobic. It is spore-forming and biofilm-forming, which presents a challenge to the food industry due to its contamination potentiality. Bacillus cereus has been identified as an uncommon cause of severe systemic disease in mammals.
Methods: On clinical examination, a 6-year-old male Nigerian Dwarf goat presented with severe edema of the head and neck. After a lack of response to treatment and the development of acute kidney injury, euthanasia with necropsy was elected. A complete necropsy was performed, and tissues were collected and fixed in 10% neutral buffered formalin solution. Tissues were processed routinely, and 4 micrometer tissue sections were stained with hematoxylin and eosin (H&E) for histopathologic examination. Aerobic and anaerobic bacterial culture was performed on the affected masticatory muscles and a Gram stain was performed on selected tissue sections.
Results: On gross examination, there was severe edema and multifocal splenic necrosis. Aerobic culture of the masticatory muscles identified moderate growth of Bacillus cereus, and on histologic examination, there was necrotizing myositis, splenitis and hepatitis, all with numerous intralesional short chains of bacilli. These bacilli were Gram-positive and measured 3 x 0.5 micrometers with square/blunted ends (morphologically consistent with Bacillus cereus).
Conclusion/Significance: Strains of Bacillus cereus have reportedly caused anthrax-like disease in mammals. This case report represents an instance of Bacillus cereus causing anthrax-like disease in a domestic goat and may correlate with previous reports of emerging virulence within this bacterium.

195. MC15CCRHOD

Effect of varying angles for needle insertion on small intestinal leakage at injection sites: An ex-vivo study

C. Pyne, K. S. Aulakh, BVSc & AH, MS, MS, CCRP, DACVS-SA; G. Castro-Ceullar, DVM, MS; C. Walls, DVM, DACVS-SA; A. W. St. Blanc, DVM, DACVS-SA; J. A. Gines, DVM, DECVS, MRCVS; C. Liu, PhD

Rationale: Intestinal closures are routinely tested for leakage by injecting saline intraluminally using a needle. However, leakage from needle tract itself could lead to septic peritonitis. The effect of needle insertion angle has not been evaluated for needle tract leakage. Our objective was to determine the influence of the angle of needle insertion on leakage at injection sites.
Methods: 54 intact 10-cm jejunal segments from three canine cadavers were randomly assigned to one of the three groups (n =18/group). A 22-Gauge needle was inserted at 90° (group-1), 45° (group-2), or tunneled into the jejunal segments (group-3). The segments were occluded with Doyen forceps and 14ml diluted methylene blue was injected. Leakage from needle tract was recorded at the time of needle removal, and at supraphysiologic peristaltic pressure. The pressure values were assessed using a mixed-ANOVA with three techniques as fixed-effect and animal as the random-effect.
Results: Initial leakage was significantly different among techniques ($p = 0.0034$). Group-1 had the highest incidence of leakage (83%), followed by Group-2 (78%), and Group-3 (28%). Leakage at supraphysiologic pressures was also significantly different among techniques ($p < .0001$). Group-1 had the highest incidence of leakage (89%), followed by Group-2 (39%), and Group-3 (11%).
Conclusions: The frequency of leakage increased when the needle was inserted perpendicular to the intestines and decreased when the needle was tunneled into the intestine.
Significance: Injection using a 22-gauge needle when tunneled through intestine may decrease the frequency of leakage, but its influence on the detection of surgical site leakage remains unknown.

197. MC16CCRHOD

Myxobolus-like Myxosporidean infection in a Coral Catfish (Plotosus lineatus)

N. Falconnier, J. Hawke, I. M. Langohr, F. Del Piero, M. Carossino

Rationale: Myxobolus cerebralis is a well-recognized myxosporidean parasite of salmonid fish and is a significant cause of hatchery mortality. This parasite is harbored within cartilage, results in skeletal deformities, and thus alters swimming patterns, hence the clinical name of whirling disease. A complete parasitic life cycle requires an environmental intermediate host, the tubificid oligochaete worm (Tubifex tubifex), which is known to live in both fresh and brackish water.
Methods: A captive hatchling coral catfish (Plotosus lineatus) was found dead in the enclosure and submitted within 10% buffered formalin for postmortem examination. Following decalcification with 15% formic acid solution, the fish was processed routinely, and sections were stained with hematoxylin and eosin as well as Fite-Faraco acid-fast.
Results: Histologic examination revealed widespread chondrolysis that predominately affected the calvarium and gill arches with numerous intralesional variably acid-fast staining myxozoan spores and trophozoites. Other parasites identified within the fish included those morphologically consistent with microsporidia, which were within peripheral nerves (suspected Pseudoloma neurophilia), as well as an encysted digenean trematode within the skeletal muscle and cestode larvae within a coelomic granuloma.
Conclusions: The morphologic and tinctorial features and location of the myxozoan organisms are most consistent with Myxobolus cerebralis which was thought to exclusively affect salmonid fish. However, this is the first report, to our knowledge, of this parasite infecting a marine fish.
Significance/Implications: Additional research is needed to speciate this Myxobolus-like organism and to establish the potential range of host species cross-infectivity.

Category: Faculty (Non-Competitive)

144. Race-related injuries in Thoroughbred and Quarter Horse Racehorses in Louisiana (2011-2021)

L. Dirikolu, P. Waller, X. Wen*

No abstract available

Category: PhD Student

159. PhD0PHD

Preovulatory LH and FSH Profiles of Aluteal Cycles

S.B. Cousseau1, E.L. Oberhaus2, C.R.F. Pinto1

Rationale: LH and FSH blood profiles and follicle development of cycling mares during the preovulatory period of aluteal cycles have not yet been described.
Methods: Eight mares in estrus were allotted into two groups in a crossover design at time of ovulation (D0): CTRL, luteal cycle; and AL, aluteal cycle (induced by the administration of 500 mcg of cloprostenol twice daily on Days 0, 1, 2 and once daily on Days 3 and 4). Daily blood samples were collected starting six days preceding ovulation, for RIA determination of hormone concentrations.
Results: Total area under the curve concentrations (±SEM) were greater in AL cycles for LH (41.57 ± 8.72 ng·day·mL-1 vs. 16.69 ± 4.17 ng·day·mL-1, p=0.012) and FSH (68.35 ± 11.44 ng·day·mL-1 vs. 45.60 ± 5.69 ng·day·mL-1, p=0.079). Mean (±SD) IOI of AL cycles was shorter (12.88 ± 1.13 days vs. 21.25 ± 1.28 days, p<0.0001). A significant number of mares (5/8, 62.5%) presented an increase in the number of dominant follicles during AL cycles (2.5 ± 1.75 vs. 1.5 ± 1; p=0.025). In contrast, no difference in the median number of ovulations was observed between groups (1 ± 0 vs. 1 ± 0.75; p=0.563). All cycles were ovulatory; however, AL cycles presented a trend to have remaining presumptive preovulatory follicles failing to ovulate (3/8 vs. 0/8; p=0.083).
Conclusions/Implications: The preovulatory period of aluteal cycles was characterized by elevated plasma concentrations of gonadotropins which were likely associated with the increase in the number of dominant follicles that became presumptive preovulatory follicles.

162. PhD2PHD

Decreased Expression of Carboxylesterase 1 (CES1) Impairs Osteogenic Differentiation of Human Bone Marrow Stem Cells (hBMSCs) during in vitro Expansion

W. Rong, S. Yao

Rationale: Human bone marrow stem cells (hBMSCs) are the workhorse of bone regeneration; in vitro expansion of primary hBMSCs is needed to obtain sufficient cell quantities for therapeutics. However, hBMSCs quickly lose their osteogenic differentiation potential following expansion, which largely limits their clinical applications. The study aims to understand the mechanisms of attenuated osteogenesis during in vitro expansion of hBMSCs.
Methods: RNA-seq was performed to screen the differentially expressed genes (DEGs) between early- and late-passage hBMSCs. CES1 knockdown and overexpression in hBMSCs were achieved with siRNA and recombinant adeno-associated virus (AAV), respectively. The osteogenic differentiation potential of hBMSCs was assessed by Alizarin Red S (ARS) staining, calcium quantification, and the expression of osteogenic markers.
Results: RNA-seq identified that CES1 was among the top ten downregulated DEGs in late-passage hBMSCs compared to early-passage cells. The expression of CES1 was progressively decreased with continued in vitro expansion of hBMSCs, while the cells gradually lost their osteogenic differentiation potential. Knockdown of CES1 by two different siRNAs targeting distinct regions of CES1 mRNA in early passage hBMSCs significantly inhibited the cells' osteogenic differentiation potential. Moreover, AAV serotype 2 (AAV2)-mediated CES1 overexpression could retard the loss of osteogenic potential during in vitro expansion of hBMSCs derived from two donors.
Conclusions/significance: Successive expansion of hBMSCs causes downregulation of CES1, which contributes to the impairment of osteogenic potential of hBMSCs. This study may shed light on the molecular mechanisms of loss of osteogenic differentiation during hBMSC expansion. CES1 could be a potential target for hBMSCs-based bone regeneration.

164. PhD3PHD

Machine-Learning-Assisted Spontaneous Raman Spectroscopy Classification and Feature Extraction for the Diagnosis of Human Laryngeal Cancer

Z. Li, S. Yao, J. Xu

Rational: The early detection of laryngeal cancer significantly increases survival rates, permits more conservative larynx sparing treatments, and reduces healthcare costs. A non-invasive optical biopsy for laryngeal carcinoma can increase the early detection rate, allow for more accurate monitoring of its recurrence, and improve intraoperative margin control.
Methods: In this study, we designed and evaluated a Raman spectroscopy system for the rapid intraoperative detection of human laryngeal carcinoma. We collected the Raman spectra from 207 normal and 500 tumor sites collected from 10 human laryngeal cancer surgical specimens. Data were subjected to spectral analysis with principal component analysis (PCA), random forest (RF), and one-dimensional (1D) convolutional neural network (CNN) methods.
Results: Random Forest analysis yielded an overall accuracy of 90.5%, a sensitivity of 88.2%, and a specificity of 92.8% on average over 10 trials. The 1D CNN demonstrated the highest performance with an accuracy of 96.1%, a sensitivity of 95.2%, and a specificity of 96.9% on average over 50 trials. In predicting the first three principal components (PCs) of normal and tumor data, both RF and CNN demonstrated high performances, except for the tumor PC2.
Conclusions: The proposed Raman spectroscopy feature extraction approach has not been previously applied to human cancer diagnosis. Raman spectroscopy, as assisted by machine learning (ML) methods, can serve as a non-invasive tool for the rapid diagnosis of laryngeal cancer and margin detection.
Significance: This is the first study in which CNN-assisted Raman spectroscopy was used to identify human laryngeal cancer tissue with extracted feature weights.

165. PhD4PHD

Peptide methionine sulfoxide reductases protect Staphylococcus aureus from killing by mammalian neutrophils

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Background and rationale: Staphylococcus aureus is a common human pathogen that causes a wide range of infections. Host immune cells use oxidative stress to eliminate these infections through the deleterious oxidation of bacterial proteins. The sulfur of methionine is susceptible to oxidation. The peptide methionine sulfoxide reductase (Msr) system evolved to repair oxidized methionine residues, preventing the organism from synthesizing proteins de novo. Staphylococci are unique among bacteria with four Msr enzymes. Our studies of Msr enzymes will identify bacterial pathways sensitive to oxidation, which will be targeted by future therapies.
Methods: Community-acquired methicillin-resistant strain USA300 and the same strain with all four msr deleted (Delta_msr) were used to understand the role of methionine oxidation by HOCl, superoxide, and H2O2 in bacterial survival. Whole blood and neutrophils from humans and mice were used to assess the differences in virulence of USA300 and delta_msr.

Results: The Msr enzymes only protect S. aureus from HOCl killing and each Msr protects S. aureus differentially. Human and murine neutrophils kill delta_msr better than USA300. Msr enzymes protect S.aureus from killing by humans but not murine whole blood, indicating species-specific roles for Msr enzymes during pathogenesis.
Conclusion: Msr enzymes protect S. aureus from distinct oxidative stressors and play a greater role in pathogenesis in humans compared to mice. Understanding the role of Msr enzymes in S.aureus pathogenesis will help identify the pathways that are susceptible to oxidative stress and can be exploited as antibiotic targets.

166. PhD5PHD

Metagenetic Analysis of the Pregnant Microbiome in Horses

V. Gomes, K. Crissman, C. Schulz, G. Childers, J. Sones, K. Beckers

Rationale: Placentitis is the leading cause of equine infectious abortion. Clinical signs of placentitis present in the last 2 months of pregnancy. We have shown that the equine placenta harbors a unique microbiome at term; however, the microbiome earlier in gestation is unknown. This study aims to identify microbial communities in the pregnant mare that may contribute to placental dysbiosis prior to the clinical presentation of placentitis. We hypothesize that the equine placental microbiome in early pregnancy will be different compared to oral, vaginal and fecal communities.
Methods: Pregnant (day 96-120) pony mares (n=5) oral cavity, vagina, anus, and the allantois sampled with a sterile swab. V4 region of 16S rRNA gene was amplified for Illumina Miseq sequencing to examine core bacterial communities present in different body sites.
Results: Microbial community composition of the pregnant ponies by body site was significantly different (p=0.001, PERMANOVA with Bray-Curtis dissimilarity of 16S Amplicon Sequence Variant's relative abundance): allantois was different from feces (p=0.027), oral cavity (p=0.046), and the vagina (p=0.038). Alpha diversity measuring Shannon diversity matrix was significant with body sites being a compounding variable (p=0.0008) suggesting a difference in richness and evenness in the microbial communities. When using Tukey's multiple comparisons, the allantois was most similar with the oral cavity, while feces showed significantly greater diversity.
Conclusions: Metagenetics revealed distinct community differences. The equine placenta microbial community has similarities to the oral cavity. Further research is needed to investigate extra-placental bacteria translocation to the placenta and the contribution to placentitis.

168. PhD6PHD

Gut Dysbiosis and Inflammation in the BPH5 Preeclamptic like Mouse Model

C. Schulz, J. Flanagan, G. Childers, J. Sones, K. Beckers

Rationale: Preeclampsia (PE) is a hypertensive disorder of pregnancy occurring in ~10% of pregnant women worldwide. Although the etiology is still unknown, obesity, which is associated gut dysbiosis and inflammation, is a known risk factor. Short chain fatty acids (SFCAs) are gut microbiome derived metabolites fueling host metabolism and signal through G protein coupled receptors (GPRs). We hypothesize that obese mice with a PE-like phenotype and have gut dysbiosis and perturbed GPR pathways with increased local inflammation.
Methods: BPH/5, an obese mouse model of superimposed PE, was utilized. Fecal samples were collected from pregnant and non-pregnant BPH5 and C57 controls for Illumina sequencing of 16S v4

rRNA. GPR41 and IL-15 mRNA were measured in pregnant colons by real time PCR. SCFAs were measured in feces and serum by mass spectrometry.
Results: Pregnant BPH/5 microbial community composition were different versus C57 using PERMANOVA/Bray-Curtis dissimilarity of 16S Amplicon Sequence Variant's relative abundance and alpha diversity increased ($p<0.05$, n=8-15). Significant differences were found with the onset of pregnancy BPH5: decreased Muribaculum spp., Muribaculaceae unclassified, Parabacteroides spp, and Lachnospiraceae_NK4A136 unclassified. Fecal SCFAs were not different between groups ($p>0.05$), but BPH/5 serum acetic and butyric acid were decreased while isobutyric and isovaleric acid were increased. BPH5 demonstrate an altered colonic signaling with decreased GPR41 mRNA ($p<0.05$, n=5-9) and increased IL-15 to represent local inflammation ($p<0.05$, n=3-5).
Conclusion: Pregnant BPH/5 have maternal-fecal microbiome dysbiosis characterized by diversity changes. Gut dysbiosis may be a key mechanism linking GPR41 signaling and inflammation to the BPH5 phenotype and PE.

170. PhD7PHD

NLRP10 Inflammasome Modulates Host Defense During Pneumonia

J. Le, S. Paudel, T. Rangasamy, A. T. Brown, and S. Jeyaseelan

Background: Pneumonia is one of the most common respiratory diseases in immunocompetent and immunocompromised populations. In particular, children and the elderly are known to have complications associated with pneumonia, which can be life-threatening. The role of NACHT, leucine-rich repeat (LRR), and PYD-containing protein 10 (NLRP10) is a recently identified inflammasome that lacks the leucine-rich domain (LRR) but its role in Gram-positive pneumonia is unknown.
Methods: We used age-matched C57BL/6 wild-type (WT) and NLRP10 knockout (KO) female mice and infected them with Methicillin-Resistant Staphylococcus aureus (MRSA USA300 strain, 5X107 Colony Forming Units/mouse) through the oropharyngeal route. The mice were euthanized at 12- and 24-hours post-infection to collect bronchoalveolar lavage (BAL) fluid, lungs, livers, and spleens. The bacterial burden was enumerated in these organs and the levels of leukocytes and inflammatory cytokines in the lungs were quantified. Isolated bone marrow-derived macrophages (BMDMs) and neutrophils (BMDNs) were used to measure functional endpoints.
Results: We found that WT mice had higher neutrophil and macrophage recruitment and lower bacterial burden in the lungs and spleens of NLRP10 KO mice. Despite low cytokine production, IFN-g level was higher in the KO mice. NLRP10 KO neutrophils show decreased extracellular bacterial killing which is neutrophil extracellular trap (NET)-dependent. NLRP10 neutrophils also show reduced intracellular bacterial killing and augmented cell death after infection. Regarding macrophage function, NLRP10 cells exhibit enhanced phagocytosis and increased cell death after infection.
Conclusions: The NLRP10 inflammasome plays a critical role during MRSA-induced pneumonia through IFN-g production and modulating myeloid (neutrophil and macrophage) function.

174. PhD8PHD

Bile Acid Profiling of Pyloric Gastric Fluid in Horses with Equine Glandular Gastric Disease

L. Paul1, F. Andrews1, A. Ericsson2, and H. Banse1

Rationale: The etiology of equine glandular gastric disease (EGGD) remains poorly characterized. In people, reflux of bile into the stomach can cause bile gastropathy and has many parallels to

hyperemic EGGD. We hypothesize that there is an increase in bile acid concentrations of pyloric gastric fluid associated with hyperemic EGGD. Our specific objective is to compare the bile acid profiles between horses with and without hyperemic EGGD.
Methods: This was a case-control study in horses with naturally-occurring EGGD. Horses from the institutional herd underwent gastroscopic evaluation. Enrolled horses were designated as control (no abnormalities observed, n=8) or affected (hyperemic EGGD observed, n=15). Concurrent lesions (mucosal surface disruption) were observed in seven affected horses. During gastroscopic evaluation, gastric fluid was collected from the pylorus. Bile acid concentrations were measured using ultra-performance liquid chromatography coupled with mass spectrometry (UPLC/MS). Concentrations were compared between groups using a t-test or Mann-Whitney U test.
Results: Thirteen bile acids were analyzed: ten had measurable concentrations in all horses (n=23), two in 22 horses, and one in 3 horses. Affected horses had increased concentrations of taurolithocholic acid (p=0.044), lithocholic acid (p=0.023), and hyodeoxycholic acid (p=0.002) compared to controls. There was no difference detected in the percentage of conjugated or unconjugated bile acids between groups .
Conclusions: The bile acid profile of pyloric gastric fluid differs between horses with and without EGGD.
Significance/Impact/Implications: These results support a role of bile acid reflux in pyloric, hyperemic EGGD. This is the first study to identify an etiology for pyloric hyperemia.

180. PhD9PHD

Myeloid cell-specific role of HMGB1 in murine lungs with muco-obstructive lung disease

Y. Mao, S. Patial, Y. Saini

Rationale: Muco-obstructive lung diseases are characterized by muco-obstructive airways, increased levels of pro-inflammatory mediators, and infiltration of immune cells. High mobility group box 1 protein (HMGB1), a ubiquitous chromatin-binding protein required for gene transcription regulation, is known to act as a pro-inflammatory mediator in various inflammatory diseases, but its role in muco-obstructive lung diseases remains poorly understood. Here, we hypothesize that myeloid cell-specific HMGB1 acts as a proinflammatory mediator in the Scnn1b-transgenic Tg+ (Scnn1b-Tg+ [Tg+]) mouse, a model that overexpresses sodium channel nonvoltage-gated 1, beta subunit (Scnn1b) transgene and exhibits muco-obstructive lung disease features of human cystic fibrosis (CF) disease.
Methods: We generated myeloid cell-specific HMGB1-deficient Tg+ mice (LysM-Cre+/+/Hmgb1flx/flx/Tg+) mice by intercrossing floxed Hmgb1 (Hmgb1flx/flx) mice, Lysozyme M-regulated Cre recombinase (LysM-Cre) mice, and Tg+ mice. Employing myeloid cell-specific HMGB1-deficient and sufficient control Tg+ mice, we evaluated the effect of myeloid cell-specific HMGB1 deletion on the muco-inflammatory features of Tg+ lungs.
Results: HMGB1 was highly expressed in BALF myeloid cell of Tg+ mice compared with wild-type (WT) mice. Myeloid cell-specific HMGB1-deficient mice had elevated immune cell recruitment in BALF and exaggerated mucoinflammation in airspaces, which was associated with significantly higher levels of inflammatory mediators, including KC, MCP-1, MIP-1a, MIP-1ß, and TNF-a. Furthermore, HMGB1 deletion in BALF myeloid cells in Tg+ mice enhanced the type 2 inflammation manifested by increased levels of Th2 cytokine such as IL-4.
Conclusion: Myeloid cell-derived HMGB1 may play an anti-inflammatory role in murine lungs with muco-obstructive lung disease.

189. PhD10PHD

miRNA species as systemic mediators of Environmentally Persistent Free Radical (EPFR)- induced endothelial dysfunction.

A. Aryal, A. Harmon, L. Khachatryan, A. Noel, A. Penn, S. Cormier, T. Dugas

Particulate matter containing environmentally persistent free radicals (EPFRs) is formed by incomplete combustion of organic pollutants when organic pollutants are incompletely burned and chemisorbed to the surface of particulate matter containing redox-active transition metals. We generated EPFR particles in the laboratory using a combustion reactor, and to investigate dose-dependent effects of free radicals on vascular function, we generated particles over varying free radical concentrations, e.g., EPFRlo: (1e16-17 radicals/g particles) and EPFRhi: (1e18-19 radicals/g). We first exposed C57BL/6 male mice by inhalation with filtered air compared to 250 μg/m3 EPFR for 4h/d for 5 d to investigate their effects on vascular endothelial function. Our studies demonstrated that EPFR inhalation results in a dose-dependent reduction in endothelium-dependent vascular relaxation. Using Nanostring digital transcript counting, we next conducted microRNA (miRNA) profiling and identified 35 miRNAs out of 577 that were dose-dependently increased in the plasma after EPFR exposure. Ingenuity Pathway Analysis (IPA) showed that five of the 35 dysregulated miRNAs are linked with endothelial function, suggesting that miRNA may be a systemic mediator promoting EPFR-induced endothelial dysfunction. Our recent data also suggest that aryl hydrocarbon receptor (AhR) signaling at the air-blood interface in the lungs plays a critical role in EPFR-induced endothelial dysfunction. Thus, to definitively link miRNA release with EPFR-induced endothelial dysfunction, ongoing studies are using mice deficient in AhR at the air-blood interface to test whether miRNA release is attenuated.

190. PhD11PHD

Non-Terminal Equine Model for Tendon and Ligament Regeneration

M.H. Mirza, C. Takawira, R. Aoun, F.J. Morales-Yniguez, J. Miller, N. Moreau, N. Rademacher, M.J. Lopez, T. Taguchi

Rationale: Tendon and ligament injuries are prevalent and debilitating for both human and horses due to poor healing capacity. Horses frequently develop overuse injuries similar to humans, making them an ideal translational model. Established equine tendon injury models that are induced surgically or chemically are cost-prohibitive and require euthanasia.
Methods: Cylindrical core defects (4 mm) were mechanically induced in the front accessory ligament of the deep digital flexor tendon (ALDDFT) of 2 adult mares. A collagen type I (COLI) sponge or allogeneic adipose-derived multipotent stromal cells (ASCs) were percutaneously injected into the defects 6 days post-injury. Each ALDDFT was harvested 12 weeks post-injury and the micro-structure assessed. Objective gait and ultrasonographic image analyses were performed up to 11 weeks after injury and harvest.
Results: There was a clinically relevant (= 5%) decrease in ground reaction forces up to 7 weeks followed by return to pretreatment levels after injury creation. Ultrasonographic core lesion area decreased 7 weeks after COLI injection, and echogenicity increased over time after both treatments. Numerous elongated cells surrounded by new extracellular matrix were present within the COLI implant. The defect distal to the COLI implant and the defect injected with ASCs has few cells surrounded by scant extracellular matrix.

Discussion: The ALDDFT injury model had limited impact on limb use and tissue harvest permitted detection of differences between treatments at the microstructural level.
Significance: A robust, humane, equine ligament injury model will accelerate translation of novel therapies for tendon and ligament pathology.

191. PhD12PHD

Polyunsaturated fatty acids: host-derived molecules that kill Staphylococcus aureus.

A. Stackhouse, A. Monteith, V. Amarnath, K. Tallman, R. Mernaugh, L. Roberts III, N. Porter, S. Davies, E. Skaar, W. Beavers

1:Rationale: Staphylococcus aureus is a Gram-positive pathogen that in the United States causes more than 900,000 severe infections annually. Given both the healthcare and economic impact of S. aureus, the need to investigate novel antimicrobial compounds is imperative to maintain human health. Arachidonic acid (AA), a polyunsaturated fatty acid (PUFA), is abundant in humans and used by the host to defend against invading pathogens. This study will test the hypothesis that lipid peroxidation is the antibacterial mechanism of PUFAs against S. aureus.
2:Methods: Growth assays determined the bactericidal activity and concentrations of PUFAs. Killing assays assessed the bactericidal activity of AA. Spontaneous mutations that convey AA resistance were selected, isolated, and characterized to identify the mechanism of action of PUFA killing. Murine models of infection defined the role of these mutants in S. aureus virulence.
3:Results: Antioxidants protect S. aureus from PUFA killing demonstrating that PUFA toxicity is driven by a lipid peroxidation mechanism. Lipid peroxidation reactions lead to the generation of toxic lipid electrophiles and electrophile scavengers abate S. aureus killing, further implicating a lipid peroxidation mechanism. Alterations in cell wall biosynthesis genes, modulate PUFA susceptibility without detectable alteration of the cell membrane.
4:Conclusions: The results of this study show that PUFAs are bactericidal against S. aureus through a lipid peroxidation mechanism. This indicates that PUFAs could serve as potent antibacterial compounds for the treatment of S. aureus infections. Future studies will focus on investigating the products of PUFA peroxidation and evaluating their effectiveness as potential therapeutic compounds.

199. PhD13PHD

Activation of the Endoplasmic Reticulum Stress Regulator IRE1a Compromises Immunity to MRSA Lung Infection

A. Sharma, L. Heffernan, B. Abuaita

Rationale: Endoplasmic reticulum (ER) stress is linked to many inflammatory diseases of lung where alveolar macrophages (AMs) are critical in disease progression and resolution. Our previous studies demonstrated that the ER stress sensor, IRE1a, promotes host defense in subcutaneous skin infections by enhancing bactericidal activity and production of inflammatory mediators. As the lung is a vital organ, AMs must adequately tune their responses to ensure effective antimicrobial function without excessive tissue damage that could impair gas exchange. Therefore, it is not well understood whether IRE1a underlies AM antimicrobial function and pulmonary host defense.

Methods: Here, we used in vitro AM culture infection model and in vivo murine lung infection model to investigate the importance of IRE1a in pulmonary host defenses during methicillin-resistant Staphylococcus aureus (MRSA) infection.
Results: We found that IRE1a is activated in AMs in response to MRSA infection, which promotes the production of inflammatory mediators (PGE2, TXB2, TNFa, and IL-1ß) by AMs. Myeloid-specific IRE1a deficient mice confer protection against MRSA lung infection and production of less IL-1ß and TNFa in the lungs. Importantly, mice treated with the IRE1a inhibitor, 4μ8C have a higher rate of survival when infected with a lethal dose of MRSA compared to DMSO control. Furthermore, the surviving mice treated with 4μ8C have reduced MRSA burdens and inflammation in the lungs.
Conclusions: Collectively, our results suggest that IRE1a activation in the lung exacerbates bacterial infection and reveals IRE1a inhibitors as a promising therapeutic strategy to fine-tune lung inflammation to enhance host defense against multidrug-resistant pathogens.

201. PhD14PHD

Deleting Caveolin-1 In Epithelial Cells Increases Doxorubicin Sensitivity in Advance Stage of Breast Cancer

A Pandit, DP Singh, R Pathak, P J Ebenezer, and J Francis

Caveolin-1 (Cav-1) is a lipid raft protein with a dual role as a tumor suppressor and persuader. We have previously shown that knocking out Cav-1 from epithelial cells reduces lung metastasis from primary tumors. In this study, we examined whether Cav-1 knockout in epithelial cells increases sensitivity to doxorubicin using both in vitro and in vivo studies. Our in vitro study showed reduced cell numbers in Dox-treated Cav-1 KO cells compared with Dox-treated 4T1 cells (WT). A significant increase in G2M phase arrest in Dox-treated Cav-1 KO cells compared with WT confirmed reduced cell growth. To demonstrate the increased sensitivity to doxorubicin in vivo, we used a syngeneic tumor model using Cav-1 KO and 4T1 WT cells injected into Balb/c mice. Subsequently, after a week, we treated both groups with Dox at a dose of 8 mg/kg body weight/week for 3 weeks (24 mg/kg BW cumulative dose). Tumor sizes were significantly reduced in Dox-treated mice, and this was further reduced in Cav-1 KO mice when compared with the WT. To quantify lung metastasis, we explanted the lungs and plated dissociated cells in complete RPMI media supplemented with 6-thioguanine (6-GT). The number of 6-TG-resistant 4T1 metastatic cells was significantly lower in the lungs' suspension of Cav-1 KO mice treated with Dox compared to WT-Dox mice. Our findings confirm that knockout of Cav-1 increased the sensitivity of Dox treatment and inhibited lung metastasis of breast cancer in Balb/c mice. Currently, mRNA sequencing analysis is underway to delineate the mechanism.

204. PhD15PHD

Blueberry Supplementation for Depression and Anxiety in a Rural Louisiana Population: Behavioral Outcomes and Inflammatory Cytokines

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Blueberries have antioxidant and anti-inflammatory properties and modulate serotonin, mood, cognition, and behavior. Depression and anxiety are prevalent psychiatric disorders and are the second and third most common causes of disability in the US. Further, emerging evidence supports a bidirectional relationship between depression and anxiety and immune, cardiovascular, and

neuroendocrine systems, which blueberries also benefit. To investigate how a medicinal dose of blueberries might affect the physiological health and emotional wellbeing of individuals diagnosed with depression and anxiety, we collaborated with a Louisiana Rural Health Clinic (RHC) system, LHCP. We designed and implemented a randomized, double blind, placebo-controlled crossover study with two 12-week experimental periods, separated by a 4-week washout. Participants received either blueberry powder or placebo powder in the first period and switched treatment in the second period; we took baseline, mid, and post treatment assessments in each arm which consisted of behavioral measures and blood draws. We calculated change from baseline to post timepoints for behavioral measures and used paired Wilcoxon tests which detected significant differences between blueberry and placebo treatment; namely blueberry significantly decreased symptoms of depression and anxiety compared to placebo on the HAM-D and GAD7, but not the MDI. We also measured inflammatory cytokines IL-1B, TNF-a, IL-6, IFN-y, and IL-10 in collected serum samples. Spearman correlation analysis revealed significant associations between IL-1B and IL-6 and behavioral measures, with relationships that differed between blueberry and placebo. This data supports blueberries as a potential treatment or adjunct treatment for depression and anxiety.

206. PhD16PHD

Horseshoe Configuration Effects on In vivo Equine Gait Kinetics and Capsule Deformation

R. Aoun, A. Williams, C. Takawira, T. Taguchi, and M. Lopez

Rationale: The equine hoof capsule is stiff enough to protect the sensitive soft tissues within it and elastic enough to allow sufficient tissue deformation to allow energy absorption and release as a part of the suspensory apparatus. Horseshoes distinctly alter hoof load distribution, but there is limited quantification of the specific effects of shoe configuration on gait kinetics and hoof capsule deformation. The hypothesis tested in this study was that equine walking ground reaction forces (GRF) and hoof capsule deformation are distinct among shoe configurations, which all vary from unshod.
Methods: The 3D location of 13 infrared markers attached to the hoof was simultaneously recorded with GRF in 4 adult horses as they walked across a force platform embedd3d in 30 m-long concrete runway. 3-D deformation of proximal and distal hemicircumferences, dorsal toe, quarters, and heels was calculated at 25% intervals over the stance cycle, while unshod or with open heel, egg bar, heart bar, or wooden clog shoes applied in a random order. The maximum change in resultant GRF vector was quantified. Outcomes were compared with repeated measures/mixed-model ANOVA ($p<0.05$).
Results: Peak vertical GRF is lower with shoes compared to unshod. Deformation of the proximal and distal hemi-circumferences and heels is higher with shoes versus unshod.
Conclusion: Equine shoes reduce both vertical GRFs and hoof deformation at a walk.
Significance/Impact/Implications: Shoes may restrict hoof tissue elasticity contributions to tissue protection and suspensory apparatus energy storage.

208. PhD17PHD

Ehrlichia chaffeensis Infection of Mammalian and Tick Cell Lines

S. Valdes, M. Carossino, U. B. R. Balasuriya

Tick-borne pathogens, including rickettsial and ehrlichial infections, are present on the Gulf Coast. This study will cultivate Ehrlichia chaffeensis in various tick and mammalian cell lines to determine relative susceptibility and infection dynamics. We hypothesize that E. chaffeensis will establish infection in all cell lines; however, there will be a difference in bacterial counts between mammalian and tick cells.
Three tick cell lines (ISE6, AAE2, and DVE1) and one mammalian cell line (Vero E6) will be maintained aseptically. Cells will be infected with E. chaffeensis and harvested at 3dpi and 7dpi. Cells from each group will be mounted on slides before performing immunohistochemistry (IHC) using a pan-Ehrlichia antibody. Slides will be made for use in immunofluorescence assay (IFA), and microscopy will be used to visualize infection with the same primary antibody.
We anticipate all the flasks inoculated with E. chaffeensis will become infected, and the mock-infected flasks will not. We expect that the IHC and IFA assay for Ehrlichia will specifically localize bacteria within the host cells. Lastly, we expect a difference in the number of bacteria between the tick and mammalian cells.
These results will determine if Ehrlichia chaffeensis can grow in each cell line. IHC is commonly used for research and diagnostics, and this work validates this assay's use and establishes infection dynamics of E. chaffeensis in various cell lines. This also lays the groundwork for developing RNAscope tools and better-visualizing bacteria within in vitro systems.

209. PhD18PHD
Viral-induced Small non-coding RNAs modulate the innate immune response to respiratory pneumovirus infection in phagocytes and epithelial cells.

Iván Martínez-Espinoza, Anang D Bungwon, and Antonieta Guerrero-Plata

Rationale: MicroRNAs (miRNAs) are small noncoding single-stranded RNAs that play an essential role in the regulation of the gene expression during cellular normal homeostasis and disease by binding to specific mRNAs; thus, regulating at the transcriptional and post-transcriptional levels with a direct impact on the immune response and other cellular processes. Human metapneumovirus is a respiratory pathogen that can infect macrophages to secrete large amounts of type I interferon and multiple inflammatory cytokines. Although macrophages are essential in defense of the respiratory epithelium against viruses, the role of viral-induced miRNAs in these cells remains largely unknown. Methods: In vitro human macrophages derived from a monocytic cell line and alveolar epithelial cells were used as our experimental model. By using a recombinant virus that expresses GFP, we characterized the viral infection in macrophages. RT-qPCR was used to determine the host miRNA profile induced by the viral infection. The effect of miRNAs on epithelial cells and macrophage immune activation was determined by electroporation assays. Appropriate statistical analysis was applied to determine the changes observed. Results: Here, we demonstrated that respiratory pneumovirus infection significantly induces specific host MicroRNAs. Transfection experiments with miRNA mimic and inhibitor demonstrated that microRNAs modulate the IFN response in virus-infected macrophages and epithelial cells. Conclusions: Overall, our results demonstrate that microRNAs are important for the regulation of the IFN response in macrophages and epithelial cells during HMPV infection, suggesting that HMPV induces miRNA expression as a subversion mechanism of the antiviral response. Significance: Our results increase our understanding

213. PhD21PHD

Repetitive exposure to ozone exaggerates inflammatory response in mice with preexisting muco-obstructive lung disease

T. Vo, S. Patial, Y. Saini

Rationale: Ozone, one of the six criteria pollutants, according to the National Ambient Air Quality Standards (NAAQS), alters muco-inflammatory responses and pathological features in muco-obstructive lungs undergoing active postnatal development. Here, we tested our hypothesis that the juvenile mice with preexisting muco-obstructive lung disease will have exaggerated responses to repetitive ozone exposure.
Methods: We exposed 3-week-old Scnn1b-Tg+ mice, a widely used animal model of Cystic Fibrosis (CF) lung disease, and their wild-type (WT) littermates to ozone (800ppb) or filtered air (FA) for 3 weeks (4h/day) and examined their muco-inflammatory endpoints 12-16h-post last exposure.
Results: Ozone-exposed Scnn1b-Tg+ mice exhibited significantly increased inflammatory cell recruitment in the lung airspaces as compared to FA-exposed Scnn1b-Tg+. The levels of neutrophil chemoattractants (KC, G-CSF, MCP-1) were upregulated in the lungs of ozone-exposed Scnn1b-Tg+ as compared to FA-exposed Scnn1b-Tg+ mice, resulting in the marked increase of neutrophils. The BALF levels of Th2 chemokines (IL-4 and IL-5) and eosinophil counts were also upregulated in ozone-exposed Scnn1b-Tg+ mice as compared to FA-exposed Scnn1b-Tg+. Furthermore, ozone-exposed Scnn1b-Tg+ mice exhibited significantly increased numbers of lipid-laden macrophages, indicating exacerbated lipid peroxidation in the airspaces. Finally, ozone-exposed Scnn1b-Tg+ mice exhibited marked reduction in immunosuppressive cytokine IL-10 levels as compared to FA-exposed Scnn1b-Tg+ mice, suggesting the likely cause of exaggerated inflammation in ozone-exposed Scnn1b-Tg+ lungs.
Conclusion: Taken together, our data suggest that 1) mice with the underlying muco-obstructive disease exhibit exaggerated muco-inflammatory responses to ozone and 2) reduced anti-inflammatory IL-10 levels is the likely cause of exaggerated inflammation in the ozone-exposed Scnn1b-Tg+ lungs.

214. PhD22PHD

Mafb promoter activity may define the alveolar macrophage dichotomy

T. Vo, Y.Saini

Rationale: Cre-LoxP system is a valuable tool for inducing recombinant cell- and tissue-specific genes of interest. Current available macrophage-specific Cre mouse strains are not perfect with regard to their depletion efficiency and targeting specificity, thus warrants the testing for additional Cre strains. V-maf musculoaponeurotic fibrosarcoma oncogene family, protein b-Cre (Mafb-Cre) mice label macrophages in most organs such as spleen, small intestine, lung, bone marrow, and peritoneal cavity. However, Mafb was never tested for its specificity in alveolar macrophages.
Methods: We performed fluorescent microscopy and flow cytometry to analyze mTOM and mEGFP expression in alveolar macrophages from the double reporter MafbCre/WTR26mTmG/WT mice.
Results: The Mafb-Cre is active in only ~40% of the alveolar macrophages in age-independent manner. While Mafb- (mTOM+/mEGFP-) and Mafb+ (mEGFP+) alveolar macrophages exhibit comparable expression of CD11b and CD11c surface markers, the surface expression of MHCII is elevated in the Mafb+ (mEGFP+) macrophages. The bone marrow-derived macrophages from

MafbCre/WTR26mTmG/WT are highly amenable to Cre-LoxP recombination in vitro. The bone marrow depletion and reconstitution experiment revealed that ~98% of alveolar macrophages from MafbCre/WTR26mTmG/WT ? WT chimera are amenable to the Mafb-Cre mediated recombination. Finally, the Th2 stimulation and ozone exposure to the MafbCre/WTR26mTmG/WT mice promote the Mafb-Cre mediated recombination in alveolar macrophages.
Conclusion: While the Mafb-/Mafb+ dichotomy thwarts the use of Mafb-Cre for the induction of floxed alleles in entire alveolar macrophage population, this strain provides a unique tool to induce gene deletion in alveolar macrophages that encounter Th2 microenvironment in the airspaces.

215. PhD23PHD

Liver-Specific Deletion of RNA-Binding Proteins ZFP36L1 and ZFP36L2 Protects Against Carbon Tetrachloride-Induced Acute Liver Injury

R. Kumar, S. Patial, and Y. Saini

Rationale: RNA-binding proteins, Zinc protein 36 like 1 (ZFP36L1) and Zinc protein 36 like 2 (ZFP36L2), bind to AU-rich elements in 3'UTR of target mRNAs and cause mRNA decay. Our preliminary data suggest that the deletion of these proteins results in inflammatory changes in the liver at the basal level. Accordingly, we hypothesized that the liver-specific loss of these proteins will exaggerate chemical-induced acute liver injury.
Methods: Liver-specific ZFP36L1 and ZFP36L2 double knockout (L1/L2KO; AlbCre+/Zfp36l1flox/flox/ Zfp36l2flox/flox) and flox-only control (L1/L2FLX; AlbCre-/Zfp36l1flox/flox/ Zfp36l2flox/flox) adult mice generated. Mice were intraperitoneally injected with carbon tetrachloride (CCL4) dissolved in corn oil (0.8 ml CCL4/Kg body weight). The basal liver glutathione (GSH) and cytochrome P450 2E1 (CYP2E1) levels were assessed in untreated mice. Liver injury-associated endpoints, including histopathology, ALT and AST levels, were assessed at 48 h post-administration.
Results: The liver GSH content was significantly elevated in L1/L2KO than in L1/L2FLX control mice at the basal level. Interestingly, basal liver CYP2E1 level, a pathogenic factor, was significantly decreased in L1/L2KO than in L1/L2FLX group. CCL4 administration resulted in milder centrilobular necrosis in the liver of L1/L2KO mice compared to L1/L2FLX mice. Further, the serum levels of liver function enzymes, ALT and AST were also significantly lower in L1/L2KO than in L1/L2FLX group.
Conclusion/Significance: The combined deletion of RNA-binding proteins, ZFP36L1 and ZFP36L2, protects against CCL4-induced acute liver injury by promoting the antioxidant defense mechanism and preventing the bioactivation of CCL4. These data suggest a pathogenic role for ZFP36L1/ ZFP36L2 in CCL4-induced acute liver injury.

216. PhD24PHD

Establishing a Mouse Model for Lineage Tracing of Mucous Cells in Allergic Asthma

D. Singamsetty, K. Paudel, Y. Saini

Background/Rationale: Asthma is a chronic inflammatory lung disease that affects more than 300 million people worldwide. Mucous cell metaplasia (MCM), a hallmark of asthma, reflects an increase in mucous cells in the airways. Our understanding of the origin of mucous cells in asthmatic airways remains elusive. Basal cells are considered to be the primary stem cells, though club cells are also reported to possess stem cell abilities. While existing research indicates that both these cell types can give rise to mucous cells, the exact lineage of mucous cell is not clearly delineated.

Methods: Because IL-33 is a master regulator of asthmatic airway inflammation, a mouse model of IL-33-induced MCM was established through a single oropharyngeal dose of IL-33 (1µg in 50 µl saline). To conduct lineage tracing of mucous cells from basal or club cells, Basal cell- or Club cell-specific Tamoxifen-inducible reporter mice were generated and employed. Airway epithelium was assessed for altered epithelial cell composition at different timepoints post-dosing.
Results: A single IL-33 dose was sufficient to induce robust basal cell proliferation and MCM, with most changes happening within 24h post-dosing. The eosinophilia and total cell counts peaked at 96h post-IL-33 dosing. Reporter studies showed that intraperitoneal Tamoxifen administration (five injections on alternate days) were sufficient to successfully induce GFP expression in basal cells and club cells, in Krt5-reporter and CCSP-reporter strains, respectively.
Conclusion: These data confirm a successful lineage tracing model to determine the origin of mucous cells in allergic asthma.

217. PhD25PHD

Acute Ozone Exposure Results in Airway Epithelial and Immune Cell Disturbances in Mice

K. Paudel, S. Patial, Y. Saini

Rationale: The ground-level ozone produced by industries and automobiles creates serious pulmonary and cardiovascular problems. Acute ozone exposure disrupts airway epithelial integrity, which compromises lung function and aggravates ongoing lung diseases. However, the kinetics of acute ozone-induced pulmonary responses are not clearly defined.
Methods: We exposed 9-10-week-old female mice to either ozone (1500ppb) or filtered air for four hours. We collected bronchoalveolar lavage fluid (BALF) from the right lung at 12 hours, 36 hours, 60 hours, 108 hours, and 204 hours post-exposure, and assessed immune cell counts, total protein contents, HMGB1 levels, and cytokine contents. The unlavaged left lung was formalin-fixed and paraffin-embedded for histopathological analyses.
Results: At 12 hours post-exposure, severe epithelial denuding of club and ciliated cells was observed. Basal cell proliferation was marked at 36h and 60h post-exposure. Restoration of ciliated cells was observed from 60h post-exposure leading to normal epithelial composition at 204h post-exposure. BALF neutrophil counts and protein concentration peaked at 12h and 36h post-exposure, respectively, with a gradual decline afterwards. A consistent increase in the levels of high mobility group box 1 (HMGB1) was observed until 60h post-exposure along with increased expression of found in inflammatory zone protein (FIZZ1) in the inflamed airway epithelium. Ozone exposure also caused significant changes in the levels of eotaxin, G-CSF, IL-6, KC, MIP-1a, MIP-1ß, IL-5, and MCP-1 levels in a time-dependent manner.
Conclusion: Our study elucidates critical events involved in the progression and resolution of pathological outcomes in ozone-exposed mice.

218. PhD26PHD

Tristetraprolin (TTP) Overexpression Alleviates Type 2 (Th2) Immune Response in Allergic Asthmatic Mice

R. Lamichhane, I. Choudhary, T. Vo, D. Singamsetty, S. Patial and Y. Saini

Rationale: Allergic asthma is a chronic inflammatory airway disease characterized by eosinophilic recruitment, mucous cell metaplasia (MCM), peribronchial fibrosis, and airway hyper-responsiveness

(AHR). Tristetraprolin (TTP) is an mRNA-binding protein that binds to AU-rich elements within the 3' untranslated regions of certain transcripts for inflammatory genes and increases their rate of decay. Hypothesis: The systemic overexpression of TTP will mitigate mixed allergen (MA)-induced allergic asthma endpoints.
Methods: TTP-overexpression (TTP?ARE) and TTP-WT (TTPWT) adult mice were intranasally challenged with a mixed allergen (MA) (Ovalbumin, Alternaria alternata, Aspergillus fumigatus, Dermatophagoides pteronyssius) or PBS for four weeks (3 doses/week). Lung injury, inflammation, and fibrosis were assessed, 48 hours post-last dose of MA or PBS. Additionally, bone-marrow chimeras (TTPWT (donor)?TTPWT(recipient), TTP?ARE?TTPWT, TTPKO?TTPWT, TTP?ARE?TTP?ARE, TTPWT?TTPARE, TTPKO?TTP?ARE) were generated and challenged to MA.
Results: As compared to the PBS-challenged mice, MA-challenged TTPWT and TTP?ARE mice showed a significant increase in eosinophilic recruitment, lung injury, consolidation, peribronchial fibrosis, and Th2 inflammation. As compared to the MA-challenged TTPWT mice, the MA-challenged TTP?ARE mice exhibited a significant decrease in eosinophilic recruitment, lung injury, consolidation, peribronchial fibrosis, and Th2 inflammation. Interestingly, as compared to TTPWT?TTPWT mice, TTP?ARE?TTPWT mice exhibited significantly decreased inflammation whereas TTPKO?TTPWT mice exhibited exaggerated inflammation post-MA-challenge. Additionally, as compared to the MA-challenged TTP?ARE?TTP?ARE mice, the MA-challenged TTPWT?TTP?ARE mice or TTPKO?TTP?ARE mice showed increased inflammation. However, the inflammation was more robust in TTPKO?TTPWT mice as compared to TTPKO?TTP?ARE mice post-MA challenge.
Conclusion: The overexpression of TTP in hematopoietic cells protects mice against MA-induced asthma endpoints.

Category: Post Doc

182. PD0PD

Differential Pulmonary Tropism, Accelerated Viral Replication, Neurodissemination, and Pulmonary Host Responses in K18-hACE2 Mice Infected with the SARS-CoV-2 MA10 Strain

C. J. Thieulent, W. Dittmar, U. B. R. Balasuriya, N. A. Crossland, X. Wen, J. A. Richt, M. Carossino

Rationale: Several models were developed to study the pathogenicity of SARS-CoV-2 as well as the in vivo efficacy of vaccines and therapeutics. Since wild-type mice are naturally resistant to infection by ancestral SARS-CoV-2 strains, several transgenic mouse models expressing human angiotensin-converting enzyme 2 (hACE2), the cellular receptor of SARS-CoV-2, were developed (e.g., K18-hACE2 mice). An alternative approach has been to develop mouse-adapted SARS-CoV-2 strains (e.g., MA10).
Methods: Clinical progression, viral replication kinetics and dissemination, pulmonary tropism, and host innate immune response dynamics between the mouse-adapted MA10 strain and its parental strain (USA-WA1/2020) following intranasal inoculation of K18-hACE2 mice were measured.
Results: Compared to its parental counterpart, the MA10 strain induced earlier clinical decline with significantly higher viral replication and earlier neurodissemination, along with a broader tropism for bronchiolar epithelia. While both SARS-CoV-2 strains induced comparable pulmonary cytokine/chemokine responses, many proinflammatory and monocyte-recruitment chemokines, such as IL-6, TNFa, IP-10/CXCL10, and MCP-1/CCL2, showed an earlier peak in MA10-infected mice. Furthermore, both strains induced a similar downregulation of murine Ace2, with only a transient downregulation of Tmprss2 and no alterations in hACE2 expression.
Conclusions/Significance: Overall, these data demonstrate that in K18-hACE2 mice, the MA10 strain has a pulmonary tropism that more closely resembles SARS-CoV-2 tropism in humans (airways and

pneumocytes) than its parental strain. Its rapid replication and neurodissemination and early host pulmonary responses can have a significant impact on the clinical outcomes of infection and are, therefore, critical features to consider for study designs using these strains and mouse model.

184. PD1PD

Exacerbated viral replication following infection of diabetic mice with the mouse-adapted SARS-CoV-2 MA10 strain

C. J. Thieulent, U. B. R. Balasuriya, N. A. Crossland, W. Dittmar, J. Staszkiewicz, J. M. Stephens, J. A. Richt, M. Carossino

Rationale: Comorbidities such as diabetes are associated with an increased rate of acute respiratory distress syndrome (ARDS) and COVID-19-associated hospitalizations in patients. Type II diabetes (T2D) is the most common form of diabetes (95%) and affects over 12% of the US population. The aim of this study is to evaluate the susceptibility of T2D mice to SARS-CoV-2.
Methods: T2D mice and lean mice were intranasally infected with the SARS-CoV-2 mouse-adapted strain MA10. Clinical progression, lung viral replication kinetics, and pulmonary tropism were measured over time. In addition, lung bulk RNAseq analysis was performed to identify transcriptional signatures associated with SARS-CoV-2 infection.
Results: Significantly higher viral titers and viral RNA were identified in the lung of T2D mice following SARS-CoV-2 infection compared to lean, heterozygotes. This difference also correlated with more severe histologic lesions and higher SARS-CoV-2 antigen expression in the lungs of T2D mice. The difference in cytokines/chemokines expression revealed a difference in immune response in both groups of mice. Furthermore, differential gene expression analysis revealed an increase in virus-induced cytokine storm signaling and interferon response pathways in T2D mice despite lack of interferon-alpha upregulation.
Conclusions/Significance: Overall, these data demonstrated that SARS-CoV-2 replicates to a higher titer in the lung of T2D mice. Its rapid replication is partially explained by the downregulation of key biological processes associated with immunity in TD2 mice. However, further studies are needed to understand why T2D patients are more prone to developing ARDS and to inform alternative therapeutic interventions for this high-risk population.

185. PD2PD

Vimentin Is Involved in Equine Arteritis Virus Infection

C. J. Thieulent, S. Sarkar, M. Carossino, U. B. R. Balasuriya

Rationale: Equine arteritis virus (EAV) is the causative agent of equine viral arteritis, a respiratory and reproductive disease of horses. CXCL16S was previously identified as a cell entry receptor for EAV. However, EAV has a broad host-cell tropism and infects a variety of cells in vitro that do not express CXCL16S. We hypothesize that other host cell-protein(s) facilitate EAV entry.
Methods: Virus overlay protein-binding assay in combination with Far-Western blot and LC-MS/MS analysis were performed to identify other EAV-binding protein(s). Virological and cell culture methods (e.g., cell transfection, immunofluorescence, plaque assays) were used to confirm the role of the putative EAV receptor.
Results: A 57 kDa protein from two EAV-susceptible equine cell lines (EECs and E. Derm) was first identified as a possible EAV-binding protein. Further investigation revealed that the unidentified 57 kDa protein is present in the membrane fraction of EECs and identified as vimentin. Screening of a

wide range of cells determined that only those expressing vimentin are susceptible to EAV infection. Overexpression of equine vimentin in HEK-293T cells results in an increase of EAV infection. Conclusions/Significance: Collectively, our data provides strong evidence that EAV binds to the host cell protein, vimentin, which possibly serves as an attachment factor, suggesting that EAV interacts with multiple host cell proteins that determine its diverse cell tropism in vitro.

186. PD3PD

Multiplex qPCR/RT-qPCR assays for detection of canine and feline respiratory pathogens

C. Thieulent, M. Carossino, L. Peak, K. Strother, W. Wolfson, G. Li, U. B. R. Balasuriya

Rationale: Canine infectious respiratory disease complex (CIRDC) and feline upper respiratory tract disease (URTD) are the primary causes of respiratory disease in companion animals and are associated with a wide array of viruses and bacteria acting as either individual etiologic agents or in combination, making etiologic diagnosis challenging. Additionally, SARS-CoV-2 has been reported to infect both dogs and cats. Therefore, the rapid detection and differentiation of SARS-CoV-2 from other common viral and bacterial agents in a single specimen is critical.
Methods: Here, two one-step, TaqMan® multiplex qPCR/RT-qPCR panels were developed and validated for the identification of CIRDC and feline URTD-associated agents and SARS-CoV-2. Clinical performance was evaluated using 68 and 63 nasal/nasopharyngeal swabs obtained from CIRDC-suspected dogs and URTD-suspected cats, respectively.
Results: All the multiplex assays demonstrated high specificity, analytical sensitivity and efficiency, and nearly perfect linearity. Among the clinical samples derived from dogs, Mycoplasma canis, M. cynos and canine respiratory coronaviruses were the most prevalent pathogens. The emerging canine pneumovirus was detected in five samples. Among the clinical samples from cats, M. felis was the most prevalent pathogen, followed by feline herpesvirus type 1, Chlamydia felis and feline calicivirus. SARS-CoV-2 was detected in four canine and two feline samples. A high prevalence of co-infection was detected, with a rate of 29% and 59% of canine and feline samples, respectively. Conclusions/Significance: These two newly developed multiplex qPCR/RT-qPCR panels are useful and reliable for the rapid detection and identification of canine and feline respiratory pathogens, along with SARS-CoV-2.

207. PD4PD

Bovine herpesvirus 1 (BoHV-1)-Vectored Rift Valley Fever-sub Vaccine Induces RVFV-Specific Humoral and Cell-mediated Immune Response and Does Not Shed upon Latency-reactivation

P. Selvaraj, S. Pavulraj, E.D. Barras, R.W. Stout, D.B. Paulsen, and S.I. Chowdhury

Rationale: Rift Valley fever virus (RVFV) is an emerging pathogen with high biodefense priority causing abortion and death in cattle and sheep. This zoonotic virus has the potential for aerosol spread and causes fatal hemorrhagic fever in humans. Currently available RVFV vaccines have safety and efficacy limitations. Therefore, we developed a BoHV-1 vectored RVFV-subunit vaccine against RVF.
Methods: We have constructed a BoHV-1 quadruple gene-deleted/mutated (BoHV-1qmv) vaccine vector expressing chimeric RVFV envelope glycoproteins, Gn ectodomain fused with GM-CSF and Gc with self-cleavable peptide 2A (BoHV-1qmv RVFV-Sub). Calves were immunized with the live BoHV-1qmv RVFV-Sub vaccine intranasally and subcutaneously. Immunogenicity against RVFV was evaluated by determining RVFV-specific neutralizing antibodies in serum and cell-mediated immune

response in peripheral blood mononuclear cells collected from the immunized calves. We also determined the latency-reactivation and nasal virus-shedding properties of the vaccine virus. Results: The BoHV-1qmv RVFV-Sub vaccine virus replicated well in vitro and expressed RVFV chimeric proteins. The live vaccine virus is highly attenuated and optimally replicated in the nasal mucosa of immunized calves. A single dose of BoHV-1qmv RVFV-sub vaccine induced both BoHV-1- and RVFV-specific neutralizing antibodies and RVFV-specific cellular immune responses. Upon dexamethasone-induced reactivation from latency, only the BoHV-1 wild-type-infected calves shed virus in the nasal secretions with memory B cell response, but not the BoHV-1qmv RVFV-Sub vaccinated calves.
Conclusions/Significance: Our live BoHV-1qmv vectored RVFV-sub prototype subunit vaccine is highly immunogenic, safe, and efficacious against RVFV in calves. The BoHV-1qmv vector is safe and has the potential to use for various subunit vaccines.

Faculty

144. FP0FAC

L. Dirikolu, P. Waller, X. Wen*

Race-related injuries in Thoroughbred and Quarter Horse Racehorses in Louisiana (2011-2021)

No abstract available