THE OHIO STATE UNIVERSITY

COLLEGE OF VETERINARY MEDICINE

COLLEGE OF VETERINARY MEDICINE RESEARCH DAY

7 APRIL 2016

BOOK OF ABSTRACTS

PROGRAM

April 7, 2016

POSTER JUDGING

Graduate Student Posters
8:00 am – 10:30 am
(closed session – only open to
those being judged)

AWARDS PRESENTATION

Veterinary Medical Center Auditorium
12:00 pm

GRADUATE STUDENT and POST DOC PLATFORM PRESENTATIONS

Dr. Dimitria Mathys
Dr. Amanda Panfil

INAUGURAL RAINIER ENDOWED CHAIR LECTURE

Veterinary Medical Center Auditorium
immediately following the awards
and platform presentations

DR. G. Gilbert Cloyd

Chief Technology Officer of Procter & Gamble (Retired)
Ohio State CVM Alumnus

"Veterinary Careers in Industrial Research and the Importance of Private Sector Innovation"

POSTER SESSION

1st and 2nd Floors – Vet Med Academic Building
11:00 am – 5:00 pm

CHAIRED BY

Dr. Patrick Green

ORGANIZED BY

Michele Morscher

Special thanks to Marc Hardman in the
College's Technology Services for printing the posters

POSTER JUDGING SESSIONS

Wednesday, April 6, 2016
2:00 – 5:00 pm
Undergraduate and
Veterinary Student Poster Judging

Thursday, April 7, 2016
8:00 – 10:30 am
Graduate Student Poster Judging

Thank you to the following faculty and guests for taking time out of their busy schedules to judge 70 posters.

Jim Belknap

Andy Bowman

Prosper Boyaka

Rachel Cianciolo

Luciana da Costa

Miles Hall

Jim Hartke

Kate Hayes-Ozello

Ryan Jennings

Sanggu Kim

Stefan Niewiesk

Mike Oglesbee

Judy Radin

Dave Ralph

Yasuko Rikihisa

Thiru Selvanantham

Barb Wolfe

THE OHIO STATE UNIVERSITY
COLLEGE OF VETERINARY MEDICINE

Office of Research
and Graduate Studies

COLLEGE OF VETERINARY MEDICINE
RESEARCH DAY

Awards Presentation, Graduate Student and Post Doc Platforms, and Inaugural Rainier Endowed Chair Lecture

Thursday, April 7th, 2016 Noon – 2 p.m.

Veterinary Medical Center Auditorium

Dr. G. Gilbert Cloyd

Chief Technology Officer
of Procter & Gamble
(Retired)

"Veterinary careers in industrial research and the importance of private sector innovation"

Poster judging:

April 6th, 2 – 5 p.m. for Professional Students

April 7th, 8 – 10:30 a.m. for Graduate Students

EAR – 16

PLATFORM PRESENTATION

***ENTEROBACTERIACEAE* PRODUCING EXTENDED SPECTRUM β-LACTAMASES (ESBL) FROM WILD BIRDS IN OHIO.** D.A. Mathys[1], B. A. Mathys[2], D.F. Mollenkopf[1], J.B. Daniels[3], T.E. Wittum[1]. [1]Department of Veterinary Preventive Medicine, College of Veterinary Medicine, Ohio State University [2]Department of Natural Sciences, Ohio Dominican University [3]Department of Veterinary Clinical Sciences, College of Veterinary Medicine, Ohio State University

ESBLs confer bacterial resistance to critically important antimicrobials. Livestock are an important reservoir for the zoonotic food-borne transmission of resistant enteric bacteria. Our aim is to describe the potential role of migratory and resident wild birds in the epidemiology of ESBL mediated bacterial resistance on dairy farms. Using mist nets, we sampled wild migratory and resident birds either immediately adjacent to or 600 feet away from free stall barns on three Ohio dairy farms during 2014/2015 spring migration. Individual swabs were used to obtain both a cloacal and external surface swab from each bird. Additionally, wild ducks were sampled either live caught or hunter harvested from hunting preserves in 2014 and 2015. Samples were inoculated into MacConkey broth containing cefotaxime and inoculated onto MacConkey Agar with cefoxitin, cefepime, or meropenem to identify the *bla*$_{CMY,}$ *bla*$_{CTX-M,}$ and carbapenemase phenotypes, respectively. Six hundred and six birds were sampled, 14 (2.3%) of which harbored bacteria with the *bla*$_{CMY}$ gene and 26 (4.3%) harbored bacteria with the *bla*$_{CTX-M}$ gene from either their cloacal sample or from their external swab. There was no difference in the prevalence of either gene between migratory and resident birds. Prevalence of the *bla*$_{CMY}$ was higher among birds sampled immediately outside the barns compared to those sampled 600 feet away. Six hundred and twenty seven ducks were sampled, with 44 (7%) harboring *bla*$_{CMY}$ bacteria and 2 (0.3%) harboring *bla*$_{CTX-M}$ bacteria. Our results suggest that wild birds can serve as mechanical and/or biological vectors for *Enterobacteriaceae* with resistance to extended spectrum cephalosporins. Birds live in close contact with dairy cows and their feed, therefore transmission locally from farm to farm is possible. Finding a similar prevalence in migratory and non-migratory birds suggests the potential for regional and intercontinental movement of these genes via birds.

Keywords: Antibiotic resistance, wildlife, vector, livestock

MCB – 15

PLATFORM PRESENTATION

PRMT5 IS UPREGULATED IN HTLV-1-MEDIATED T-CELL TRANSFORMATION AND SELECTIVE INHIBITION ALTERS VIRAL GENE EXPRESSION AND INFECTED CELL SURVIVAL. A. Panfil, J. Al-Saleem, C. Howard, J. Mates, J. Kwiek, R. Baiocchi, and P. Green. Depts. of Veterinary Biosciences

Human T-cell leukemia virus type-1 (HTLV-1) is a tumorigenic retrovirus responsible for development of adult T-cell leukemia/lymphoma (ATLL). This disease manifests after a long clinical latency period of up to 2-3 decades. Two viral gene products, Tax and HBZ, have transforming properties and play a role in the pathogenic process. Genetic and epigenetic cellular changes also occur in HTLV-1-infected cells, which contribute to transformation and disease development. However, the role of cellular factors in transformation is not completely understood. Herein, we examined the role of protein arginine methyltransferase 5 (PRMT5) on HTLV-1-mediated cellular transformation and viral gene expression. We found PRMT5 expression was upregulated during HTLV-1-mediated T-cell transformation, as well as in established lymphocytic leukemia/lymphoma cell lines and ATLL patient PBMCs. shRNA-mediated reduction in PRMT5 protein levels or its inhibition by a small molecule inhibitor (PRMT5i) in HTLV-1-infected lymphocytes resulted in increased viral gene expression and decreased cellular proliferation. PRMT5i also had selective toxicity in HTLV-1-transformed T-cells. Finally, we demonstrated that PRMT5 and the HTLV-1 p30 protein had an additive inhibitory effect on HTLV-1 gene expression. Our study provides evidence for PRMT5 as a host cell factor important in HTLV-1-mediated T-cell transformation, and a potential target for ATLL treatment.

Keywords: ATLL; HBZ; HTLV-1; PRMT5; Tax; lymphoma; transformation

CLINICAL RESEARCH

CR - 1

MORPHOMETRIC DIFFERENCES OF COMPUTED TOMOGRAPHIC IMAGES BETWEEN THE CERVICAL VERTEBRAL FORAMEN OF GREAT DANES WITH AND WITHOUT SUBCLINICAL NEUROLOGIC DEFICITS. J. Arbogast, R. C. Da Costa DVM, MS, ACVIM. The Ohio State University, College of Veterinary Medicine, Columbus OH

CR - 2

ASSESSMENT OF BIOMARKERS OF PAIN AND ACTIVITY PATTERNS IN LACTATING DAIRY COWS DIAGNOSED WITH CLINICAL METRITIS. A.A. Barragan[1], J.J. Piñeiro[1], G. M. Schuenemann[1], P.J. Rajala-Schultz[1], D.E. Sanders[2], S. Bas[1].
[1]Department of Veterinary Preventive Medicine, College of Veterinary Medicine, The Ohio State University, Columbus, OH 43210, [2]Vaca Resources, Urbana, OH 43078

CR - 3

CLINICAL CHARACTERISTICS OF PRESUMPTIVE OR CONFIRMED FIBROCARTILAGINOUS EMBOLIC MYELOPATHY (FCE): A SYSTEMATIC REVIEW OF 393 CASES FROM 1973 TO 2013. K. Bartholomew, S. Moore, K. Stover, and N. Olby. Dept. of Veterinary Clinical Sciences, College of Veterinary Medicine, The Ohio State University (Bartholomew and Moore); and the Dept of Clinical Sciences, College of Veterinary Medicine, North Carolina State University (Stover and Olby).

CR - 4

COMPARISON OF ALBUMIN, COLLOID OSMOTIC PRESSURE, VON WILLEBRAND FACTOR, AND COAGULATION FACTORS IN CANINE CRYOPOOR PLASMA, CRYOPRECIPITATE, AND FRESH FROZEN PLASMA. C. Culler[1], M. Iazbik M[1], J Guillaumin[2] [1]The Ohio State University Veterinary Medical Center. [2] Department of Veterinary Clinical Sciences, Ohio State University

CR - 5

ANDROGEN AND PREGNANE RESPONSE TO STRESS IN CRITICALLY ILL FOALS. K. Dembek[1], K. Timko[1], L. Johnson[1], B. David[2], B. Barr[3], K. Hart[4], and R. Toribio[1], [1]Department of Veterinary Clinical Sciences, The Ohio State University, [2]Hagyard Equine Medical Institute, [3]Rood and Riddle Equine Hospital, [4]College of Veterinary Medicine, University of Georgia

CR - 7

USE OF FOOD TO FACILITATE HANDLING OF DOGS DURING VETERINARY VISITS: EFFECTS ON GASTROINTESTINAL FUNCTION AND CLIENT PERCEPTIONS OF THE VISIT. M. Forman, T. Shreyer, T. Buffington, S. Barrett
The Ohio State University, Department of Veterinary Clinical Sciences

CR - 8

FIBROBLAST GROWTH FACTOR-23 IN CANINE CHRONIC KIDNEY DISEASE. L. Harjes, V. Parker, K. Dembek, L. Giovanni, M. Kogika, D. Chew, and R.E. Toribio. Department of Veterinary Clinical Sciences, The Ohio State University

CR - 9

LACTOFERRIN REDUCES MORTALITY IN PRE-WEANED CALVES WITH DIARRHEA. K. Harris and G. Habing. Department of Veterinary Preventive Medicine

CR - 10

COMPUTATIONAL FLUID DYNAMICS USING COMPUTED TOMOGRAPHY TO ASSESS AIRWAY RESISTANCE IN ENGLISH BULLDOGS. E.T. Hostnik[1], B.A. Scansen[1], R.E. Zielinski[2], and S.N. Ghadiali[2]. [1]Department of Veterinary Clinical Sciences and [2]Department of Biomedical Engineering, The Ohio State University, Columbus, OH 43210.

CR - 11

THE FGF-23/KLOTHO AXIS AND ITS ASSOCIATION WITH PHOSPHORUS, CALCIUM, VITAMIN D, PARATHYROID HORMONE, DISEASE SEVERITY AND OUTCOME IN HOSPITALIZED FOALS. A. Kamr[1,4], K.A. Dembek[1], B.E. Hildreth III[1], S.M. Reed[2], N.M. Slovis[3], T.A. Burns[1], A. Zaghawa[4], R.E. Toribio[1]. [1] Veterinary Clinical Sciences, College of Veterinary Medicine, The Ohio State University, Columbus, OH; [2]Rood and Riddle Equine Hospital, Lexington, KY; [3]Hagyard Equine Medical Institute, Lexington, KY; [4]Faculty of Veterinary Medicine, University of Sadat City, Sadat City, Egypt

CR - 12

THE EFFECTS OF HYALURONAN ALONE OR IN COMBINATION WITH CHONDROITIN SULFATE AND N- ACETYL-D-GLUCOSAMINE ON LIPOPOLYSACCHARIDE-CHALLENGED EQUINE FIBROBLAST-LIKE SYNOVIAL CELLS. A. Kilborne, H. Hussein, A. Bertone. Department of Veterinary Clinical Sciences. College of Veterinary Medicine, The Ohio State University, Columbus, OH, USA.

CR - 13

ADRENOCORTICAL STEROID RESPONSE TO A HIGH DOSE OF ACTH IN HEALTHY AND CRITICALLY ILL FOALS. J.S. Minuto, K.A. Dembek, R.E. Toribio. Department of Veterinary Clinical Sciences, College of Veterinary Medicine, The Ohio State University, Columbus, OH

CR - 14

REGIONAL DIFFERENCE IN THE SPINAL EPENDYMAL LAYER OF NORMAL DOGS A Muir, SA Moore. Department of Clinical Sciences, College of Veterinary Medicine, The Ohio State University, Columbus, Ohio

CR - 15

EVALUATION OF KINEMATIC MAGNETIC RESONANCE IMAGING IN DOGS WITH OSSEOUS-ASSOCIATED CERVICAL SPONDYLOMYELOPATHY. M. Provencher, A. Habing, S. Moore, L. Cook, G. Phillips, and R. da Costa. Departments of Veterinary Clinical Sciences and the Center for Biostatistics

CR - 16

CLINICAL STUDY OF ECHOCARDIOGRAPHIC VARIABILITY IN ESTIMATING PULMONARY ARTERY PRESSURE AND PULMONARY VASCULAR RESISTANCE IN DOGS. J. Rhinehart, K. Schober. B. Scansen, J. Bonagura. Depts. of Veterinary Clinical Sciences

CR - 17

BEHAVIORAL EFFECTS OF TRAZODONE ON HOSPITALIZED DOGS.
S. Gilbert-Gregory, M.R. Rice, J. Stull, K. Proudfoot, M. Herron. Depts. of Veterinary Clinical Sciences and Preventative Medicine.

CR - 18

THE EFFECT OF INTRAVENOUS MAGNESIUM SULFATE (MgSO4) ADMINISTRATION IN THE HORSE. S. Schumacher DVM, A. Bertone DVM, PhD, and R.Toribio DVM, PhD. Departments of Veterinary Clinical Sciences. The Ohio State University, Columbus, Ohio 43210

EPIDEMIOLOGY AND APPLIED RESEARCH

EAR - 1

EXTENDED-SPECTRUM CEPHALOSPORIN, CARBAPENEM, AND FLUOROQUINOLONE RESISTANT COLIFORM BACTERIA FROM A LARGE EQUINE TEACHING HOSPITAL AND A REFERRAL EQUINE SPECIALTY HOSPITAL. R. Adams, D. Mathys, D. Mollenkopf, A. Whittle, M. Mudge, A. Bertone, J. Daniels, T. Wittum. Depts. of Veterinary Preventive Medicine and Veterinary Clinical Sciences

EAR - 2

***SALMONELLA ENTERICA* PREVALENCE IN THE OHIO STATE UNIVERSITY VETERINARY MEDICAL CENTER ENVIRONMENT**. A. Albers, D. Mollenkopf, D. Mathys, T. Wittum. Department of Veterinary Preventive Medicine

EAR - 3

INFLUENCE OF A PLANT QUATERNARY BENZO[C]PHENANTHRIDINE ALKALOID-SUPPLEMENTED DIET ON THE INTESTINAL MICROBIOTA PROFILE OF FINISHING PIGS CHALLENGED WITH *SALMONELLA.* V. Artuso-Ponte, S. Moeller, P. Rajala-Schultz, P.N. Boyaka, and W. Gebreyes. Depts. of Veterinary Preventive Medicine, Animal Sciences and Veterinary Biosciences.

EAR - 4

COMPARATIVE HEALTH ANALYSIS OF ENDANGERED MASSASAUGA RATTLESNAKES ACROSS OHIO AND ILLINOIS. K. Backus, M. Freeman, B. Wolfe, G. Lipps, College of Veterinary Medicine.

EAR – 5

COMPARATIVE STUDY OF COMMERCIALLY SOLD RAW PET FOOD PROCESSING. P. H. Bellen and T. Wittum. Department of Veterinary Preventive Medicine

EAR - 6

CHARACTERIZATION OF BEHAVIORAL INDICATORS FOR EQUINE PROTOZOAL MYELOENCEPHALITIS (EPM). L. Diangelo, W. Saville, S. Reed, and K. Proudfoot. The Ohio State University Department of Veterinary Preventive Medicine, Columbus, OH (Diangelo, Saville, Proudfoot)

EAR - 7

DISSEMINATION OF ANTIMICROBIAL RESISTANT ENTERIC BACTERIA IN A ZOO ENVIRONMENT. S. M. Feicht, D. A. Mathys, D. F. Mollenkopf, T. E. Wittum, Department of Veterinary Preventive Medicine

EAR - 8

NON-TYPHOIDAL *SALMONELLA* IN VEAL CALVES. S. Finney, L. Munoz, H. Hutchinson, A. Ascot, A. Strait, M. Masterson, G. Habing. Dept. Of Veterinary Preventive Medicine.

EAR - 9

DEVELOPMENT OF MULTILOCUS SEQUENCE TYPING (MLST) ASSAY FOR *MYCOPLASMA IOWAE*. M Ghanem[a] and M El-Gazzar [a,*]
[a]*Department of Veterinary Preventive Medicine, College of Veterinary Medicine, The Ohio State University, Columbus, OH, 43210, USA.*

EAR - 10

NON-WOVEN FABRICS FOR NASAL WIPE SAMPLING OF INFLUENZA A VIRUS IN SWINE. CT Hammons, N Bliss, JM Nolting, and AS Bowman. Department of Veterinary Preventive Medicine, College of Veterinary Medicine, The Ohio State University, Columbus, Ohio

EAR - 11

CHANGES IN THE PREVALENCE OF ANTIMICROBIAL RESISTANCE THROUGH A VERTICALLY INTEGRATED VEAL CALF PRODUCTION SYSTEM H. Hutchinson, S. Finney, A. Ascott, A. Strait L. Munoz-Vargas and S. Feicht, M. Masterson and G. Habing. Dept. of Veterinary Preventative Medicine.

EAR - 12

ENVIRONMENTAL SURVEILLANCE FOR EXTENDED SPECTRUM β-LACTAMASE GENES IN *ESCHERICHIA COLI* AT A MUNICIPAL WASTEWATER TREATMENT PLANT. CA King, DF Mollenkopf, DA Mathys, DM Stuever, JB Daniels, TE Wittum. Departments of Veterinary Preventive Medicine and Veterinary Clinical Sciences, College of Veterinary Medicine, The Ohio State University.

EAR - 13

COMPARISON OF THE MICROBIOLOGICAL QUALITY OF FRESH PRODUCE FROM SEASONAL FARMER'S MARKETS AND RETAIL GROCERY STORES IN OHIO. D. I. Korec, D. A. Mathys, D. F. Mollenkopf, T. E. Wittum. The Ohio State University, College of Veterinary Medicine, Department of Veterinary Preventive Medicine, Columbus, OH

EAR - 14

DETECTION OF PORCINE HEMAGGLUTINATING ENCEPHALOMYELITIS VIRUS IN EXHIBITION SWINE WITH INFLUENZA-LIKE ILLNESS AT AGRICULTURAL FAIRS IN MICHIGAN IN 2015. J. Lorbach, S. Nelson, M. Zentkovich, J. Nolting, A. Bowman. Department of Veterinary Preventive Medicine, The Ohio State University

EAR - 15

DAIRY CALF PREFERNCE FOR ENRICHMENT ITEMS ADDED TO AN OUTDOOR HUTCH. H. Manning, E. Cosentino, J. Pempek, M. Eastridge, K. Proudfoot. Dept. of Veterinary Preventive Medicine

EAR – 16
PLATFORM PRESENTATION

***ENTEROBACTERIACEAE* PRODUCING EXTENDED SPECTRUM β-LACTAMASES (ESBL) FROM WILD BIRDS IN OHIO.** D.A. Mathys[1], B. A. Mathys[2], D.F. Mollenkopf[1], J.B. Daniels[3], T.E. Wittum[1]. [1]Department of Veterinary Preventive Medicine, College of Veterinary Medicine, Ohio State University [2]Department of Natural Sciences, Ohio Dominican University [3]Department of Veterinary Clinical Sciences, College of Veterinary Medicine, Ohio State University

EAR - 17

AMYLOIDOSIS IN CHEETAHS (*Acinonyx jubatus*)
K.M. McLean,[1] R.B. Garabed,[1] and B.A. Wolfe. [1,2] [1]Dept. of Veterinary Preventive Medicine. [2]Morris Animal Foundation

EAR - 18

GENOTYPIC CHARACTERIZATION OF EXTENDED-SPECTRUM CEPHALOSPORIN RESISTANT NONTYPHOIDAL *SALMONELLA* FROM THE NAHMS FEEDLOT 2011 STUDY. D. Mollenkopf[1], D. Mathys[1], D. Dargatz[2], M. Erdman[3], J. Daniels[4], T. Wittum[1]. [1]Dept. of Veterinary Preventive Medicine, College of Veterinary Medicine, The Ohio State University, Columbus, OH. [2]USDA, APHIS, VS Centers for Epidemiology and Animal Health, Fort Collins, Colorado, [3]Diagnostic Bacteriology Laboratory, National Veterinary Services Laboratories, USDA, Ames, IA, [4]Dept. of Veterinary Clinical Science, College of Veterinary Medicine, The Ohio State University, Columbus, OH

EAR - 19

HOST SPECIES HETEROGENEITY IN THE EPIDEMIOLOGY OF *NESOPORA CANINUM*. K. Moreno-Torres, L. W. Pomeroy, B. Wolfe, W. Saville, M. Moritz and R. Garabed. Depts. of Veterinary Preventive Medicine and Anthropology

EAR - 20

TRANSMISSION OF *SALMONELLA* FROM FARM TO FOOD: THE IMPACT OF CLINICAL OUTBREAKS OF SALMONELLOSIS IN CALVES ON RECOVERY OF *SALMONELLA* FROM LYMPH NODES AT HARVEST. L.M. Muñoz-Vargas[1], S. Finney[1], H. Hutchinson[2] and G. Habing[1]. [1]Dept. of Veterinary Preventive Medicine, The Ohio State University, Columbus, OH, USA. [2]Dept. of Animal Sciences, The Ohio State University, Columbus, OH, USA.

EAR - 21

FLOW CYTOMETRIC CHARACTERIZATION OF SIALIC ACID RECEPTORS ON MDCK CELLS MAINTAINED UNDER DIFFERENT MEDIA CONDITIONS AND IMPLICATIONS FOR DETECTION OF INFLUENZA A VIRUS. S. Nelson, I. Davis, A. Bowman. Departments of Veterinary Biosciences and Veterinary Preventive Medicine

EAR - 22

EFFECTS OF POSTPARTUM UTERINE DISEASES ON MILK YIELD, MILK COMPONENTS, AND CULLING IN DAIRY COWS UNDER CERTIFIED ORGANIC MANAGEMENT. J. Piñeiro[‡], M. Maquivar[&], A. Barragan[‡], J. Velez[†], H. Bothe[†], and G. Schuenemann[‡] [‡]*Department of Veterinary Preventive Medicine, College of Veterinary Medicine, The Ohio State University, Columbus, OH, USA*
[&]*Department of Animal Sciences, Washington State University, Pullman, WA*
[†]*Aurora Organic Farms, Boulder, CO, USA*

EAR - 23

DISTRIBUTION AND DIVERSITY OF *SALMONELLA* IN SHIPMENTS OF HATCHLING POULTRY, UNITED STATES, 2013-2015. A. Sharma[1], M.M. Erdman[2], L. Muñoz-Vargas[1], R. O'Shaughnessy[1], G.G. Habing[1]. (1) The Ohio State University, (2) National Veterinary Services Laboratories, APHIS, USDA

EAR - 24

DETECTION OF *HAMMONDIA HEYDORNI* OOCYSTS IN WILD AND DOMESTIC CANID FECES. D. Sinnott, K. Moreno Torres, B. Wolfe, R. Garabed, and A. E. Marsh. Dept. of Veterinary Preventive Medicine.

EAR - 25

EVALUATION OF RISK FACTORS AND TRANSMISSION PATHWAYS OF SALMONELLA AND ESβL-PRODUCING ORGANISMS FOR DOGS ON OHIO LIVESTOCK FARMS. A. Smith, N. Moran, T. Mills, D. Mollenkopf, D. Mathys, T. Wittum, and J. Stull. Dept. of Veterinary Preventative Medicine.

EAR - 26

ASSESSMENT OF THE CANINE RABIES PROGRAM IN ETHIOPIA: A PROJECT OF RIGHT PARTNERSHIP'S PILOT PROGRAM IN NORTH GONDAR Waibel, S., O'Quin, J., and Gebreyes, W. The Department of Veterinary Preventative Medicine

IMMUNOLOGY AND INFECTIOUS DISEASES

IMID-1

SAMHD1-MEDIATED HIV-1 RESTRICTION IN CELLS DOES NOT INVOLVE RIBONUCLEASE ACTIVITY. JM Antonucci [1, 2], C St. Gelais [1], S de Silva [1], JS Yount [3], C Tang [4]

IMID - 2

REGULATION OF IMMUNOGLOBULIN CLASS SWITCH BY PHARMACOLOGICAL INHIBITORS OF INFLAMMATION AND NEUTROPHIL FUNCTIONS. Z.Attia[1,2], H.E.Steiner1, E.Kim[1], T.L.Martin1, A.Zaghawa[2], E.Cormet-Boyaka[1], P.N.Boyaka[1]. [1]Veterinary Biosciences, College of Veterinary Medicine, Ohio State University, Columbus, OH; [2]Faculty of Veterinary Medicine, University of Sadat City, Sadat City, Egypt . , X Ji [4], C Shepard [5], Y Xiong [4], B Kim [5], L Wu [1-]

IMID - 3

RANDOM MUTAGENESIS OF *EHRLICHIA* SP. HF STRAIN FOR IDENTIFICATION OF VIRULENCE GENES. H. Bekebrede, M. Lin, Y. Rikihisa. Dept. of Veterinary Biosciences

IMID - 4

POLY-LACTIC-CO-GLYCOLIC ACID (PLGA) NANOPARTICLE DELIVERY OF SWINE INFLUENZA VIRUS VACCINE PROVIDES HETEROLOGOUS PROTECTION THROUGH CELL MEDIATED IMMUNITY IN PIGS. S. Dhakal, J. Hiremath[1], K. Bondra[1], Y. SL[1], B. Shyu[1], K. Oyuang[1], B. Binjawadagi[1], K.I. Kang[1], J. Goodman[2], B. Narasimhan[2], C.W. Lee[1], R.J. Gourapura[1]; [1]Food Animal Health Research Program, Department of Veterinary Preventive Medicine, The Ohio State University, Wooster, OH, USA, [2]Department of Chemical and Biological Engineering, Iowa State University, Ames, IA, USA.

IMID - 5

THE EFFECT OF HYPOTHERMIA ON INFLUX OF MONONUCLEAR CELLS IN THE DIGITAL LAMELLAE OF HORSES WITH OLIGOFRUCTOSE-INDUCED LAMINITIS. J.D. Godman[1], T.A. Burns[1], C.S. Kelly[1], M. Watts[1], B.S. Leise[2], E.L. Schroeder[1], A.W. van Eps[3], J.K. Belknap[1] 1. The Ohio State University, Columbus OH, 2. Louisiana State University, Baton Rouge, LA, 3. The University of Queensland, Brisbane, Australia

IMID - 6

CX3CR1 IN COTTON RATS IS THE RECEPTOR FOR RESPIRATORY SYNCYTIAL VIRUS AS IT IS IN HUMANS. G Green[1], S. Johnson[2], A. Oomens[4], M. Teng[3], M. Peeples[2], S. Niewiesk[1]
[1]Department of Veterinary Biosciences, The Ohio State University, Columbus, Ohio; [2]Center for Vaccines and Immunity, The Research Institute at Nationwide Children's Hospital, Columbus, Ohio; [3]Division of Allergy and Immunology, Department of Internal Medicine, Morsani College of Medicine, University of South Florida, Tampa, Florida; [4]Department of Veterinary Pathobiology, Oklahoma State University, Stillwater, Oklahoma.

IMID - 7

EVALUATION OF THE VIRULENCE OF A PORCINE EPIDEMIC DIARRHEA VIRUS WITH A 197 AMINO ACID-DELETION IN THE SPIKE PROTEIN
Y. Hou, C.M Lin, X. Gao, Z. Lu, X. Liu, Y. Qin, L. J. Saif and Q. Wang
Food Animal Health Research Program, Ohio Agricultural Research and Development Center, College of Food, Agricultural and Environmental Sciences, Department of Veterinary Preventive Medicine, The Ohio State University, Wooster, Ohio, USA

IMID - 8

CATHEPSIN K INHIBITION RENDERS EQUINE BONE MARROW NUCLEATED PROGENITOR CELLS HYPO-RESPONSIVE TO LPS AND UNMETHYLATED CPG STIMULATION *IN VITRO.* H. Hussein[1], P. Boyaka[2], J. Dulin[1], A. Bertone[1, 2]. [1].Dept. of Veterinary Clinical Sciences. [2]. Dept. of Veterinary Biosciences. College of Veterinary Medicine, The Ohio State University, Columbus, OH, USA.

IMID - 9

ANTIMICROBIAL USE AND RESISTANCE IN ZOONOTIC BACTERIA RECOVERED FROM NONHUMAN PRIMATES. J. Kim, The Ohio State University, College of Veterinary Medicine, Department of Veterinary Preventive Medicine, College of Public Health, Columbus, Ohio, United States of America; D. J. Coble, The Ohio State University, College of Veterinary Medicine, Department of Veterinary Preventive Medicine, University of Laboratory Animal Resources, Columbus, Ohio, United States of America; G. W. Salyards, University of California, Davis, California National Primate Research Center, Davis, California, United States of America; W. Rinaldi, Alpha Genesis Incorporated, Yemassee, South Carolina, United States of America; G. Plauche, University of California, Davis, California National Primate Research Center, Davis, California, United States of America; G. H. Habing, The Ohio State University, College of Veterinary Medicine, Department of Veterinary Preventive Medicine, Columbus, Ohio, United States of America

IMID - 10

EPITHELIAL CELL IKKβ REGULATES EOSINOPHIL LEVELS IN THE INTESTINE AND SEVERITY OF ALLERGIC RESPONSES TO INGESTED ALLERGENS E. Kim, M. M. Lembert, T. L. Martin, J. C. Rowe, H. E. Steiner, E. Cormet-Boyaka, P. N. Boyaka. Depts. of Veterinary Biosciences

IMID - 11

DEVELOPING A CRYOPRESERVATION METHOD THAT PRESERVES FUNCTION OF CANINE AND FELINE PERIPHERAL BLOOD MONONUCLEAR CELLS. Y. Lin, R. Vicetti Miguel, N. Quispe Calla, K. Henschel, and T. Cherpes. Depts. of Microbial Infection and Immunity and Obstetrics and Gynecology

IMID - 12

EXPERIMENTAL MODELING OF THE NONSPECIFIC PROTECTIVE EFFECTS WITH MEASLES VIRUS VACCINATION. S. C. Linn, D. Huey, and S. Niewiesk.Department of Veterinary Biosciences, College of Veterinary Medicine, The Ohio State University

IMID - 13

3'3'-CGAMP INDUCES A BALANCED TH1 AND TH2 CYTOKINE PROFILE FOLLOWING SUBLINGUAL IMMUNIZATION. T. Martin, E. Kim, J. Jee, H.E. Steiner, and P.N. Boyaka. Dept. of Veterinary Biosciences

IMID - 14

MATERNAL ANTIBODY TRANSFER IN THE COTTON RAT PLACENTA

M. E. Martinez[1], K. M. D. La Perle[1,2], S. Niewiesk[1]

[1]Department of Veterinary Biosciences and the [2]Comparative Pathology and Mouse Phenotyping Shared Resource, The Ohio State University, Columbus, Ohio

IMID - 15

EFFECT OF NF-κB PATHWAY IN INTESTINAL EPITHELIAL CELLS DURING INGESTION OF LOW DOSES OF CADMIUM. J. Rowe, E. Kim, H. Steiner, E. Cormet-Boyaka, and P. Boyaka. Dept. Veterinary Biosciences

IMID - 16

EXAGGERATED PRO-INFLAMMATORY INNATE IMMUNE RESPONSE OF CYSTIC FIBROSIS AIRWAY EPITHELIA CELLS TO H1N1 INFLUENZA A INFECTION. S. YOUNG[1], P. Woods[1], M. Peeples[2], and I. Davis[1]. [1]The Ohio State University College of Veterinary Medicine; [2]Nationwide Children's Hospital Medical Center

IMID - 17

MIR-155 IMPACTS T CELL MIGRATION IN ACUTE GRAFT-VERSUS-HOST-DISEASE (AGVHD). N.C. Zitzer[1], P.A. Taylor[2], A. Ngankeu[1], Y.A. Efebera[1], S.M. Devine[1], B.R. Blazar[2], R. Garzon[1], P. Ranganathan[1]. [1]Comprehensive Cancer Center, The Ohio State University, Columbus, OH; [2]Blood and Marrow Transplantation, Division of Pediatrics, Department of Medicine, University of Minnesota, Minneapolis, MN

IMID – 18

INHIBITION OF LUNG TISSUE NON-SPECIFIC ALKALINE PHOSPHATASE ATTENUATES INFLUENZA-INDUCED ACUTE LUNG. P. S. Woods[1,2], L. Doolittle[1,2], and I. C. Davis[1] Department of Veterinary Biosciences[1], The Ohio State University. The Ohio State School of Medicine[2], The Ohio State University

MOLECULAR AND CELLULAR BIOLOGY

MCB - 1

IDENTIFYING THE ROLE OF NOVEL TAX-1 INTERACTING PROTEIN SNX27 IN HTLV-1 INFECTION. Jacob Al-Saleem[1,2,3], Nikoloz Shkriabai[1,4], Mamuka Kvaratskhelia[1,4], Lee Ratner[6], and Patrick L. Green[1,2,3,4]
[1]Center for Retrovirus Research, The Ohio State University, Columbus, OH, USA; [2]Department of Veterinary Biosciences, The Ohio State University, Columbus, OH, USA; [3]College of Veterinary Medicine, The Ohio State University, Columbus, OH, USA; [4]Department of Pharmaceutics and Pharmaceutical Chemistry, The Ohio State University, Columbus, OH, USA; [5]Department of Molecular Virology, Immunology, and Medical Genetics, The Ohio State University, Columbus, OH, USA; [6]Division of Oncology, Washington University, St Louis, MO, USA

MCB - 2

SALMON POISONING DISEASE: CANINE IMMUNE RECOGNITION OF *NEORICKETTSIA HELMINTHOECA.* K. Bachman, M. Lin, Y. Rikihisa. Department of Veterinary Biosciences, College of Veterinary Medicine, The Ohio State University

MCB - 3

IMPROVING EFFICIENCY IN SAUGEYE PRODUCTION USING CRYOPRESERVED MILT. B.Blawut[1], M. Krcmarik[1], B. Wolfe[3], M.C. da Silva[2], R. D. Zweifel[4], D. Sweet[4], & S.Hale[4]
1 Ohio State University, College of Veterinary Medicine, Department of Veterinary Preventive Medicine, 1920 Coffee Rd. Columbus, OH 43210
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3 Morris Animal Foundation, 720 S. Colorado Blvd., Suite 174A Denver, CO 80246
4 Ohio Division of Natural Resources, 2045 Morse Rd Service Road, Columbus, OH 43229

MCB - 4

THE EFFECT OF TRYPAN BLUE ON POSTERIOR CAPSULE OPACIFICATION IN AN EX VIVO CANINE MODEL BM Brash, DA Wilkie, AJ Gemensky-Metzler, HL Chandler, Department of Veterinary Clinical Sciences, The Ohio State University

MCB - 5

ANTITUMOR ACTIVITY OF SELECTED CHEMOTHERAPY AGENTS ON A FELINE BRONCHIOLOALVEOLAR LUNG CARCINOMA CELL LINE. D. L. Burroughs, S. Roy, and G. Lorch. Department of Veterinary Clinical Sciences.

MCB - 6

CANINE MODEL OF PROSTATE CANCER AND THE ROLE OF THE GASTRIN-RELEASING PEPTIDE RECEPTOR (GRPR). R. Y. Camiener, S. M. Elshafae, W. P. Dirksen, and T. J. Rosol, Department of Veterinary Biosciences, College of Veterinary Medicine, The Ohio State University, Columbus, OH, USA.

MCB - 7

TOPOGRAPHY INFLUENCES GLIAL AND NEURONAL MIGRATION UNDER INFLUENCE OF LAMININ IN VITRO. J Cronin[1,2]; C Czeisler, PhD[1,3]; A Short, PhD[1,4]; J Winter, PhD[1,4]; JJ Otero, MD, PhD[1,3]
[1]The Ohio State University, [2]College of Veterinary Medicine, [3]College of Medicine, [4]College of Engineering

MCB - 8

ANALYSIS OF FAS-MEDIATED APOPTOSIS IN CANINE CERVICAL SPONDYLOMYELOPATHY. E. Curtis, R.C. da Costa. Department of Veterinary Clinical Sciences

MCB - 9

THE EFFECT OF HYPOTHERMIA ON INFLAMMATORY AND GROWTH FACTOR SIGNALING PATHWAYS IN ACUTE LAMINITIS. K. Dern, M. Watts, A. van Eps, J. Belknap. Dept of Veterinary Clinical Sciences

MCB - 10

TRACKING TRANSCRIPTOME MODIFICATIONS RESPONSIVE TO THE ESTROUS CYCLE IN THE MOUSE UTERUS. A Diedrich, C Koivisto, G Leone. College of Veterinary Medicine (Diedrich, Koivisto), School of Biological Sciences-Molecular Virology, Immunology and Molecular Genetics, College of Medicine (Leone) The Ohio State University

MCB - 11

THE EFFECT OF HDACI (AR-42) ON CANINE PROSTATE CANCER METASTASIS. S. Elshafae[1], N. Kohart[1], L. Altstadt[1], W. Dirksen[1] and T. Rosol[1]. Department of Veterinary Biosciences[1], The Ohio State University, Columbus, OH, USA.

MCB - 12

INSULIN-RELATED GROWTH FACTOR SIGNALING EVENTS IN THE EQUINE LAMINAE USING A MODEL OF EQUINE METABOLIC SYNDROME. O. Hegedus, M. Watts, P. Weber, K. Woltman, J. Belknap. Dept. of Veterinary Clinical Sciences, College of Veterinary Medicine, Ohio State University, Columbus, OH (Hegedus, Watts, Balknap). Dept. of Large Animal Clinical Sciences, College of Veterinary Medicine, Michigan State University, East Lansing, MI (Weber and Woltman).

MCB - 13

DOWNREGULATION OF SAMHD1 EXPRESSION CORRELATES WITH INCREASED MICRORNA-181 LEVELS IN SÉZARY SYNDROME PATIENT CD4+ T-CELLS. R. Kohnken[1], K.M. Kodigepalli[1], A. Mishra[2,3], P. Porcu[2,3,4] and L. Wu[1,2,5]
[1]Center of Retrovirus Research, Department of Veterinary Biosciences; [2]Comprehensive Cancer Center; [3]Division of Hematology; [4]Department of Internal Medicine; [5]Department of Microbial Infection and Immunity, The Ohio State University, Columbus, OH, 43210, USA

MCB - 14

INDUCIBLE CRE-MEDIATED ABLATION OF E2F7 AND E2F8 IN THE MOUSE SMALL INTESTINE. M. Maglaty[1], M. Cuitino[2], J. Rakijas[2], and G. Leone[2]. [1]College of Veterinary Medicine; [2]Department of Molecular Virology, Immunology, and Medical Genetics, College of Medicine, The Ohio State University.

MCB – 15
PLATFORM PRESENTATION

PRMT5 IS UPREGULATED IN HTLV-1-MEDIATED T-CELL TRANSFORMATION AND SELECTIVE INHIBITION ALTERS VIRAL GENE EXPRESSION AND INFECTED CELL SURVIVAL. A. Panfil, J. Al-Saleem, C. Howard, J. Mates, J. Kwiek, R. Baiocchi, and P. Green. Depts. of Veterinary Biosciences

MCB - 16

CHARACTERIZATION OF LIVING SYNOVIAL EXTRACELLULAR MATRIX SCAFFOLDS FOR GENE DELIVERY. N. Reisbig, H. Hussein, E. Pinnell, A. Bertone. Department of Veterinary Clinical Sciences. College of Veterinary Medicine, The Ohio State University, Columbus, OH, USA.

MCB - 17

MICRORNA AS A HOST DETERMINANT OF SEVERITY IN INFLUENZA A VIRUS INFECTION. L.D. Schermerhorn*, P. Woods*, S.P. Nana-Sinkam[&]. I.C. Davis*
*Department of Veterinary Biosciences, The Ohio State College of Veterinary Medicine
[&]Division of Pulmonary, Allergy, Critical Care, and Sleep Medicine, The Ohio State University College of Medicine

MCB - 18

WNT SIGNALING IN PROSTATE CANCER GROWTH AND BONE METASTASIS.
W. Supsavhad, W. Dirksen, S. Elshafae, B. Hassan, N. Kohart, L. Altstadt and T. Rosol. Department of Veterinary Biosciences, College of Veterinary Medicine, Ohio State University

MCB - 19

ROLE OF STAT3 IN PROSTATE INVOLUTION AND CANCER CELL DEATH
KA Zabrecky[1], BW Simons[2], and EM Schaffer[2]
[1]The Ohio State University CVM, Columbus, OH; [2]The Brady Urological Institute, Johns Hopkins University, Baltimore, MD

STRUCTURE/FUNCTION

SF - 1

INTRAVENOUS ADMINISTRATION OF COBALT CHLORIDE IS ASSOCIATED WITH HEMODYNAMIC ALTERATIONS IN HORSES. Burns TA, Dembek K, Kamr A, Dooley B, Dunbar LK, Brewington S, Aarnes TK, Bednarski KS, O'Brien C, Lakritz J, Toribio RE.

CLINICAL RESEARCH

CR - 1

MORPHOMETRIC DIFFERENCES OF COMPUTED TOMOGRAPHIC IMAGES BETWEEN THE CERVICAL VERTEBRAL FORAMEN OF GREAT DANES WITH AND WITHOUT SUBCLINICAL NEUROLOGIC DEFICITS. J. Arbogast, R. C. Da Costa DVM, MS, ACVIM. The Ohio State University, College of Veterinary Medicine, Columbus OH

Cervical spondylomyelopathy (CSM), also known as Wobbler's syndrome, is the most common disease of the cervical spine in giant breed dogs. Great Danes suffer from the osseous form of CSM, which results in severe, absolute vertebral canal stenosis secondary to proliferation of the vertebral arch, articular facets, and/or vertebral pedicles. A previous study conducted by Dr. da Costa revealed that more than 50% (17/32) of clinically normal Great Danes displayed neurological deficits upon further evaluation. Our aim is to compare the vertebral foramen of these subclinical dogs to those that are CSM-affected and those that are normal in order to find the cause of these subclinical neurologic deficits. 10 adult Great Danes were enrolled in this study; each participant was clinically normal in its everyday life, but displayed neurologic deficits during a complete neurologic exam. The morphometry of the cervical vertebrae (C2-C7) of each participant was studied using transverse computed tomographic (CT) images and compared to the morphometry of 10 CSM-affected Great Danes and 10 normal Great Danes all of similar age and gender. Subjectively, there didn't appear to be a drastic difference in the vertebrae of the normal and subclinical dogs. However, morphometric analysis revealed that the area of the caudal vertebrae (C5-C7) was a bit smaller in the subclinical dogs in comparison to the normal. Our results indicate that although there does appear to be a minute difference between the vertebrae of normal and subclinical Great Danes, further statistics are needed to determine if they are relevant.

Keywords: Cervical Spodylomyelopathy, wobblers syndrome, Great Danes, Computed Tomography, morphometry, cervical spine

CR - 2

ASSESSMENT OF BIOMARKERS OF PAIN AND ACTIVITY PATTERNS IN LACTATING DAIRY COWS DIAGNOSED WITH CLINICAL METRITIS. A.A. Barragan[1], J.J. Piñeiro[1], G. M. Schuenemann[1], P.J. Rajala-Schultz[1], D.E. Sanders[2], S. Bas[1].

[1]Department of Veterinary Preventive Medicine, College of Veterinary Medicine, The Ohio State University, Columbus, OH 43210, [2]Vaca Resources, Urbana, OH 43078

Post-partum uterine diseases such as clinical metritis (MET) are associated with substantial economic losses due to reduced milk yield, delayed time to conception, treatment costs, and increased culling and death rates. Furthermore, MET has been characterized by bovine veterinarians as a painful event and can be regarded as a welfare concern since it can be associated with systemic signs, such as fever, depression, loss of appetite, and visceral pain. The objectives of this study were to: 1) assess circulating concentrations of substance P, and 2) daily activity patterns (i.e. lying and standing time) in lactating dairy cows diagnosed with MET. Lactating dairy cows (n=200) from two commercial dairy herds were enrolled in the present study. Cows diagnosed with MET (n=100) at 7 ± 3 days in milk (DIM) were matched according to parity and DIM to cows without MET (noMET; n=100). On study d 1, MET was diagnosed (using a metricheck device) by the presence of watery, reddish or brownish foul smelling vaginal discharge; blood samples were collected for assessment of circulating concentration of substance P. in addition, on study d 1 activity monitors were placed on the hind leg of cows (MET; n = 56; CON; n = 56) and were kept until study d 7. Cows showing any other signs of disease were not included in the study. Cows with MET had higher ($P<0.05$) plasma concentration of substance P when compared to noMET cows (MET = 72.44 pg/ml; noMET = 55.73 pg/ml). Furthermore, cows with MET tended ($P = 0.06$) to spend more time lying (635.60 vs. 603.02 min/day) and less time standing (804.08 vs. 837.25 min/day) than noMET cows. These findings provide evidence that biomarkers of pain are increased and activity is affected in cows with MET.

Keywords: Dairy Cattle, Metritis, Substance P, Activity

CR - 3

CLINICAL CHARACTERISTICS OF PRESUMPTIVE OR CONFIRMED FIBROCARTILAGINOUS EMBOLIC MYELOPATHY (FCE): A SYSTEMATIC REVIEW OF 393 CASES FROM 1973 TO 2013. K. Bartholomew, S. Moore, K. Stover, and N. Olby. Dept. of Veterinary Clinical Sciences, College of Veterinary Medicine, The Ohio State University (Bartholomew and Moore); and the Dept of Clinical Sciences, College of Veterinary Medicine, North Carolina State University (Stover and Olby).

Objective – To summarize data from a large cohort of dogs with a clinical diagnosis of fibrocartilaginous embolic myelopathy (FCE) to provide a clear understanding of the natural history of this common cause of spinal cord injury in dogs.
Design – Meta-analysis
Animals – 322 previously reported cases from the literature and 71 previously unreported cases identified by retrospective medical record review at two veterinary teaching hospitals.
Procedures – Source publications were identified through a PubMed central search as well as references from a recent review article and resources from any publication obtained thereby. Previously unreported cases were identified via computerized medical records search at The Ohio State University and North Carolina State University.
Results and conclusions– A diagnosis of FCE was most common in middle aged large breed dogs (30%), although a significant number of small breed dogs (24%) were also reported. The most common neuro-anatomic localization was a T3-L3 myelopathy (33.1%), although other presentations including multifocal signs were observed. CSF findings were normal in most cases, but some dogs had profound increases in total nucleated cell count and protein concentration. Prognosis for recovery of ambulation was good to excellent with 85% of cases regaining the ability to walk unassisted within 3 weeks. Persistent neurologic deficits were common in patients that recovered ambulation (49.1%). When nociception was absent in the affected limbs at initial presentation rate of recovery was lower (10%); however, this data may be confounded by limited follow up in more severe cases. Future prospective studies should prospectively evaluate prognosis for more severely affected patients.

Keywords: FCE, FCEM, fibrocartilaginous embolism, fibrocartilaginous embolic myelopathy, canine

CR - 4

COMPARISON OF ALBUMIN, COLLOID OSMOTIC PRESSURE, VON WILLEBRAND FACTOR, AND COAGULATION FACTORS IN CANINE CRYOPOOR PLASMA, CRYOPRECIPITATE, AND FRESH FROZEN PLASMA. C. Culler[1], M. Iazbik M[1], J Guillaumin[2] [1]The Ohio State University Veterinary Medical Center. [2] Department of Veterinary Clinical Sciences, Ohio State University

Objective— To compare albumin and coagulation factors levels and colloid osmotic pressure (COP) of cryoprecipitate (CRYO) and cryopoor plasma (CPP), to that of source fresh frozen plasma (FFP).

Design—Prospective in-vitro study.

Setting— University teaching hospital.

Animals—Ten healthy, non-Greyhound dogs enrolled in an academic teaching hospital blood donor program.

Interventions—Fresh blood was obtained from canine blood donors and was separated into FFP and packed red blood cells. The source FFP was further separated into CRYO and CPP. Albumin, COP, fibrinogen, coagulation factors II, V, VII, VIII, IX, X, and von Willebrand factor (vWf) were assessed for each FFP, CRYO, and CPP. Measured variables were compared between the three products.

Measurements and Main Results— The mean albumin and COP in CPP were significantly higher than in FFP, with 31.7±6 g/L in CPP compared to 28.9±0.5 g/L in FFP ($p<0.001$) and 14.5±0.65 mmHg in CPP compared 12.73±0.31 mmHg in FFP ($p = 0.03$), respectively. CRYO had significantly higher levels of fibrinogen (median 3.8 g/L, 95% CI 2.79-4.91 g/L), factor VIII (mean 427.0±95.4%), and vWf (mean 504.7±41.39%) as compared to the other products (all p values <0.05). The levels of vitamin K dependent factors II, VII, and X were similar in CPP compared to FFP, although factor IX was lower in CPP ($p = 0.036$). There was no significant difference in factor II or VII levels between the three products.

Conclusions— The mean albumin and COP were highest in CPP, suggesting that CPP may be an alternative for oncotic support and albumin replacement. CRYO could be used to treat vWf, factor VIII, and factor IX deficiencies. As factors II, VII and X in CPP were similar to FFP, CPP may be an option for replacement of most vitamin K dependent factors.

Keywords: Plasma, transfusion, coagulation factors, oncotic pressure

CR - 5

ANDROGEN AND PREGNANE RESPONSE TO STRESS IN CRITICALLY ILL FOALS. K. Dembek[1], K. Timko[1], L. Johnson[1], B. David[2], B. Barr[3], K. Hart[4], and R. Toribio[1], [1]Department of Veterinary Clinical Sciences, The Ohio State University, [2]Hagyard Equine Medical Institute, [3]Rood and Riddle Equine Hospital, [4]College of Veterinary Medicine, University of Georgia

Neonatal infection (sepsis) remains the main cause of death in foals. The hypothalamic-pituitary-adrenal axis regulates the response to sepsis-associated stress. We have shown that relative adrenal insufficiency (RAI), characterized by an impaired cortisol response to stress, is associated with mortality and severity of disease in foals. Most studies in foals have been focused on cortisol, while other adrenocortical steroids (pregnane, androgen) have not been investigated.

We hypothesized that RAI in critically ill foals will involve multiple adrenocortical layers, resulting in decreased glucocorticoid, mineralocorticoid, androgen and pregnane concentrations, which will be associated with severity of disease and non-survivor. We also proposed that septic foals with RAI will have higher ACTH/steroid ratios than healthy foals.

Foals were classified into 3 categories based on severity of disease (septic, sick non-septic [SNS] and healthy) and likelihood of survival (Group-1: 3-18%; Group-2: 38-62%; Group-3: 82-97%). Blood concentrations of adrenocorticotropin (ACTH) and steroid were determined by immunoassays. RAI was defined based on the ACTH/cortisol ratio in healthy foals.

Septic foals had higher ACTH, cortisol, 17α-OH-progesterone, progesterone, pregnenolone, and androstenedione concentrations as well as ACTH/cortisol, ACTH/progesterone and ACTH/aldosterone ratios compared to SNS and healthy foals ($P<0.01$). The prevalence of RAI was 30% in septic and 18% in SNS foals. Foals with dehydroepiandrosterone (DHEAS) of 0.4-5.4 ng/mL were 2.5 times more likely to have RAI than those with DHEAS of 5.5-30.5 ng/mL. Foals in Group 1 had higher ACTH, aldosterone, progesterone, and cortisol concentrations as well as ACTH/cortisol, and ACTH/progesterone ratios than foals in Groups 2 and 3 ($P<0.01$). The progesterone cutoff value below which survival could be predicted was 23.5 ng/mL with 75% sensitivity and 72% specificity.

Our study demonstrated that adrenocortical response to critical illness involves multiple adrenal steroids in addition to cortisol. DHEAS and progesterone were good predictors of RAI and mortality in hospitalized foals.

Keywords: sepsis, equine neonates, endocrinology, adrenal insufficiency

CR - 6

IMPACT OF HEAT TREATMENT ON PREVALENCE OF DIROFILARIA IMMITIS ANTIGEN DETECTION IN FRANKLIN COUNTY SHELTER DOGS. M. Elser, A.E. Marsh, B. DiGangi, C. Dworkin, J. Stull, and J. O'Quin. Dept. of Veterinary Preventative Medicine and the University of Florida, College of Veterinary Medicine.

Diagnosis and management of canine heartworm disease is a significant concern for animal shelters across the United States. As many as 7% of samples from shelter dogs may falsely test negative for the detection of *Dirofilaria immitis* antigen. This effect, thought to be the result of antigen blocking due to immune complex formation, can be minimized with heat treatment of serum samples prior to antigen detection. This study determined the prevalence of antigen blocking in dogs entering the Franklin County Animal Shelter, summer and autumn of 2015. We included secondarily, risk factors for positive antigen test results in the analysis. Physical examination of the dogs, blood sampling, and any history about the dog was recorded. The blood samples collected from dogs >6 months of age were tested on site for *Dirofilaria immitis* antigen using a commercially-available microwell ELISA both before and after heat treatment. Whole blood was also evaluated for the presence of microfilariae using modified Knott's testing. Our results include the prevalence of false negative antigen test and the detection of the microfilaria, *Acanthocheilonema reconditum*, in several samples. Historical factors, clinical factors, and the degree of microfilaremia are included in the analysis. Of the 162 shelter dogs that were included in the study, six dogs were found to be heartworm antigen positive (3.70%). Four of those six antigen positive dogs tested positive only after heat treatment, making the prevalence of antigen blocking 2.47% in the sample population. This suggests that antigen blockers could represent a significant portion of the heartworm positive dogs in our community, and heat treating samples could be a valuable method of detecting them.

Keywords: Heartworm, Shelter Medicine, *Dirofilaria immitis*

CR - 7

USE OF FOOD TO FACILITATE HANDLING OF DOGS DURING VETERINARY VISITS: EFFECTS ON GASTROINTESTINAL FUNCTION AND CLIENT PERCEPTIONS OF THE VISIT. M. Forman, T. Shreyer, T. Buffington, S. Barrett
The Ohio State University, Department of Veterinary Clinical Sciences

Veterinary visits induce variable combinations of fear and anxiety in many pets. Provision of palatable food (Counterconditioning- CC), which changes animals' perceptions of stimuli from negative (fear) to positive (pleasure), is one low stress patient handling strategy used to reduce negative perceptions and make veterinary visits a more positive experience for both patients and clients. Neither the incidence of gastrointestinal (GI) distress after typical veterinary visits, nor those where food is utilized as a low stress handling tool, have ever been quantified to our knowledge. To investigate these effects, the incidence of GI distress in patients after visiting our Community Practice Service (CP), where food is commonly used to facilitate patient handling was documented. Client perceptions about the value of using food for low stress handling, with their pet was also assessed. Food types utilized, and amounts offered and consumed during appointments were recorded. Historical behavioral and GI health were also recorded to determine if these variables affected the incidence of GI distress following appointments. Clients were first contacted the day after the appointment to determine their pet's response(s). In addition, an anonymous survey was sent to all clients to ask their opinion about the use of food as a low stress handling technique. Quantifying the possible GI effects of providing high value foods as CC during veterinary visits, and a better understanding of client perceptions about their use, will help veterinary professionals gain insight into the value of this approach to increasing patient comfort and client satisfaction.

Keywords: low stress handling, behavior, veterinary visit

CR - 8

FIBROBLAST GROWTH FACTOR-23 IN CANINE CHRONIC KIDNEY DISEASE. L. Harjes, V. Parker, K. Dembek, L. Giovanni, M. Kogika, D. Chew, and R.E. Toribio. Department of Veterinary Clinical Sciences, The Ohio State University

Fibroblast growth factor-23 (FGF-23) is recently discovered phosphaturic hormone (phosphatonin). In humans and cats with chronic kidney disease (CKD), FGF-23 concentrations are associated with disease progression and development of renal secondary hyperparathyroidism (RHPT). An increase in FGF-23 is one of the earliest biomarkers of CKD, often preceding hyperphosphatemia and RHPT. It is an independent risk factor for both progression of CKD in humans and cats. The objectives of this study were to measure plasma FGF-23 concentrations in healthy dogs and dogs with CKD and to determine its association severity of CKD as well as phosphorus and parathyroid hormone (PTH) concentrations.

Thirty-four dogs with CKD and 10 healthy dogs were included. Dogs with CKD were staged according to International Renal Interest Society (IRIS) guidelines. A human-specific FGF-23 ELISA was validated for canine samples, showing linearity and intra- and interassay coefficients of variation <7%. Values are presented as median (range). Plasma FGF-23 concentrations in healthy dogs and dogs with IRIS stages 3 and 4 CKD were 315 pg/mL (211-449), 2,302 (455-24,409) and 7,733 (2,520-41,265), respectively (P<0.01).

Plasma FGF-23 concentrations were positively correlated with creatinine (r=0.86, P<0.01), phosphorus (r=0.69, P<0.01), and PTH (r=0.72, P<0.01) concentrations. Nineteen (56%) CKD dogs had an FGF-23 concentration above the upper range of normal dogs. Based on healthy dog phosphorus concentrations, 11 (32%) CKD dogs had elevated phosphorus concentrations. Only eight (24%) CKD dogs had hyperparathyroidism.

Plasma FGF-23 concentrations were measurable in normal dogs and in dogs with various stages of CKD. Plasma FGF-23 concentrations increase in proportion to severity of CKD, as has been reported in other species. This study showed that plasma FGF-23 has clinical value in assessing early canine CKD, has prognostic value, and provides better insight on the pathophysiology of CKD and RHPT in dogs.

Keywords: fibroblast growth-factor 23, FGF-23, chronic kidney disease

CR - 9

LACTOFERRIN REDUCES MORTALITY IN PRE-WEANED CALVES WITH DIARRHEA. K. Harris and G. Habing. Department of Veterinary Preventive Medicine

According to NAHMS, calf diarrhea is the most common illness in young calves, and nearly 8% die as a result. Alternatives to antimicrobials are frequently used to treat calf diarrhea on organic operations, but there is little data confirming their effectiveness. The availability of effective antibiotic alternatives could help improve antimicrobial stewardship and reduce usage in cases of diarrhea. Lactoferrin and garlic extract have antimicrobial properties and have shown positive impacts on growth in preweaned calves. We hypothesized that lactoferrin and garlic extract would decrease mortality, improve weight gain, and decrease disease duration in pre-weaned calves with diarrhea. In total, 633 calves with diarrhea were enrolled in a blinded, randomized field trial. Upon diagnosis of diarrhea (fecal score>3), calves were randomized to 3 consecutive days of oral treatments with garlic extract, lactoferrin, or water (control). Calves were clinically evaluated for up to 10 days following enrollment, and body weight was measured at enrollment and 10 days later. Mortality, culling, and farm treatments were recorded. Lactoferrin significantly ($p < 0.05$) reduced the risk of death and culling in the preweaning period. In total, 7.5% (15/198) of calves in the control group died compared to 3% (8/201) of calves treated with lactoferrin. Lactoferrin was similarly effective in reducing mortality in older calves (11-21days of age), with severe diarrhea (fecal score= 4), without hyperthermia (temperature<103.0) and absence of depression (depression score=1) ($p < 0.05$). Neither garlic nor lactoferrin had a significant effect on disease duration or average weight gain during the 10 day period ($p >0.1$). These results suggest that treatment with lactoferrin is effective as an alternative to antimicrobials to reduce mortality in calves between 11 and 21 days of age with watery diarrhea in the absence of systemic signs of dehydration or depression. If confirmed with additional research, lactoferrin has the potential to reduce antimicrobial use and improve calf health.

Keywords: calf diarrhea, lactoferrin

CR - 10

COMPUTATIONAL FLUID DYNAMICS USING COMPUTED TOMOGRAPHY TO ASSESS AIRWAY RESISTANCE IN ENGLISH BULLDOGS. E.T. Hostnik[1], B.A. Scansen[1], R.E. Zielinski[2], and S.N. Ghadiali[2]. [1]Department of Veterinary Clinical Sciences and [2]Department of Biomedical Engineering, The Ohio State University, Columbus, OH 43210.

Introduction/Purpose

Obstructive airway disease is common in brachycephalic dogs. Stenotic nares, edematous intranasal turbinates, mucosal swelling, and an elongated, thickened soft palate are sources of airflow resistance. Surgery has traditionally focused on resection of excessive nares and soft palate, without objective measures to validate efficacy.

Methods

Twenty-three non-operated brachycephalic dogs were recruited for this pilot study. A 128 multi-detector computed tomography (MD-CT) scan was performed in all dogs, from rostral nares to diaphragm (SOMATOM Definition Flash; Siemens Healthcare). MD-CT examinations were performed using conscious sedation and without endotracheal intubation.

Raw MD-CT data were imported into ScanIP software (Simpleware, Version 7.0) to render a three-dimensional surface mesh model by automatic segmentation using -1024 to -450 Hounsfield units to isolate the air-filled nasal passage from the nares to the caudal soft palate. Three-dimensional surface models were then imported into COMSOL Multiphysics 5.0 with MATLAB (COMSOL, Inc., Version 5.0.1.276) for computational fluid dynamic modeling and calculation of airway resistance.

Results

The nasal passages were modeled and airway resistance calculated in all dogs. Airway resistance varied widely; mean and SD of 9,859.19 +/- 12,818.53 Pa/L/s. Airway resistance did not correlate with age ($r = 0.344$, $P = 0.126$) or weight ($r = -0.058$, $P = 0.803$). In 19/21 dogs, the rostral third of the nasal passage showed the greatest step-up of airflow resistance.

Discussion/Conclusion

Computational fluid dynamics derived from nasal MD-CT can quantify airway resistance in dogs. This methodology may have utility for objectively studying surgical interventions in canine brachycephalic airway syndrome.

Keywords Computational fluid dynamics, Computed tomography, Brachycephalic airway syndrome, English Bulldog

CR - 11

THE FGF-23/KLOTHO AXIS AND ITS ASSOCIATION WITH PHOSPHORUS, CALCIUM, VITAMIN D, PARATHYROID HORMONE, DISEASE SEVERITY AND OUTCOME IN HOSPITALIZED FOALS. A. Kamr[1,4], K.A. Dembek[1], B.E. Hildreth III[1], S.M. Reed[2], N.M. Slovis[3], T.A. Burns[1], A. Zaghawa[4], R.E. Toribio[1]. [1] Veterinary Clinical Sciences, College of Veterinary Medicine, The Ohio State University, Columbus, OH; [2]Rood and Riddle Equine Hospital, Lexington, KY; [3]Hagyard Equine Medical Institute, Lexington, KY; [4]Faculty of Veterinary Medicine, University of Sadat City, Sadat City, Egypt

Hypocalcemia and hyperphosphatemia, low vitamin D metabolite and elevated parathyroid hormone (PTH) concentrations are frequent in critically ill foals; however, the mechanisms leading to these abnormalities remain unclear. Fibroblast growth factor-23 (FGF-23) is secreted by osteocytes in response to increased $1,25(OH)_2D_3$, PTH, and phosphorus concentrations. FGF-23 with its co-receptor klotho inhibits PTH synthesis, as well as renal 1α-hydroxylase activity and phosphorus reabsorption. However, information on FGF-23 and klotho in hospitalized foals is lacking. The goal of this study was to investigate the FGF-23/klotho axis and its relationship with phosphorus, calcium, PTH, vitamin D, disease severity and mortality in hospitalized foals. A total of 91 newborn foals ≤ 3 days old divided into hospitalized (n=81; 58 septic, 23 sick non-septic [SNS]) and healthy (n=10) groups were included. Blood samples were collected on admission. Serum FGF-23, klotho, PTH, and vitamin D metabolites were measured by immunoassays. Data were analyzed by non-parametric methods and logistic regression. Serum FGF-23 concentrations were significantly higher while klotho, $25(OH)D_3$, and $1,25(OH)_2D_3$ concentrations were lower in septic and SNS compared to healthy foals ($P < 0.05$). Septic foals had higher phosphorus and PTH, and low calcium concentrations than SNS and healthy foals ($P < 0.05$). In hospitalized and septic foals, serum FGF-23 concentrations were associated with phosphorus and PTH ($P < 0.05$). In septic foals, serum klotho concentrations were positively associated with low $1,25(OH)_2D_3$ concentrations ($r_s = 0.42$; $P = 0.01$). Hospitalized foals with the highest FGF-23 and lowest klotho concentrations were more likely to die (OR= 3.3; 95% CI = 1.1-10.3; OR=3.1; 95% CI=1.1-8.7, respectively). Elevated FGF-23 and reduced klotho concentrations in combination with high phosphorus and PTH concentrations suggest that FGF-23 resistance may be implicated in the pathogenesis of hyperphosphatemia and elevated PTH concentrations in critically ill foals.

Keywords: FGF-23; klotho; phosphorus; PTH; vitamin D; sepsis; mortality; hospitalized foals.

CR - 12

THE EFFECTS OF HYALURONAN ALONE OR IN COMBINATION WITH CHONDROITIN SULFATE AND N- ACETYL-D-GLUCOSAMINE ON LIPOPOLYSACCHARIDE-CHALLENGED EQUINE FIBROBLAST-LIKE SYNOVIAL CELLS. A. Kilborne, H. Hussein, A. Bertone. Department of Veterinary Clinical Sciences. College of Veterinary Medicine, The Ohio State University, Columbus, OH, USA.

Lipopolysaccharide (LPS) is an established model for induction of inflammatory and degradation cascades associated with arthritis. While the anti-inflammatory efficacy of hyaluronan (HA) is documented, combination therapeutics may have the potential to provide an additive or synergistic anti-inflammatory effect as well as anti-catabolic effect and warrant investigation. Our hypothesis was that HA with chondroitin and N-acetyl-glucosamine (HA-CS-NAG) would be superior to HA alone in cellular protection and anti-inflammatory profiles produced by LPS challenge. The cellular and inflammatory response of equine synovial cells to 2 hour (hr) LPS challenge (20 ng/mL or 50ng/ml) with pre (24hr) and sustained (24hr) HA or HA-CS-NAG incubation have been investigated using an *in vitro* model. The LPS treatment induced a decrease in cell viability ($P < 0.01$) and loss of characteristic fibroblast-like synovial cell culture morphology including loss of cell attachment, cell contraction and rounding, and cell death that was LPS-concentration dependent ($P<0.001$). The expression of inflammatory products; prostaglandin E_2, interleukin-6, matrix metalloproteinase-3 and cyclo-oxygenase 2, were increased in response to LPS challenge ($P<0.05$). Both HA and HA-CS-NAG protected synovial cells from the negative effects of LPS ($P<0.001$). HA-CS-NAG treatment had greater anti-inflammatory effect than HA alone ($P<0.03$). Our work demonstrated that HA and HA-CS-NAG can protect synovial cells and the use of a combination product may have additional clinical advantage.

Keywords: equine, hyaluronan, polyglycan, synovitis, lipopolysaccharide.

CR - 13

ADRENOCORTICAL STEROID RESPONSE TO A HIGH DOSE OF ACTH IN HEALTHY AND CRITICALLY ILL FOALS. J.S. Minuto, K.A. Dembek, R.E. Toribio. Department of Veterinary Clinical Sciences, College of Veterinary Medicine, The Ohio State University, Columbus, OH

Neonatal infections are the leading causes of mortality in newborn foals. In response to sepsis-related stress, the hypothalamic-pituitary-adrenal axis (HPAA) is activated, resulting in increased concentrations of adrenocorticotropin (ACTH) and cortisol adrenocortical steroids. However, preliminary studies from our group suggest that some critically ill foals have abnormally low cortisol concentrations despite elevated ACTH, indicating relative adrenal insufficiency (RAI). Cortisol and other adrenocortical steroids are essential for energy and blood pressure regulation, as well as organ differentiation and function. We hypothesized that the response of multiple adrenocortical steroids to a high ACTH dose (100 µg) will be lower in septic foals compared to healthy foals, and those with lowest steroid concentrations and poor response to ACTH (supporting RAI)_will have more severe disease and be more likely to die. Foals <4 days old were divided into: healthy, sick non-septic (SNS), and septic. Blood samples were collected at admission, then foals received 100 µg of ACTH (cosyntropin, IV). Additional blood samples were collected 30 and 90 minutes post ACTH administration. Concentrations of cortisol, aldosterone, and steroid precursors were determined via immunoassays. Changes in steroid concentration over 30 minutes were calculated.

In septic foals, cortisol, 17β-estradiol, pregnenolone, and 17α-OH-progesterone concentrations were significantly increased at all time points compared to healthy foals ($P<0.05$). Dehydroepiandrosterone (DHEA) concentrations were not significantly different between groups at any time. However, healthy, SNS, and septic foals showed 1-fold, 2-fold, and 4-fold increases in DHEA concentrations respectively 30 minutes after ACTH stimulation ($P<0.05$). Cortisol response to ACTH was lower in non-survivors compared to survivors. However, the difference was not statistically different.

RAI involves multiple adrenocortical steroids in addition to glucocorticoids. High DHEA and low cortisol responses to high dose of ACTH are good indicators of RAI and disease severity.

Key Words: Hypothalamic-Pituitary-Adrenal Axis, ACTH Stimulation Test, Relative Adrenal Insufficiency, Cortisol, DHEA, Sepsis, Equine, Neonate, Foal

CR - 14

REGIONAL DIFFERENCE IN THE SPINAL EPENDYMAL LAYER OF NORMAL DOGS A Muir, SA Moore. Department of Clinical Sciences, College of Veterinary Medicine, The Ohio State University, Columbus, Ohio

The mammalian spinal cord has restricted ability for regeneration and repair after spinal cord injury (SCI). In rodents, a subpopulation of cells in the spinal ependymal layer (SEL) exhibits neural stem cell characteristics and contributes to tissue repair and regeneration. Dogs are an important spontaneous model through which to study SCI, but little is known about the SEL in this species. Rodent studies indicate important regional differences in the SEL, but this has not been studied in the dog. Our aim was to evaluate the normal canine SEL for regional differences that may impact recovery after SCI. We examined 4-5 consecutive tissue sections of cervical, thorax and lumbar spinal cord from normal dogs (n=5) using hematoxylin and eosin (H&E), and immunohistochemistry for GFAP, S100, and ki67. We observed statistically significant regional differences in number of total cells in the SEL ($p<0.05$) with the highest number of cells located in the lumbar region (152 ± 29) and the lowest number located in the thoracic region (109 ± 24) of the spinal cord. GFAP was expressed intermittently in cells of the SEL, while S100 was expressed almost universally consistent with neural crest cell origin. We did not identify significant regional differences in GFAP or S100 expression.. Minimal Ki-67 expression was noted in all regions. These results form a basis to compare regional responses after SCI.

Keywords: Spinal cord injury, immunohistochemistry, spinal ependymal layer, neural stem cell, dog

CR - 15

EVALUATION OF KINEMATIC MAGNETIC RESONANCE IMAGING IN DOGS WITH OSSEOUS-ASSOCIATED CERVICAL SPONDYLOMYELOPATHY. M. Provencher, A. Habing, S. Moore, L. Cook, G. Phillips, and R. da Costa. Departments of Veterinary Clinical Sciences and the Center for Biostatistics

Osseous-associated cervical spondylomyelopathy (OA-CSM) is a condition characterized by static and dynamic spinal cord compressions. The dynamic component of cervical spondylotic myelopathy in humans (hCSM) is evaluated with kinematic MRI (kMRI). The purpose of this study was to evaluate kMRI in dogs with OA-CSM using a positioning device that allowed controlled flexion and extension of the cervical vertebral column. We hypothesized that kMRI would reveal new compressive lesions not identified with standard positioning.

Ten Great Danes and 2 Doberman pinschers with a cervical myelopathy were prospectively evaluated. All dogs underwent MRI in a neutral position using a 3.0-Tesla magnet. The patients were then placed on a positioning device and the cervical vertebral column was first flexed and then extended. Additional images were acquired. Morphologic and morphometric assessments were performed.

In neutral 4 patients had 1 compression, 4 patients had 2 compressions, 3 patients had 3 compressions, and 1 patient had 4 compressions. In flexion 1 patient had 0 compressions, 4 patients had 1 compression, 4 patients had 2 compressions, 2 patients had 3 compressions, and 1 patient had 4 compressions. In extension 2 patients had 1 compression, 1 patient had 2 compressions, 8 patients had 3 compressions, and 1 patient had 4 compressions. Extension was associated with mild compression at C4-C5 (p=0.02) that was not noted in neutral or flexion. There were 11/32 compressions in extension that were not present in neutral. The presence of dorsal compression with extension was significant at C4-C5 (p=0.01). In 1 patient, a synovial cyst that was not identified in neutral was noted to cause mild spinal cord compression in extension.

Our results support the use of kMRI in patients with OA-CSM to reveal new compressive sites, dorsal compressions and to enhance visualization of extradural compressive lesions, such as synovial cysts.

Keywords: OA-CSM, Wobbler, flexion, extension, dynamic

CR - 16

CLINICAL STUDY OF ECHOCARDIOGRAPHIC VARIABILITY IN ESTIMATING PULMONARY ARTERY PRESSURE AND PULMONARY VASCULAR RESISTANCE IN DOGS. J. Rhinehart, K. Schober. B. Scansen, J. Bonagura. Depts. of Veterinary Clinical Sciences

Pulmonary hypertension (PH) is an important clinical entity and is related to clinical symptoms and prognosis. We hypothesized that Doppler echocardiographic (DE) indices of PH and pulmonary vascular resistance (PVR) are influenced by a variety of independent factors leading to clinically important variability of DE estimates of PH and PVR in dogs.

Dogs with naturally acquired tricuspid regurgitation (TR) were studied prospectively. All dogs had degenerative valve disease. Target variables during 4 study periods (dogs imaged in lateral recumbency, dogs standing, after defined exercise (6-minute walk test [6-MWT]), and after sedation [0.25mg/kg butorphanol, IM]), were quantified by two different observers. Heart rate (HR), TR flow velocity (TRFV), systolic pulmonary artery pressure (sPAP), PVR, estimates of right atrial pressure, stroke volume, cardiac output (CO), and 23 other echocardiographic variables were quantified. Statistical methods included repeated-measures ANOVA and linear mixed model analysis. $P<0.05$ was considered significant.

Thirty-eight dogs of 15 small breeds with varying TRFVs (2.33-5.64 m/s) and PVR (2.3-22.0 WU) were studied. Observer and body position during echocardiography (lateral recumbency vs. standing) did not have a significant effect on the target variables. Heart rate declined after sedation (mean reduction 13±24 bpm; $P<0.05$) and increased after 6-MWT (mean increase 18±24 bpm; $P<0.05$). Sedation significantly increased mean TRFV ($P<0.001$; mean±SD; 3.43±0.95 m/s vs. 3.75±0.88 m/s) and sPAP ($P<0.001$; 57±30 mmHg vs. 64±31 mmHg) but did not significantly affect PVR ($P=0.38$). Post-sedation, TRFV increased in 78% of dogs (range of increase 0.02-1.2 m/sec; 12 dogs increased >0.5 m/sec). Six-MWT had no effect on TRFV ($P>0.05$; 3.47±1.03 m/s). Multivariate analysis found a significant association between TRFV, HR, and right ventricular shortening fraction but CO was not significantly associated with TRFV.

These data document relevant variability of DE estimates of PH with sedation being the most important cause.

Keywords: pulmonary hypertension, pulmonary vascular resistance, echocardiography, six-minute walk test, dogs

BEHAVIORAL EFFECTS OF TRAZODONE ON HOSPITALIZED DOGS.

S. Gilbert-Gregory, M.R. Rice, J. Stull, K. Proudfoot, M. Herron. Depts. of Veterinary Clinical Sciences and Preventative Medicine.

The hospital setting can be frightening and anxiety producing, even petrifying, for many dogs. The increase in stress during hospitalization can lead to decreased immune function, delayed wound healing, gastric ulcerations, and cardiovascular abnormalities in canine patients. These factors can affect the outcome of the patient, in addition to the primary reason for hospitalization. Even short-term stress can be detrimental to their health and any effort in recognizing and alleviating their stress will be beneficial. Quantification of stress in animals can be difficult, thus recognizing body language, or behavior signals, has the advantage of being a less invasive method for monitoring stress. Supplementing dogs with medication during hospitalization may help decrease the stress-related behaviors thus decrease anxiety. Trazodone has been studied to aid with post-surgical cage rest in dogs. Trazodone not only induces calmness in dogs, but also decreases anxiety as a serotonin antagonist. During the study, seventeen behaviors were observed to ascertain stress in hospitalized dogs and four (lip licking, panting, whining, and whale eye) were found to have a significant decrease in expression between first and second observation in those dogs administered trazodone. There was significant differences seen in total anxiety and also in the frenetic and freeze summation behaviors following trazodone administration. The decrease in frenetic and freeze summation behaviors in the treatment group, compared to the control group, also supports trazodone reduces signs of stress in the treated patients. It is important for clinicians and general practitioners to recognize behaviors that can convey stress/anxiety. Trazodone is a safe and effective anxiolytic for hospitalized dogs. It can be used during hospital stays to improve the welfare of these patients and this should be the goal of every practitioner, in addition to treating any medical/surgical condition.

Keywords: trazodone, behavior, stress, anxiety, frenetic, welfare, hospital, dogs

CR - 18

THE EFFECT OF INTRAVENOUS MAGNESIUM SULFATE (MgSO4) ADMINISTRATION IN THE HORSE. S. Schumacher DVM, A. Bertone DVM, PhD, and R.Toribio DVM, PhD. Departments of Veterinary Clinical Sciences. The Ohio State University, Columbus, Ohio 43210

Magnesium is a highly abused substance in equine competition when used as a calming agent. In racing and show horses, magnesium sulfate ($MgSO_4$) has become a substitute for training. Magnesium sulfate has been used for the treatment of preeclampsia in women and in stroke patients; however the use of $MgSO_4$ in equine competition horses is not for therapeutic reasons. The mechanism of action for $MgSO_4$ administration is thought to be multifactorial through peripheral vasodilation and its antagonism at N-methyl-D-aspartate receptors (NAMDR). The subsequent reduction in mean arterial pressure and a reduction in sensitivity to glutamate, an excitatory neurotransmitter, may be the cause of the behavior modifying effects claimed by horsemen. The goal of this study was to document plasma, cerebrospinal fluid (CSF), and urine changes in electrolytes (total magnesium [tMg], ionized magnesium [Mg^{2+}], total calcium [tCa], ionized calcium [Ca^{2+}], sodium [Na^{+}], and potassium [K^{+}]) following $MgSO_4$ administration. Cardiac ventricular function was evaluated by echocardiography.
A lumbosacral catheter was placed for collection of cerebrospinal fluid. Hypermagnesemia was induced by administering 50% $MgSO_4$ solution (30 grams/horse) intravenously over 5 minutes. Serum tMg and Mg^{2+} concentrations increased 2-3 fold while serum total calcium tCa and Ca^{2+} concentrations decreased by 15-20% from baseline values. Plasma Ca^{2+} to Mg^{2+} ratio [Ca^{2+}/Mg^{2+}] decreased by 65% within five minutes and remained below baseline values for the duration. Differences were seen in post administration left ventricular fractional shortening as well. This work provides novel information on the interactions between Mg^{2+} with electrolytes, and may serve to improve regulatory measures on the indiscriminate use of magnesium in competing horses.

Keywords: Magnesium, calcium, hypermagnasemia,

EPIDEMILOGY
AND
APPLIED RESEARCH

EAR - 1

EXTENDED-SPECTRUM CEPHALOSPORIN, CARBAPENEM, AND FLUOROQUINOLONE RESISTANT COLIFORM BACTERIA FROM A LARGE EQUINE TEACHING HOSPITAL AND A REFERRAL EQUINE SPECIALTY HOSPITAL. R. Adams, D. Mathys, D. Mollenkopf, A. Whittle, M. Mudge, A. Bertone, J. Daniels, T. Wittum. Depts. of Veterinary Preventive Medicine and Veterinary Clinical Sciences

Objective: The heightened use of broad-spectrum antibiotics in veterinary and human medicine provides selection pressure for dangerous antibiotic resistance genes in bacteria. Surveillance of bacterial resistance to clinically important antimicrobials is necessary to maintain the effectiveness of antimicrobials for critical medical cases. Our objective was to estimate the prevalence of clinically significant resistance genes in equine veterinary hospital environments and from feces of their hospitalized patients.

Methods: Environmental and fecal samples were collected from The Ohio State University Galbreath Equine Center (OSUGEC) and a referral equine hospital in Kentucky from May 2015 through the present. Fecal swabs were obtained from equine patients upon admission, at 48 hours, and post 48 hours. Environmental and fecal samples were enriched and inoculated onto selective media to identify extended-spectrum cephalosporin, carbapenem, and fluroquinolone resistance.

Results: Of the 80 hospitalized horses enrolled, patients were significantly more likely to harbor antimicrobial resistance after 48 hours of hospitalization, with odds ratios of 4.14 ($p<0.0001$) 2.02 ($p=0.034$), and 3.13 ($p<0.0001$) for cefoxitin, cefepime, and ciprofloxacin, respectively. Patients were significantly less likely to harbor antimicrobial resistance if they were hospitalized at OSUGEC, with odds ratios of 0.29 ($p=0.012$), 0.26 ($p=0.006$), and 0.14 ($p<0.0001$) for cefoxitin, cefepime, and ciprofloxacin. From the Kentucky hospital, 52%, 38%, and 34% of the 166 surfaces sampled over 3 visits housed isolates resistant to cefoxitin, cefepime, and ciprofloxacin respectively. Over 3 similar visits, 80%, 47%, and 38% of the 96 surfaces from OSUGEC harbored bacteria resistant to cefoxitin, cefepime, and ciprofloxacin.

Discussion: These results show that hospital environmental surfaces are contaminated with resistant bacteria and can serve as reservoirs for antibiotic resistant bacteria. Additionally, longer hospitalization lead to increased carriage of clinically important antimicrobial resistance genes. Antibiotic stewardship and preventing environmental contamination is essential to protect both animal and public health.

Keywords: antimicrobial resistance, equine, nosocomial

EAR - 2

***SALMONELLA ENTERICA* PREVALENCE IN THE OHIO STATE UNIVERSITY VETERINARY MEDICAL CENTER ENVIRONMENT**. A. Albers, D. Mollenkopf, D. Mathys, T. Wittum. Department of Veterinary Preventive Medicine

Salmonella is a harmful, often food-borne pathogen that can cause severe dehydration and diarrhea in humans and animals. In a veterinary teaching hospital, the health risk associated with direct *Salmonella* exposure threatens the safety of patients, staff and students. The objectives of this study are to measure the frequency of *Salmonella* in the OSU-VMC hospital environment, and determine if there are resident *Salmonella* strains which are maintained in the VMC. Samples were aseptically collected with an electrostatic cloth from twenty combined floor drains from the equine and food animal areas of the OSU-VMC between February 16 2015, and November 3, 2015. The samples were added to buffered peptone water, transferred to Rappaport-Vassiliadis broth, and inoculated onto XLT-4 and MacConkey agar. To determine if the bacterial growth was *Salmonella* a polyvalent antisera test was performed and the isolates were inoculated onto TSI slants. Pulsed-field gel electrophoresis was used to determine bacterial relatedness using banding patterns of recovered *Salmonella* isolates. A total of 23 *Salmonella* isolates were recovered from 360 (6.4%) environmental samples with prevalence ranging from 0 to 40% on 18 individual sampling dates. A total of 8.9% of food animal service drain samples and 3.9% of equine service drain samples were positive for *Salmonella*. The PFGE indicates that eleven unique *Salmonella* strains were recovered. A single *Salmonella* strain did not appear to persist within the OSU-VMC environment for an extended period of time. The presence of the same *Salmonella* clones recovered from both equine drains and food animal drains on the same date of sampling indicates the possibility of *Salmonella* being transferred between the two services, in addition to the rest of the hospital.

Keywords: Salmonella, environment, veterinary hospital, antibiotic resistance

EAR - 3

INFLUENCE OF A PLANT QUATERNARY BENZO[C]PHENANTHRIDINE ALKALOID-SUPPLEMENTED DIET ON THE INTESTINAL MICROBIOTA PROFILE OF FINISHING PIGS CHALLENGED WITH *SALMONELLA.* V. Artuso-Ponte, S. Moeller, P. Rajala-Schultz, P.N. Boyaka, and W. Gebreyes. Depts. of Veterinary Preventive Medicine, Animal Sciences and Veterinary Biosciences.

In this study we evaluated the effect of Quaternary-Benzo[c]phenanthridine Alkaloids (QBA) supplementation on the intestinal microbiome of *Salmonella*-challenged pigs. The influence of the transportation stress was also investigated. Fecal samples collected from a total of 47 pigs from 3 treatment groups (T1: in-feed QBA, *n* = 16; T2: in-feed and water soluble QBA, *n* = 15; CON: control non-supplemented, *n* = 16). Specimens were collected from all pigs 14 days after treatment initiation (day 27) and after transport to the slaughterhouse (day 28). Genomic DNA was extracted and used to amplify the V4 variable region of the *16S rRNA* gene. The amplicons were sequenced on a MiSeq Illumina® Sequencer. Finally, the SILVA *rRNA* gene Database Project was implemented in mothur to assign the unique sequences to phylotypes at a 0.03 dissimilarity cutoff. Using analyses of alpha diversity, we found significant differences in the microbial communities of pigs receiving QBA in the feed and the drinking water as compared to non-supplemented and in-feed QBA supplemented pigs after two weeks of treatment. This was mainly attributed to the significantly lower relative abundance of the family Succinivibrionaceae among pigs in the T2 as compared to T1 and CON groups. Additionally, the microbial community structure in these pigs tended to be different as compared to non-supplemented and in-feed QBA supplemented pigs as implied by the Analysis of Molecular Variance (AMOVA) findings. However, after the pigs were transported to the slaughterhouse differences in alpha diversity were only detected within non-supplemented pigs. No differences in species richness were found within and between treatment groups at day 27 or day 28. Our results suggest that transportation to the slaughterhouse is a stressful event for pigs that can affect intestinal microbiome and QBA supplementation may be a good strategy to maintain the gastrointestinal tract ecosystem.

Keywords: quaternary benzo[c]phenanthridine alkaloids, stress, intestinal microbiota

EAR - 4

COMPARATIVE HEALTH ANALYSIS OF ENDANGERED MASSASAUGA RATTLESNAKES ACROSS OHIO AND ILLINOIS. K. Backus, M. Freeman, B. Wolfe, G. Lipps, College of Veterinary Medicine.

Massasauga rattlesnakes are found throughout parts of the United States and are native to Ohio where they are recognized as endangered. Massasaugas will likely be listed under the federal Endangered Species Act within the next few years due to their declining numbers. Research has shown that there is very little correlation between genetics and the body condition and health of massasaugas, suggesting their environment and stressors play a larger role on their success. Blood, body weight, snout-vent length, and *Ophidiomyces ophidiicola* fungal swabs for culture were collected from 23 Massasaugas in the Northeast Ohio region. We are comparing health parameters; such as neutrophil to lymphocyte ratios, body weights and lengths, and snake fungal disease occurrence from the 23 snakes captured in Northeast Ohio to previously published data from Allender et al. (2013) on populations in Illinois. We are also looking at the snake populations' health status as compared to habitat parameters from the 11 different sites in which snakes were collected. All snakes in our population tested negative for *Ophidiomyces ophidiicola.* Analysis on blood parameters and habitat data are pending but initial comparisons show a much lower Neutrophil:Lymphocyte ratio in the snake populations in Ohio than those published for populations in Illinois, possibly suggesting a lower level of chronic stress and inflammation in the Ohio population. These parameters can serve as a baseline for comparison for Ohio populations of Massasauga rattlesnakes in the future to monitor their health and population status.

Keywords: Massasauga, rattlesnakes, endangered, wildlife, ophidiomyces ophidiicola

EAR – 5

COMPARATIVE STUDY OF COMMERCIALLY SOLD RAW PET FOOD PROCESSING.

P. H. Bellen and T. Wittum. Department of Veterinary Preventive Medicine

Commercial raw et food is the fastest growing segment in the pet food industry despite having high risk for food-borne pathogens. *Listeria monocytogenes*, was recently discovered in commercial raw pet foods (Nemser, 2014) prompting numerous product recalls as they pose health risks particularly to the immunocompromised population (Jason Ward Stull, 2015). Conversely, in 2014, sales increased by 64% ($25M to $40M) in raw freeze-dried and 32% ($52M to $69M) in frozen products.

Products are processed under one of four methodologies: raw freeze-dried, frozen, dehydrated and supplemented with high pressurized processing (HPP). The study tested 89 products to compare efficacy between the processing technologies in preventing *L. monocytogenes, Salmonella* and multi resistant strain *E.coli* contamination by directly comparing recovery rates. Each product was stored and prepared following product labels. 4 grams samples in 36mL listeria enrichment broth were incubated at 30ºC for 48 hours. Broth samples were inoculated to a modified oxford agar plate, incubated at 35ºC for another 24 hours. Any growth was inoculated in motility agar and blood plate and incubated for 24 hours at room temperature. Any positive growth for *L. monocytogenes* were confirmed using matrix-assisted laser desorption ionization (MALDI-TOF) system. Results showed 0 *L. monocytogenes, 25 E.coli (23 from raw frozen; 2 raw frozen with HPP) and 7 Salmonella (7 from raw frozen)* contaminations. The study is ongoing and more data are being collected. Probable correlation in protein type and contamination risk is also analyzed.

The goal is to produce scientifically based data about differences in processing, if any, in efficacy of eliminating pathogen contamination. This will provide guidance regarding the safety of this emerging pet food niche to guide veterinarians and other healthcare professionals in effectively educating pet advocates of the risks and how to mitigate them via right product choices and strict adherence to safe food handling.

Keywords: Raw Pet Food, L. monocytogenes, Commercial raw pet food, Food borne pathogens, Zoonotic diseases from pets, Pet food

EAR - 6

CHARACTERIZATION OF BEHAVIORAL INDICATORS FOR EQUINE PROTOZOAL MYELOENCEPHALITIS (EPM). L. Diangelo, W. Saville, S. Reed, and K. Proudfoot. The Ohio State University Department of Veterinary Preventive Medicine, Columbus, OH (Diangelo, Saville, Proudfoot)

Equine protozoal myeloencephalitis (EPM) is a debilitating disease that affects the central nervous system of horses. Measuring behavioral changes associated with EPM may aid in early diagnosis and treatment. EPM often affects primarily one side of the body, thus, we hypothesized that EPM horses show more asymmetric behavior compared to horses with another neurological disease, cervical vertebral stenosis myelopathy (CVM). Patient records from 20 confirmed EPM and 20 CVM cases were collected from an equine veterinary hospital. The records were entered into a computer by an observer blind to disease. Records included a 5-point gait assessment (0 = normal to 5 = recumbent) assessing ataxia, dysmetria, paresis, and spasticity at a walk and trot. Weakness was evaluated with a tail-pull test on each side. Twenty-six records included a complete gait assessment (13 per group) and all 40 included a tail-pull. To estimate the severity of gait deficits, a score was calculated by summing the gait assessment for all 4 limbs. A Wilcoxon Two-Sample Test was used to determine if gait severity differed between EPM and CVM. A Fisher's exact test was used to determine if there was a difference in the probability that EPM horses showed more asymmetric tail-pull weakness compared to horses with CVM. There were no differences in any gait category at a walk ($P>0.05$). However, EPM horses had higher scores of dysmetria ($P=0.03$), and tended to have higher scores for spasticity ($P=0.06$) at a trot. A majority of horses with EPM (70%) had asymmetric weakness in the tail-pull test compared to 25% of CVM horses ($P=0.01$). These findings suggest that EPM horses show more asymmetric behavior and gait deficits compared to horses with CVM, which may aid in our ability to detect and treat these horses earlier.

Keywords: Asymmetric gait, Tail pull, Lameness

EAR - 7

DISSEMINATION OF ANTIMICROBIAL RESISTANT ENTERIC BACTERIA IN A ZOO ENVIRONMENT. S. M. Feicht, D. A. Mathys, D. F. Mollenkopf, T. E. Wittum, Department of Veterinary Preventive Medicine

Both antimicrobial resistant bacteria and *Salmonella* can contaminate the environment of public animal exhibits such as zoos, which can pose a potential health hazard to both the visitors and the animal population. The objective of this study is to determine the prevalence *Salmonella* contamination as well as extended-spectrum beta-lactam and fluoroquinolone resistant *Enterobacteriaceae* on surfaces of human and animal areas of a large metropolitan zoo. Individual electrostatic cloths were used on flat surfaces of human and animal contact areas, and then enriched in nutrient broth with 2 µg/ml cefotaxine or 16 µg/ml naladixic acid. Incubated cefotaxine broth was inoculated onto MacConkey agar with 8 µg/ml of cefoxitin, 4 µg/ml of cefepime, or 1 µg/ml of meropenem, to identify the *bla*$_{CMY,}$ *bla*$_{CTX-M,}$ and carbapenemase phenotypes. Naladixic acid broth was inoculated onto MacConkey agar with 2 µg/ml of ciprofloxacin or 16 µg/ml naladixic acid, to identify fluoroquinolone resistant phenotypes. A third cloth was enriched in buffered peptone water and Rappaport-Vassiliadis broth, and subsequently inoculated onto XLT-4 agar for the isolation of *Salmonella*. Phenotypic *bla*$_{CMY}$ isolates were found on 34.9% of surfaces, while *bla*$_{CTX-M}$ isolates were found on 12.7% of surfaces. Naladixic acid resistant isolates were found on 36.7% of surfaces, but ciprofloxacin resistant isolates were found on only 18.1% of sampled surfaces. Meropenem resistant isolates were recovered from 4.8% of surfaces sampled. Recovery of antimicrobial resistant bacteria varied between human and animal contact surfaces, with no consistent pattern observed. *Salmonella* were recovered from only 0.6% of surfaces. These results suggest that the zoo environment harbors coliform bacteria resistant to clinically important antimicrobials, and provides an opportunity for a diverse population of humans and animals to be exposed to bacteria expressing multiple antimicrobial resistant phenotypes.

Keywords: Pathogen, Antimicrobial Resistance, Zoo, Environment

EAR - 8

NON-TYPHOIDAL *SALMONELLA* IN VEAL CALVES. S. Finney, L. Munoz, H. Hutchinson, A. Ascot, A. Strait, M. Masterson, G. Habing. Dept. Of Veterinary Preventive Medicine.

Non-typhoidal *Salmonella* (NTS) is one of the most important foodborne pathogens in the U.S., causing over 1,000,000 foodborne illnesses annually. *Salmonella* found in the lymphatic tissue of animals at the slaughterhouse is believed to be a source of foodborne *Salmonella* infections. Previous studies have shown an on-farm prevalence of 3.8% to 16.7%, but have not determined associations between on-farm prevalence and prevalence in lymphatic tissue at slaughter. The purpose of this study was to use a longitudinal observational study and vertically integrated veal production system to test the hypothesis of a positive correlation between the prevalence of *Salmonella* recovered on-farm and at slaughter.

Fecal samples were collected from 9 cohorts of calves on 5 different veal farms in addition to environmental and water samples. Four cohorts of calves were followed to slaughter, where mesenteric and pre-femoral lymph nodes and fecal samples were collected from the same calves sampled on-farm. Associations between on-farm shedding and slaughter recovery of *Salmonella* were tested using Chi-square analysis.

The overall prevalence of *Salmonella* on-farm was 1.07% (4/374), but ranged from 0.0% to 4.8% amongst groups. At slaughter, fecal prevalence was found to be 3.75% (6/160), mesenteric lymph nodes showed 20.9% (33/158) and 0.68% (1/148) in pre-femoral lymph nodes. None of the calves that were shedding on-farm were shedding at slaughter. Overall, there was very little correlation between the presence of *Salmonella* in farm fecal samples, slaughter fecal samples, and mesenteric lymph nodes; however, calves with positive mesenteric lymph nodes tended to be more likely to have positive pre-femoral lymph nodes (p=0.07). Mesenteric lymph node recovery demonstrates colonization prior to harvest, but low on-farm recovery suggests either infection during lairage or infrequent shedding following infection. *Salmonella* infection in veal calves infrequently led to colonization in peripheral lymph nodes.

Keywords: *Salmonella*, prevalence, farm, slaughterhouse

EAR - 9

DEVELOPMENT OF MULTILOCUS SEQUENCE TYPING (MLST) ASSAY FOR *MYCOPLASMA IOWAE*. M Ghanem[a], and M El-Gazzar [a,*]

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Mycoplasma iowae (MI) infection is an economically and commercially important disease of turkeys. There are no sequence typing assays available for MI strain identification, the only available molecular tools for this purpose, are DNA fingerprinting assays. In addition to their low reproducibility, fingerprinting assays require isolation of the microorganism in pure culture, which is difficult in avian mycoplasma. Therefore, here, we propose a multilocus sequence typing (MLST) assay as the first sequence-typing assay for identification of MI. Based on the two available MI genomes on GenBank, 26 loci of housekeeping genes were identified and studied in a diverse sample set. Six genes were selected for the newly developed MLST assay. The final sequence analysis of six loci (total of 5019bp) (*dppC, ulaA, valS, rpoC, leuS, kdpA*) allowed the differentiation of 47 MI samples into 23 unique sequence types. Moreover, when only 4 loci were used to type the same set of samples, they resulted in 20 unique sequence types. Analysis of phylogenetic trees and clonal groups generated by MLST displayed a high degree of agreement with geographical and temporal information of the tested samples. MLST results were compared to those of RAPD (Random Amplified Polymorphic DNA), a commonly used DNA fingerprinting assay for avian mycoplasma. MLST results was more consistent than RAPD with epidemiological information. MLST is a highly reproducible molecular epidemiology assay that can be used to identify positive clinical cases directly from DNA samples. Therefore, it provides a useful tool allowing for better identification, control and eradication efforts.

Key words: MLST; *Mycoplasma iowae*; turkeys; Molecular typing

Abbreviations: MLST, multi locus sequence typing; ST, sequence type; RAPD, random amplified polymorphic DNA

EAR - 10

NON-WOVEN FABRICS FOR NASAL WIPE SAMPLING OF INFLUENZA A VIRUS IN SWINE. CT Hammons, N Bliss, JM Nolting, and AS Bowman. Department of Veterinary Preventive Medicine, College of Veterinary Medicine, The Ohio State University, Columbus, Ohio

Influenza A virus (IAV) is a pathogen with detrimental effects to human and animal health by causing disease in a variety of host species. Pigs can serve as mixing vessels for IAV reassortment and contact between swine and human populations can result in bi-directional zoonotic IAV transmission. Therefore, it is important to optimize IAV surveillance methods in swine populations to monitor the rapid, ongoing IAV evolution occurring in pigs. Cotton gauze is currently used for non-invasive nasal wipe sampling in swine and the objective of this study was to improve the method by investigating the molecular detection and viable IAV recovery from six alternative wipe materials, a variety of non-woven polyester fabrics. Three 25.08 cm^2 swatches of each fabric were inoculated with IAV (1.0×10^7 $TCID_{50}$/swatch), placed in vials containing 5 ml viral transport media, and frozen at -80^{o}C until testing was initiated. Quantitative reverse transcription polymerase chain reaction (qRT-PCR) was used to measure molecular detection of virus, and viable IAV recovered from each sample was quantified in cultured MDCK cells. Pairwise comparison between fabrics ($TCID_{50}$ and number of target copies) was performed using Mann-Whitney rank sum. While none of the fabrics yielded significantly more IAV copies using qRT-PCR, significantly more viable IAV was recovered from fabrics A, B, and C than cotton ($p=0.05$). Fabric A yielded significantly more IAV than both B and C ($p=0.05$). Many factors may play a role in fabric efficacy for virus collection, including fabric composition and absorbency. The present study demonstrates that there are alternatives to cotton gauze that can improve nasal wipe sampling methods for IAV detection in pigs.

Keywords: influenza; IAV; swine influenza; nasal wipe sampling; fabric comparison; influenza surveillance

EAR - 11

CHANGES IN THE PREVALENCE OF ANTIMICROBIAL RESISTANCE THROUGH A VERTICALLY INTEGRATED VEAL CALF PRODUCTION SYSTEM H. Hutchinson, S. Finney, A. Ascott, A. Strait L. Munoz-Vargas and S. Feicht, M. Masterson and G. Habing. Dept. of Veterinary Preventative Medicine.

Antimicrobial resistance is a public health concern for both human and veterinary medicine. In food animal production systems, medically important antimicrobials are used for both prophylactic and therapeutic purposes; therefore, food animals have the potential to serve as a reservoir for antimicrobial resistant bacteria. Previous research has shown an uneven distribution of resistance with a higher prevalence within young animals; however, limited research has addressed antimicrobial resistance within veal production systems. Vertically integrated veal production systems provide a unique opportunity to study the transmission of resistance through the food supply. The study's objective was to estimate the prevalence of antimicrobial resistant *Escherichia coli* within different stages of a vertically integrated veal production system. A total of 377 fecal samples were collected from nine different calf cohorts on six farms, where the average age was 69 days (range: 8-115). Four of these cohorts were followed to harvest for additional sample collection. At harvest, a total of 159 fecal samples, 161 pre-evisceration and 150 post-evisceration carcass swabs were collected. A single *E. coli* isolate from the samples was subjected to twelve antimicrobials using Kirby-Bauer disk diffusion assays. Zones of growth inhibition were measured for each antimicrobial and determined resistant based on CLSI standards. Isolates were obtained from 100% of fecal samples, 52% (84/161) of pre-evisceration swabs and 16% (24/150) of post-evisceration swabs. Greater than 98% (372/377) of isolates obtained from farm fecal samples were resistant to two or more antimicrobials. A decrease in resistance was seen at harvest where only 46.9% (73/159), 69.0% (58/84), and 29.2% (7/24) of isolates from fecal samples, pre-evisceration and post-evisceration carcass swabs, were resistant to two or more antimicrobials. These results provide insight to the current prevalence of resistance among the production system and the opportunity for further research to determine factors affecting the prevalence of resistance.

Key Words: *Escherichia coli*, antimicrobials, resistance, veal

EAR - 12

ENVIRONMENTAL SURVEILLANCE FOR EXTENDED SPECTRUM β-LACTAMASE GENES IN *ESCHERICHIA COLI* AT A MUNICIPAL WASTEWATER TREATMENT PLANT. CA King, DF Mollenkopf, DA Mathys, DM Stuever, JB Daniels, TE Wittum. Departments of Veterinary Preventive Medicine and Veterinary Clinical Sciences, College of Veterinary Medicine, The Ohio State University.

In response to ever increasing use of antibiotics, bacteria are evolving resistance to critical frontline antimicrobial drugs that treat invasive Gram-negative infections. The most serious threat is bacteria that are resistant to carbapenem drugs. Bacteria may gain this resistance by acquiring mobile resistance genes that confer the ability to produce enzymes that inactivate the antibiotic. Numerous genes, including the *bla*$_{KPC}$ and *bla*$_{NDM-1}$ are known to encode bacteria the ability to produce cabapenemase. While both are present in the US, *bla*$_{KPC}$ has emerged and disseminated primarily in the US, while *bla*$_{NDM-1}$ has primarily disseminated in SE Asia. Because of the frequency of international travel we hypothesized that both *bla*$_{KPC}$ and *bla*$_{NDM-1}$ could be present in Ohio waste-water treatment plants. The purpose of this study was to determine if carbapenem-resistant *E. coli* were present in Columbus wastewater, and to fully characterize those isolates and their resistance mechanisms. We collected 334 samples of untreated sewage water at the Jackson Pike Wastewater Plant between June and August of 2011 and 2012. Using selective media, we identified 158 (47.3%) samples with suspect colonies that grew in the presence of 1 mg/L of meropenem. Of these, 51 (32.9%) were classified as meropenem resistant using Kirby-Bauer disk diffusion assay and 29 isolates were also confirmed to be *E. coli* using biochemical tests and PCR. These isolates were resistant to most of the 26 drugs on our MIC panels using micro-broth dilution. Carbapenemase production was verified for 76 isolates using the Modified Hodge test. However, none of the isolates were positive on the EDTA Double Disk Diffusion test, indicating absence of metallo-β-lactamase production. Our detection of these isolates suggests the presence of a reservoir of important resistance genes for pathogens. Surveillance is an important component of education, awareness, and prevention of antimicrobial resistance in the public health sector.

Keywords: Antibiotic resistance, carbapenems, β-lactamase, *E. coli*

EAR - 13

COMPARISON OF THE MICROBIOLOGICAL QUALITY OF FRESH PRODUCE FROM SEASONAL FARMER'S MARKETS AND RETAIL GROCERY STORES IN OHIO. D. I. Korec, D. A. Mathys, D. F. Mollenkopf, T. E. Wittum. The Ohio State University, College of Veterinary Medicine, Department of Veterinary Preventive Medicine, Columbus, OH

The frequent use of antimicrobial drugs in veterinary medicine can results in the emergence and dissemination of antimicrobial resistance in a variety of animal populations. β-lactamases confer bacterial resistance to critically important antimicrobial drugs used in both human and veterinary medicine. Livestock are an important emergence reservoir for zoonotic food-borne transmission of resistant enteric bacteria including *Salmonella* spp. Our aim is to describe the role of fresh produce, which may have been fertilized with livestock feces, in the zoonotic food-borne transmission of antimicrobial resistant bacteria. Samples of leafy greens, tomatoes, and cucumbers were purchased each week from various local farmer's markets and grocery stores. These samples were placed in buffered peptone water (BPW) and inoculated onto spread plates for detection and quantification of coliform bacteria. An aliquot of the BPW was cultured for the presence of *Salmonella*. To test for the presence of β-lactamase-producing bacteria, samples were enriched in a nutrient broth 2 µg/ml cefotaxime, then inoculated onto 3 MacConkey agar containing Cefoxitin, Cefepime, or Meropenem. We sampled 93 farmer's markets and 67 grocery stores. There are 6 samples which produced isolates resistant to cefoxitin and cefotaxime antimicrobials, indicating the *bla*$_{CMY}$ phenotype. No cefepime or carbapenem resistant isolaes were recovered. The mean coliform count was 27 and 22 CFU per 100 µl BPW rinsate for farmer's markets and grocery stores, respectively. No *Salmonella* spp. were detected. Our results indicate that there is little difference in microbiological quality between farmer's market and grocery store produce measured by the presence of antimicrobial resistant enteric bacteria or coliform contamination.

Keywords: antimicrobial, resistance, lactamases, enteric, Salmonella, greens, coliform, bacteria, markets, grocery, mirobiological, veterinary

EAR - 14

DETECTION OF PORCINE HEMAGGLUTINATING ENCEPHALOMYELITIS VIRUS IN EXHIBITION SWINE WITH INFLUENZA-LIKE ILLNESS AT AGRICULTURAL FAIRS IN MICHIGAN IN 2015. J. Lorbach, S. Nelson, M. Zentkovich, J. Nolting, A. Bowman. Department of Veterinary Preventive Medicine, The Ohio State University

Swine exhibitions at agricultural fairs represent a swine-human interface and necessitate active surveillance for zoonotic agents like influenza A virus (IAV). During routine IAV surveillance activities in the summer of 2015, 6 fairs in Michigan noted acute outbreaks of influenza-like illness (ILI) in exhibition swine. Samples from pigs at these sites tested negative for typical swine respiratory pathogens including IAV. Additional diagnostics detected porcine hemagglutinating encephalomyelitis virus (PHEV) in the samples. Subsequent testing of all 14 Michigan fairs participating in IAV surveillance detected PHEV in 108 of 279 individual samples (38.7%) and at 10 of the 14 fairs (71.4%). Twenty-eight selected Ohio and Indiana fairs participating in IAV surveillance during the summer of 2015 were chosen on the basis of clinical signs and IAV-negative status to serve as controls in a case-control study of the PHEV outbreak in Michigan fairs. PHEV was detected in 23 of 560 control samples (4.1%) and at 4 of 28 control fairs (14.3%). The detection of PHEV was strongly associated with samples from Michigan fairs compared to Ohio and Indiana fairs (OR 14.7; 95% CI, 9.1 to 23.9). PHEV is a known enzootic pathogen of many swine herds, classically causing wasting, vomiting, and encephalitis among piglets. Given these findings typically associated with PHEV infection, the ILI in swine in this study is considered an uncommon presentation. The association of PHEV in exhibition swine with clinical respiratory signs not attributable to typical respiratory agents indicates the virus could play a role in respiratory disease in market age swine. Whether this reflects an under described presentation of PHEV in naïve swine populations, an atypical form of disease, or increased virulence of a particular strain of virus remains unclear. Additionally, this particular outbreak highlights an undescribed exhibition swine network in Michigan that appears segregated from Ohio and Indiana.

Keywords: Influenza A virus, orthomyxovirus, Porcine hemagglutinating encephalomyelitis virus, coronavirus, swine, agricultural fair

EAR - 15

DAIRY CALF PREFERNCE FOR ENRICHMENT ITEMS ADDED TO AN OUTDOOR HUTCH. H. Manning, E. Cosentino, J. Pempek, M. Eastridge, K. Proudfoot. Dept. of Veterinary Preventive Medicine

Housing pre-weaned dairy calves in individual pens or hutches is commonplace; however, this housing restricts social contact, and may hinder the behavioral repertoire of calves. This study aimed to determine if calves would use enrichment items if they were added to the hutch, and what type of enrichment they prefer. Ten Jersey heifer calves were housed in individual hutches. The outdoor enclosure of each hutch (1.2m x 2.7m) contained: two artificial teats (1 perpendicular, 1 a 45-degree angle), a stationary brush (L-shaped, two 46cm push brooms), a calf 'lollie' (60cm x 7.2cm PVC pipe with 9.5mm holes for the throughput of dried molasses), and a rubber chain link (30.5cm). The location of each item was alternated per hutch. Video recordings, taken twice weekly during wk 1, 3, and 5 of age from 0800 to 2000h, were used to determine calf preference and use of the enrichment items. Behavior data were not normal, so each variable was log transformed before analysis. A t-test was used to compare the frequency at which calves used each item (averaged across periods), and a repeated measures ANOVA was used to determine if enrichment use changed over time (SAS, Version 9.4). Preliminary analysis revealed no difference between usage of the two teats; thus, these variables were combined. Calves used the brush most frequently, followed by the lollie, chain, and teats (mean±SE: 16.9±1.2; 13.0±1.2; 8.9±1.2; 4.7±1.2 no./12h, respectively; $P<0.01$). Brush and lollie use increased as calves aged (brush: 10.0 to 25.8±1.3 no./12h, $P<0.05$; lollie: 7.6 to 18.5±1.3 no./12h, $P<0.05$; wk 1 to 5), but chain and teat use remained similar over time. Results indicate that calves preferred the brush to the other enrichment items. Further analysis is needed to determine the impact of enrichment on positive behaviors (e.g., play) and abnormal behaviors (e.g., non-nutritive or cross-sucking).

Keywords: brush, pre-weaning calf, environmental enrichment

EAR – 16

PLATFORM PRESENTATION

***ENTEROBACTERIACEAE* PRODUCING EXTENDED SPECTRUM β-LACTAMASES (ESBL) FROM WILD BIRDS IN OHIO.** D.A. Mathys[1], B. A. Mathys[2], D.F. Mollenkopf[1], J.B. Daniels[3], T.E. Wittum[1]. [1]Department of Veterinary Preventive Medicine, College of Veterinary Medicine, Ohio State University [2]Department of Natural Sciences, Ohio Dominican University [3]Department of Veterinary Clinical Sciences, College of Veterinary Medicine, Ohio State University

ESBLs confer bacterial resistance to critically important antimicrobials. Livestock are an important reservoir for the zoonotic food-borne transmission of resistant enteric bacteria. Our aim is to describe the potential role of migratory and resident wild birds in the epidemiology of ESBL mediated bacterial resistance on dairy farms. Using mist nets, we sampled wild migratory and resident birds either immediately adjacent to or 600 feet away from free stall barns on three Ohio dairy farms during 2014/2015 spring migration. Individual swabs were used to obtain both a cloacal and external surface swab from each bird. Additionally, wild ducks were sampled either live caught or hunter harvested from hunting preserves in 2014 and 2015. Samples were inoculated into MacConkey broth containing cefotaxime and inoculated onto MacConkey Agar with cefoxitin, cefepime, or meropenem to identify the *bla*$_{CMY,}$ *bla*$_{CTX-M,}$ and carbapenemase phenotypes, respectively. Six hundred and six birds were sampled, 14 (2.3%) of which harbored bacteria with the *bla*$_{CMY}$ gene and 26 (4.3%) harbored bacteria with the *bla*$_{CTX-M}$ gene from either their cloacal sample or from their external swab. There was no difference in the prevalence of either gene between migratory and resident birds. Prevalence of the *bla*$_{CMY}$ was higher among birds sampled immediately outside the barns compared to those sampled 600 feet away. Six hundred and twenty seven ducks were sampled, with 44 (7%) harboring *bla*$_{CMY}$ bacteria and 2 (0.3%) harboring *bla*$_{CTX-M}$ bacteria. Our results suggest that wild birds can serve as mechanical and/or biological vectors for *Enterobacteriaceae* with resistance to extended spectrum cephalosporins. Birds live in close contact with dairy cows and their feed, therefore transmission locally from farm to farm is possible. Finding a similar prevalence in migratory and non-migratory birds suggests the potential for regional and intercontinental movement of these genes via birds.

Keywords: Antibiotic resistance, wildlife, vector, livestock

EAR - 17

AMYLOIDOSIS IN CHEETAHS (*Acinonyx jubatus*)

K.M. McLean,[1] R.B. Garabed,[1] and B.A. Wolfe. [1,2] [1]Dept. of Veterinary Preventive Medicine. [2]Morris Animal Foundation

Amyloidosis is a chronic, protein misfolding disorder that causes pathology through the accumulation of misfolded amyloid A protein in visceral organs, often leading to death of the animal. The continued increase of amyloidosis in captive cheetahs (*Acinonyx jubatus*) is of grave concern for the species, yet nothing is definitively known about its mechanism of transmission. Several hypotheses have been presented suggesting varying modes of transmission, including infectious, genetic, or catalyst-dependent transmission. To compare all hypotheses, an agent-based disease model was designed, then populated with demographic and past captive transfer data collected from the 2013 cheetah studbook. Simulation outputs were then compared to historical amyloidosis infection data supplied by the cheetah species survival plan pathologist. Our analysis does not disprove any one hypothesized route of transmission, but rather suggests a multi-faceted route of transmission. Only a subset of the captive population's post mortem disease data were available for this study, and given that the results contradict previous reports, a broader population survey should be pursued.

Keywords: *Acinonyx jubatus*, amyloidosis, cheetah, metapopulation, odds ratio, agent-based disease model

EAR - 18

GENOTYPIC CHARACTERIZATION OF EXTENDED-SPECTRUM CEPHALOSPORIN RESISTANT NONTYPHOIDAL *SALMONELLA* FROM THE NAHMS FEEDLOT 2011 STUDY. D. Mollenkopf[1], D. Mathys[1], D. Dargatz[2], M. Erdman[3], J. Daniels[4], T. Wittum[1]. [1]Dept. of Veterinary Preventive Medicine, College of Veterinary Medicine, The Ohio State University, Columbus, OH. [2]USDA, APHIS, VS Centers for Epidemiology and Animal Health, Fort Collins, Colorado, [3]Diagnostic Bacteriology Laboratory, National Veterinary Services Laboratories, USDA, Ames, IA, [4]Dept. of Veterinary Clinical Science, College of Veterinary Medicine, The Ohio State University, Columbus, OH

In the US, nontyphoidal *Salmonella* are a common foodborne zoonotic gastroenteritis pathogen. Invasive *Salmonella* infections caused by extended-spectrum cephalosporin resistant (ESCR) phenotypes are more likely to result in treatment failure and adverse health outcomes, especially in severe pediatric *Salmonella* infections where the extended-spectrum β-lactams are the therapy of choice.

To examine the genetic characteristics of ESCR *Salmonella* which may enter the food chain, we characterized 44 ceftiofur–resistant *Salmonella* isolates from the National Animal Health Monitoring System (NAHMS) 2011 beef cattle feedlot health and management project.

As part of the NAHMS Feedlot study, 5,050 individual fecal samples from 68 large (1,000+ head capacity) feedlots were cultured for *Salmonella spp*. The resulting 460 positive samples yielded 571 Salmonella isolates with 111 samples (24%) having multiple serotypes. The most prevalent serotypes were S. Anatum (n=103, 18%), S. Montevideo (n=98, 17%), and S. Kentucky (n=87, 15%).

Of the 571 feedlot Salmonella isolates, 44 (8%) expressed an AmpC β-lactamase phenotype. These phenotypic *bla*$_{CMY}$ *Salmonella* isolates represented 8 serotypes, most commonly *S.* Newport (n=14, 32%), *S.* Typhimurium (n=13, 30%), and *S.* Reading (n=5, 11%), followed by S. Dublin, S. Infantis, S. Montevideo, S. Rough O:i;v:1;7, and S. Uganda.

Carriage of the *bla*$_{CMY}$ gene was confirmed for all isolates by PCR. Additionally, all 44 isolates were PCR-positive for the presence of an Inc A/C plasmid which has been previously reported to harbor *bla*$_{CMY}$ in multiple species. Other plasmids, including Inc N, FIC, and FIIA, were also detected in some isolates.

Most *Salmonella* infections are the result of zoonotic foodborne transmission from livestock reservoirs where extended-spectrum cephalosporins are commonly used. Our characterization of the NAHMS Feedlot Surveillance ESCR *Salmonella* shows that while other cephalosporin resistance mechanisms have been reported in US cattle, specific serotypes harboring *bla*$_{CMY}$ on Inc A/C plasmids may be the dominant resistance genotype.

Keywords: *Salmonella*, extended-spectrum cephalosporin resistance, beef feedlot

EAR - 19

HOST SPECIES HETEROGENEITY IN THE EPIDEMIOLOGY OF *NESOPORA CANINUM*. K. Moreno-Torres, L. W. Pomeroy, B. Wolfe, W. Saville, M. Moritz and R. Garabed. Depts. of Veterinary Preventive Medicine and Anthropology

The role of host species heterogeneity in the epidemiology of Neosporosis remains under studied, although it is clear that a number of herbivores species are susceptible to *Neospora caninum* infection. Our goal was to better understand the role of host species heterogeneity in the epidemiology of *N. caninum* circulating in a community. We determined immunological and transmission dynamics by comparing catalytic and reverse catalytic infectious disease models with age-structured and constant force of infection in three co-located ruminant populations. Also, we estimated the species-specific contribution to the persistence of this pathogen in the community by calculating the reproductive number of each population. Finally, we calculated the critical vaccination coverage to prevent an outbreak. Results show that immunity in cattle and Pere David's deer wanes over time, suggesting that boosting immunity with vaccines might be a venue to prevent infection within those populations. For white-tailed deer, immunity is lifelong, thus natural boosting of the immune system might be occurring. Cattle's reproductive number was below threshold ($R_t < 1$), meaning that transmission cannot be maintained within cattle, thus an outside source is needed to re-introduce the pathogen and highlighting the importance of controlling outside sources. Pere David's deer and white-tailed deer, both can maintain continues chains of transmission ($R_t > 1$) within their populations. Therefore, control of outside sources might not do a difference. Understanding the epidemiology of multi-host pathogens at the community level allow us to better evaluate processes and transmission dynamic heterogeneities, that could ultimately guide targeted control and with further evaluation the confirmation of reservoirs.

Keywords: catalytic model, community, ruminant, heterogeneity, reservoirs, targeted control, multi-host parasite

EAR - 20

TRANSMISSION OF *SALMONELLA* FROM FARM TO FOOD: THE IMPACT OF CLINICAL OUTBREAKS OF SALMONELLOSIS IN CALVES ON RECOVERY OF *SALMONELLA* FROM LYMPH NODES AT HARVEST. L.M. Muñoz-Vargas[1], S. Finney[1], H. Hutchinson[2] and G. Habing[1]. [1]Dept. of Veterinary Preventive Medicine, The Ohio State University, Columbus, OH, USA. [2]Dept. of Animal Sciences, The Ohio State University, Columbus, OH, USA.

Cattle are an important reservoir of Non-typhoidal *Salmonella* (NTS) which can be transmitted to humans by consumption of contaminated meat. *Salmonella* can colonize peripheral lymphatic tissues of infected animals that can later be ground with muscles and adipose tissue into ground beef. Outbreaks of salmonellosis occur frequently in cattle on dairy farms, and may result in a higher probability of foodborne transmission of pathogenic strains of NTS. The aims of this study were to 1) compare the prevalence of NTS of cohorts of veal calves with or without a documented recent outbreak of salmonellosis, and 2) assess the genetic relatedness of NTS isolated at farm and slaughter level to evaluate the farm to food transmission. We hypothesized that 1) farms having a recent salmonellosis outbreak would have higher prevalence of NTS in lymph nodes than farms with non-outbreak, and that 2) subtypes found on farm would be closely related genetically to those isolated from lymph nodes. Fecal swabs, mesenteric and pre-femoral lymph nodes of 242 calves from 6 farms (two outbreak and four non-outbreak herds) were collected at harvest. All samples were cultured for *Salmonella* isolation, and 76 isolates were characterized by pulsed-field gel electrophoresis (Xba1-PFGE). Prevalence of *Salmonella* was significantly different ($p \leq 0.05$) between outbreak and non-outbreak farms in feces, mesenteric and pre-femoral lymph nodes, with 11.25%(9/80), 1.25%(1/80), 6.25%(5/80), and 4.3%(7/162), 19.7%(32/162), and 0.6%(1/162), respectively. Indistinguishable PFGE subtypes were recovered from samples between clinically infected farms. These findings suggest that transmission of NTS strains can occur from veal farms to food through lymphatic tissues, and that a highly pathogenic strain has been propagated between some veal farms causing clinically infections. These data demonstrate that implementation of pre-harvest biosecurity measures should be highly recommended in order to decrease the prevalence of NTS in farms, and to prevent the meat contamination at harvesting.

Keywords: *Salmonella*, lymph nodes, veal, calves, PFGE

EAR - 21

FLOW CYTOMETRIC CHARACTERIZATION OF SIALIC ACID RECEPTORS ON MDCK CELLS MAINTAINED UNDER DIFFERENT MEDIA CONDITIONS AND IMPLICATIONS FOR DETECTION OF INFLUENZA A VIRUS. S. Nelson, I. Davis, A. Bowman. Departments of Veterinary Biosciences and Veterinary Preventive Medicine

Influenza A virus (IAV) initiates infections by binding to host-cell surface receptors containing sialic acid. Avian-lineage IAVs preferentially bind α-2,3-linked sialic acids while human-lineage IAVs prefer α-2,6-linked sialic acid receptors. Historically, Madin Darby Canine Kidney (MDCK) cells have been used to isolate IAVs from many species because these cells express both α-2,3-linked and α-2,6-linked receptors. Our hypothesis was that cell culture mediums would alter the relative proportions of α-2,3-linked and α-2,6-linked sialic acid receptors on MDCK cells. Cells were cultured in either serum free media (SFM) or medium containing fetal bovine serum (FBS). Cells from each treatment were stained with sialic acid residue specific dyes, which were subsequently detected using flow cytometry. Cells cultured in SFM consistently expressed both sialic acids whereas cells cultured with FBS had varying proportions that alternated passage by passage. To confirm the biological significance of these differences, 50% tissue culture infectious dose experiments were performed at two successive passage points. Serial dilutions were made of one swine origin IAV and one avian origin IAV and each dilution was inoculated into 8 wells of three 96 well tissue culture plates per media group. The swine IAV grew to similar titers in both culture mediums, while the avian IAV grew to significantly ($p=.014$ for trial 1 and $p=.003$ for trial 2) higher titers in cells maintained in SFM. The cells maintained in SFM were shown to be expressing more α-2,6-linked sialic acids while the cells maintained with FBS were expressing mostly α-2,3-linked sialic acids. The results indicate that culture media can influence the sialic acid expression of MDCK cells and this can alter the efficiency of IAV isolation.

Keywords: MDCK, cell culture, flow cytometry, influenza

EAR - 22

EFFECTS OF POSTPARTUM UTERINE DISEASES ON MILK YIELD, MILK COMPONENTS, AND CULLING IN DAIRY COWS UNDER CERTIFIED ORGANIC MANAGEMENT. J. Piñeiro[‡], M. Maquivar[&], A. Barragan[‡], J. Velez[†], H. Bothe[†], and G. Schuenemann[‡] [‡]*Department of Veterinary Preventive Medicine, College of Veterinary Medicine, The Ohio State University, Columbus, OH, USA*
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The objective was to assess the effect of postpartum uterine diseases on milk yield (kg), milk components (SCC and percent fat and protein), and culling up to 300 days in milk (DIM). Cows (n = 3,227) from 2 dairies were screened for retained placenta (RP; > 24 h after parturition), metritis (within 20 d in milk [DIM]), and purulent vaginal discharge (PVD) at 26 ± 3 DIM. Weekly, a list of cows by DIM was obtained using on-farm computer records and screened for RP (presence of fetal membranes outside the vulva), metritis (fetid brown-red watery vaginal discharge and fever), and PVD (gloved hand technique). Parity (lactations 1, 2 and ≥3) of cows was considered for milk yield, milk components, and culling. The statistical analyses were performed using SAS. Cows with metritis, RP or PVD had an additive effect on milk yield, milk components, and culling. Regardless of parity, lactating cows diagnosed with uterine diseases (all combined) had significantly reduced milk yield (by 2–3.9 kg/cow/d) for at least one of the first 4 DHIA test-days ($P < 0.05$), but was not different at later tests. For the first 2 DHIA test-days, lactating cows diagnosed with uterine disease (all combined) had significantly higher SCC (232 × 103 cells/mL) and fat content (3.7%) compared with cows without uterine diseases (164 × 103 cells/mL and 3.5%, respectively; $P < 0.05$). Milk protein content (%) was not different between cows with or without uterine diseases. Cows with uterine diseases had higher ($P < 0.05$) culling within 60 DIM and significantly lower ($P < 0.05$) pregnancy hazard up to 300 DIM compared with cows without uterine diseases, regardless of parity. Uterine diseases decreased milk yield and changed milk components early in lactation; and these diseases were a substantial risk factor within 60 DIM for culling.

Keywords: Organic, dairy cattle, uterine disease, milk yield, culling

EAR - 23

DISTRIBUTION AND DIVERSITY OF *SALMONELLA* IN SHIPMENTS OF HATCHLING POULTRY, UNITED STATES, 2013-2015. A. Sharma[1], M.M. Erdman[2], L. Muñoz-Vargas[1], R. O'Shaughnessy[1], G.G. Habing[1]. (1) The Ohio State University, (2) National Veterinary Services Laboratories, APHIS, USDA

Direct contact is an important route of transmission for non-typhoidal *Salmonella* in the United States. Every year, multiple outbreaks of salmonellosis are linked to contact with live poultry. This study describes the distribution and diversity of serotypes, genotypes, and antimicrobial resistance phenotypes of *Salmonella* recovered from shipped boxes of mail-order hatchling poultry in 2015, and makes comparison to the population of *Salmonella* in prior comparable studies conducted in 2013 and 2014. In 2015, employees of 50 feed stores from a single national chain with spring sales of hatchling poultry submitted hatchling pads, a questionnaire, and shipment tracking information from hatchling boxes to the investigators. A total of 552 hatchling pads from 298 shipment boxes were received and cultured for *Salmonella* between February and May 2015. Isolates were sent to the National Veterinary Services Laboratory (Ames, IA) for serotyping, pulsed-field gel electrophoresis and antimicrobial resistance testing. The PFGE patterns of isolates from hatchling boxes were compared with isolates from human outbreaks of non-typhoidal *Salmonella*. In 2015, the sample level and the box level prevalence of *Salmonella* was 19.9% (110/552) and 27.2% (81/298), respectively. Of the recovered isolates, 18 different serovars and 36 different PFGE patterns were identified, including 5 serovars and 10 PFGE patterns that were indistinguishable from strains linked to concurrent human outbreaks of salmonellosis associated with contact with live poultry. Fourteen of 110 isolates (12.7%) isolates were resistant to cephalosporins. Relative to comparable studies in prior years, the prevalence of *Salmonella* Enteritidis and *Salmonella* Kentucky increased from 2013 to 2015. Additionally, the proportion of isolates resistant to >2 classes of antimicrobials increased in 2014 and 2015 compared to that in 2013. The results indicate a need to strengthen *Salmonella* control measures in hatcheries and create awareness of zoonotic transmission of the pathogen among backyard poultry owners.

Keywords: salmonella, zoonotic transmission, poultry, antimicrobial resistance, outbreak, chicks

EAR - 24

DETECTION OF *HAMMONDIA HEYDORNI* OOCYSTS IN WILD AND DOMESTIC CANID FECES. D. Sinnott, K. Moreno Torres, B. Wolfe, R. Garabed, and A. E. Marsh. Dept. of Veterinary Preventive Medicine.

The coccidian parasite *Hammondia heydorni* is a close relative of and morphologically indistinguishable from *Neospora caninum*, and oocyst shedding of both parasites has been documented in several canid species. This study aimed to identify *H. heydorni* oocysts in the feces of wild canids and a domestic dog. Two hundred and eighty-five wild canid fecal samples were analyzed in addition to a domestic canine patient presenting to The Ohio State University Veterinary Medical Center. PCR with melting curve analysis was used to detect coccidian DNA. Coccidia-positive samples were further subjected to a *H. heydorni*-specific PCR assay targeting the ITS-1 region and a *N. caninum*-specific PCR assay targeting the Nc5 gene. Samples positive by the *H. heydorni*-specific assay were also analyzed with a PCR assay targeting the alpha tubulin gene to distinguish *H. heydorni* from *Hammondia triffittae*. *Hammondia heydorni* was detected in 3 wildlife samples (1.1%) as well as the dog sample. All samples were negative for *N*. *caninum*. The coccidia-specific, *H. heydorni*-specific, and *N. caninum*-specific assays were tested against several other coccidia species to assess their analytic specificity. Determining the presence of *H. heydorni* in wild canids will contribute to a greater understanding of the role these hosts play in the disease ecology of this parasite.

Keywords: *Hammondia*, fecal, coccidia, wild canids, dog, PCR

EAR - 25

EVALUATION OF RISK FACTORS AND TRANSMISSION PATHWAYS OF SALMONELLA AND ESβL-PRODUCING ORGANISMS FOR DOGS ON OHIO LIVESTOCK FARMS. A. Smith, N. Moran, T. Mills, D. Mollenkopf, D. Mathys, T. Wittum, and J. Stull. Dept. of Veterinary Preventative Medicine.

Livestock, the environment, humans, dogs and their diets are all theorized to be involved in the transmission of *Salmonella* spp. and extended-spectrum-beta-lactamase (ESβL)-producing organisms on livestock farms. Dogs may play a unique role due to their many on-farm roles and high human and livestock contacts. This study aimed to determine the prevalence of *Salmonella* and ESβL-producing organisms (*bla*$_{CTX-M}$ and *bla*$_{CMY-2}$) in dogs on Ohio livestock farms and identify likely domains (farm environment/livestock, dog diet, humans, other dogs) involved in the transmission of these organisms to dogs. Surveys gathering individual dog-level exposures and overall farm husbandry were collected from 71 livestock farmers, along with fecal samples from 100 dogs on these farms. Dog samples were tested for *Salmonella* spp. and ESβL-producing organisms. Survey data were categorized into domains to identify significant predictors (within and between domains) for dog carriage of *Salmonella* and ESβLs. Seven percent of dogs were shedding *Salmonella* spp., and 4% and 39% *Escherichia coli* carrying *bla*$_{CTX-M}$ and *bla*$_{CMY-2}$, respectively. Multivariable logistic regression models for each pathogen identified significant domain-associated predictors of dog carriage: *Salmonella* (farm domain): farms for personal use (OR=0.1), dog access to livestock bedding (OR=13); *bla*$_{CTX-M}$ (farm domain): meals fed in farm building (OR=23), presence of swine (OR=18); *bla*$_{CMY-2}$ (farm domain): working dogs (OR=22), goat exposure (OR=4), presence of goats (OR=9), (dog diet domain): fed raw diet (OR=3), (human domain): enrolled through 4H recruitment (OR=4), dogs allowed to sleep in all locations in house (OR=9), dogs go on car rides (OR=21), (other dogs domain): multiple dogs on the farm (OR>33). This study demonstrated the likely on-farm transmission of these pathogens to dogs from multiple domains, highlighting the need for dynamic, multi-domain approaches to pathogen canine prevention and control on livestock farms.

Keywords: dogs, livestock, *Salmonella*, *E. coli*, extended-spectrum-beta-lactamase (ESβL)-producing organisms, antimicrobial resistance, infection control, biosecurity, zoonoses

EAR - 26

ASSESSMENT OF THE CANINE RABIES PROGRAM IN ETHIOPIA: A PROJECT OF RIGHT PARTNERSHIP'S PILOT PROGRAM IN NORTH GONDAR Waibel, S., O'Quin, J., and Gebreyes, W. The Department of Veterinary Preventative Medicine

Rabies is a deadly viral disease that is almost always fatal unless timely post-exposure prophylaxis is initiated. This disease is entirely preventable yet remains a significant public health risk in developing countries. Ethiopia has the highest reported incidence of rabies in Africa (1.6 deaths /100,000 population) causing at least 1,456 human fatalities/year. Domestic dogs are the natural reservoir and are responsible for approximately 95% of human rabies cases. To address this concern, The Rabies and Infections on Global Health in the Tropics (RIGHT) partnership was established in 2012. The goal is to operationalize One Health and devise a reproducible yet versatile approach to building rabies prevention and control programs. To accomplish this goal a systematic review of the current rabies surveillance and monitoring program in Ethiopia was conducted. The report includes an in-depth analysis of current protocols and practices at the national level at the Ethiopian Public Health Institute (EPHI), in Addis Ababa, as well as an implementation review at the local level in North Gondar. Data collection involved interviewing officials and reviewing records from the following organizations/agencies: EPHI (1), local Gondar veterinary clinics (4), Gondar healthcare centers (3), a hospital (1), the Gondar Public Health Department (1), and the Amhara Zonal Agricultural Office (1). Comparison of the national protocols to the current practices at the local level identified infrastructure gaps. Similarly, comparison of the current program to the proposed RIGHT plan further identified specific needs to be addressed. Key results include: 1) None of the clinics (0/4) had appropriate safety equipment for restraining potentially rabid dogs or staff who were vaccinated against rabies, 2) major preventive vaccine shortage for both dogs and humans 3) funding and technology deficiencies promote fragmented reporting 4) attempted treatment by traditional healers may underestimate the true incidence of human rabies cases.

Keywords: canine rabies, Ethiopia

IMMUNOLOGY
AND
INFECTIOUS DISEASES

IMID-1

SAMHD1-MEDIATED HIV-1 RESTRICTION IN CELLS DOES NOT INVOLVE RIBONUCLEASE ACTIVITY. JM Antonucci [1, 2], C St. Gelais [1], S de Silva [1], JS Yount [3], C Tang [4], X Ji [4], C Shepard [5], Y Xiong [4], B Kim [5], L Wu [1-3]

[1] Center for Retrovirus Research, Department of Veterinary Biosciences; [2] Department of Microbiology; [3] Department of Microbial Infection and Immunity; The Ohio State University, 1900 Coffey Road, Columbus, OH; [4] Department of Molecular Biophysics and Biochemistry, Yale University, New Haven, CT; [5] Department of Pediatrics, Center for Drug Discovery, Emory University School of Medicine, 1760 Haygood Drive, Atlanta, GA.

SAMHD1 restricts HIV-1 replication in non-dividing cells by degrading dNTPs to a level that limits efficient HIV-1 reverse transcription (RT). It's been reported that SAMHD1 acts as an RNase and restricts HIV-1 replication in non-dividing cells through degradation of viral genomic RNA (gRNA), which challenged the established mechanism of HIV-1 restriction. To clarify these conflicting results, we independently generated stable U937 cell lines expressing SAMHD1 wild-type (WT) and mutants purported to specifically retain dNTPase (Q548A) or RNase (D137N) activities. Our results show WT SAMHD1 and the two mutants equally restricted HIV-1 infection and decreased dNTP levels in differentiated U937 cells. To determine whether SAMHD1 degrades HIV-1 gRNA, we measured HIV-1 gRNA levels in HIV-1-infected cells. We found similar levels of HIV-1 gRNA among the three SAMHD1-expressing cell lines compared to the vector control cells, indicating SAMHD1 does not degrade HIV-1 gRNA. Furthermore, we measured the levels of HIV-1 late RT products in infected cells and observed a significant decrease relative to vector control cells, suggesting SAMHD1 restricts HIV-1 infection at the level of RT. This correlates with the reduced dNTP pools measured in SAMHD1-expressing cell lines. Overexpression of SAMHD1 in virus producer cells didn't affect HIV-1 Gag expression, viral release or infectivity, suggesting that SAMHD1 does not degrade HIV-1 mRNA. To clarify whether SAMHD1 has a nuclease activity, we measured the ability of stringently purified full-length recombinant SAMHD1 to degrade ssDNA and ssRNA *in vitro.* All SAMHD1 preparations maintained a robust dNTPase activity; however, only background nuclease activity was observed in some preparations, indicating that the inconsistency of RNase activity is likely due to contamination. Overall, our data indicate that Q548A and D137N mutants of SAMHD1 do not distinguish the dNTPase and RNase function, and that dNTP hydrolysis is the most likely mechanism of SAMHD1-mediated HIV-1 restriction in non-dividing cells.

Keywords: SAMHD1, HIV-1, Restriction Factor, RNA

IMID - 2

REGULATION OF IMMUNOGLOBULIN CLASS SWITCH BY PHARMACOLOGICAL INHIBITORS OF INFLAMMATION AND NEUTROPHIL FUNCTIONS.

Z.Attia[1,2], H.E.Steiner1, E.Kim[1], T.L.Martin1, A.Zaghawa[2], E.Cormet-Boyaka[1], P.N.Boyaka[1]. [1]Veterinary Biosciences, College of Veterinary Medicine, Ohio State University, Columbus, OH; [2]Faculty of Veterinary Medicine, University of Sadat City, Sadat City, Egypt.

Different immunoglobulin isotopes and subclasses play distinct roles in host protection against bacterial, viral and parasitic infections. Each immunoglobulin isotope and immunoglobulin subclass is produced after IgM-bearing B cells receive stimuli that allow immunoglobulin class and transcription of immunoglobulin γ, ε or α chain genes corresponding to IgG, IgE and IgA. It is now well established that the anti-inflammatory cytokine IL-10 and TGF-β promote immunoglobulin class witch and production of IgA, and our group has recently shown that depletion of neutrophils facilitates generation of IgA responses by experimental sublingual vaccines. Since vaccines can be given to animal or human undergoing treatment with pharmacological inhibitors of inflammation (i.e., aspirin) or neutrophil functions (i.e., sivelestat and sulfasalazine), we tested the effect of such inhibitors on IgG and IgA production *in vitro*. Our results show that addition of aspirin, sivelestat or sulfasalazine to culture of LPS-stimulated murine spleen cells down regulates expression of B220 by B cells while increasing the expression of the plasma cell marker Syndecan1. Interestingly, these pharmacological inhibitors has similar effect of plasma cell differentiation than cholera toxin, one of the most describe adjuvant for inducing IgA responses in experimental animals. Flow cytometry analysis of surface immunoglobulin on B cells and quantification of immunoglobulin secreted in culture supernatants further demonstrated that aspirin, sivelestat and sulfasalazine increase production of both IgG and IgA. Taken together, our these findings suggest that addition of inhibitors of inflammation or neutrophil function to vaccine may represent a potential strategy for fine tuning immune response to vaccines and promoting mucosal IgA responses.

KeyworDs: Immunoglobulin class switch, inflammation, neutrophils, IgA

IMID - 3

RANDOM MUTAGENESIS OF *EHRLICHIA* SP. HF STRAIN FOR IDENTIFICATION OF VIRULENCE GENES. H. Bekebrede, M. Lin, Y. Rikihisa. Dept. of Veterinary Biosciences

Ehrlichia spp. (*E. canis, E. ruminantium, E. ewingii*, and *E. chaffeensis*) are tick-borne obligatory intracellular bacteria that infect variety of mammals including dogs, ruminants, deer, and human, causing severe and sometimes fatal systemic disease. Research to identify virulence factors of *Ehrlichia* spp. is hampered by the lack of small laboratory animal models and is inaccessible to stable genetic manipulations. The Rikihisa laboratory isolated a novel *Ehrlichia* species named “HF strain” from ticks in Japan. The HF strain is most closely related to *E. chaffeensis* human isolates, and notably kills laboratory mice in 10 days. The Rikihisa laboratory also recently completed whole genome sequencing of the HF strain. My research seeks to analyze gene function of the HF strain by using Himar transposon mutagenesis. A random mutant HF strain library will be created in canine macrophage cell line, DH82 cells. Mutant HF strains will be cloned, and genomic loci of transposon insertion will be identified by inverse PCR. Isolated mutants that can disrupt the promoter region or open reading frame will be confirmed by RT-PCR for the lack of mRNA. Ten distinct mutants will be selected to determine effects of the mutant HF strain on mice pathogenesis. I have so far isolated a single stable mutant clone that expresses mCherry fluorescence. The transposon insertion site was determined to be in the intergenic region between EHF_0098 and EHF_0097. Currently, we are seeking to obtain more mutants suitable for *in vitro* and *in vivo* pathogenesis analysis with optimal plasmid preparation and transformation methods. These studies will be expected to elucidate virulence factors of the HF strain. Because *Ehrlichia* spp. share homologus genes, the proposed study will help understanding virulence factors of other *Ehrlichia* spp. as well.

Keywords: Ehrlichia, HF strain, obligate intracellular bacteria, virulence, mutagenesis

IMID - 4

POLY-LACTIC-CO-GLYCOLIC ACID (PLGA) NANOPARTICLE DELIVERY OF SWINE INFLUENZA VIRUS VACCINE PROVIDES HETEROLOGOUS PROTECTION THROUGH CELL MEDIATED IMMUNITY IN PIGS. S. Dhakal, J. Hiremath[1], K. Bondra[1], Y. SL[1], B. Shyu[1], K. Oyuang[1], B. Binjawadagi[1], K.I. Kang[1], J. Goodman[2], B. Narasimhan[2], C.W. Lee[1], R.J. Gourapura[1]; [1]Food Animal Health Research Program, Department of Veterinary Preventive Medicine, The Ohio State University, Wooster, OH, USA, [2]Department of Chemical and Biological Engineering, Iowa State University, Ames, IA, USA.

Swine influenza is one of the major economic burdens to swine farmers in US. Current vaccines have failed to provide heterologous (cross) protection, warranting the need of innovative vaccine delivery platform. PLGA is a biodegradable polymer, Food and Drug Administration approved, and widely used in drug and vaccine delivery system. In this study, PLGA nanoparticle containing killed swine influenza virus (SwIV) H1N2 (KAg) vaccine (PLGA-KAg) was developed; and evaluated *in vitro* and *in vivo* in a typical vaccination and heterologous SwIV H1N1 challenge trial in pigs. Our results showed that PLGA-KAg induced maturation of antigen presenting cells *in vitro*. In pigs intranasally vaccinated with PLGA-KAg, at 35 days post-vaccination, increased frequencies of cytotoxic T cells (CTLs), memory T helper cells and gamma-delta T cells, and enhanced antigen specific proliferation of lymphocytes were observed. After heterologous virus challenge in PLGA-KAg vaccinated pigs: (i) absence of clinical flu symptoms like fever, anorexia and lethargy; (ii) significantly reduced virus induced lung pathology and antigenic mass; (iii) significantly higher CTLs and total interferon gamma producing cells; and (iv) virus clearance in the respiratory tract of most of the pigs compared to KAg vaccinated animals was observed. But PLGA-KAg vaccine failed to boost the antibody response both in pre- and post-challenged pigs. In summary, our study showed the particulate delivery of killed SwIV vaccine induced protective immune response was mediated through cellular (CTLs) but not humoral (antibody) immune response in pigs. Upon a few important improvements to this vaccine delivery platform, it can serve as a potent candidate vaccine to use in swine herds to mitigate flu outbreaks.

Keywords: Swine influenza, Poly-lactic-co-glycolic acid, Nanoparticle, Pig, Vaccine

IMID - 5

THE EFFECT OF HYPOTHERMIA ON INFLUX OF MONONUCLEAR CELLS IN THE DIGITAL LAMELLAE OF HORSES WITH OLIGOFRUCTOSE-INDUCED LAMINITIS. J.D. Godman[1], T.A. Burns[1], C.S. Kelly[1], M. Watts[1], B.S. Leise[2], E.L. Schroeder[1], A.W. van Eps[3], J.K. Belknap[1] 1. The Ohio State University, Columbus OH, 2. Louisiana State University, Baton Rouge, LA, 3. The University of Queensland, Brisbane, Australia

Sepsis-related laminitis (SRL) is a common complication in the septic/endotoxemic critically-ill equine patient. Similar to organ injury in human sepsis, lamellar injury in SRL has been associated with inflammatory events, including the influx of leukocytes into the lamellar tissue and markedly increased expression of a wide array of inflammatory mediators at the onset of Obel grade 1 (OG1) laminitis. The only treatment reported to protect the lamellae in SRL, local hypothermia, has been demonstrated to effectively inhibit lamellar expression of multiple inflammatory mediators. However, the effect of hypothermia on leukocyte influx into affected tissue has not been assessed. We hypothesized that hypothermia inhibits leukocyte emigration into the digital lamellae in SRL.

Immunohistochemical staining using leukocyte markers MAC387 (neutrophils, activated monocytes) and CD163 (monocyte/macrophage-specific) was performed on archived lamellar tissue samples from a carbohydrate overload model. One forelimb was maintained at ambient temperature (AMB) and one forelimb was immersed in ice water (ICE) immediately following oligofructose administration (10g/kg, n=14 horses). Lamellae were harvested at 24 hours post-oligofructose administration (DEV, n=7) or at the onset of OG1 laminitis (OG1, n=7). Leukocytes were counted by a single blinded investigator on images [n=10 (20x fields/digit for MAC387; 40x fields/digit for CD163)] obtained using Aperio software. Data were assessed for normality and analyzed with a paired t-test and one-way ANOVA with significance set at $p<0.05$. MAC387(+) cells were present in low numbers in the lamellar tissue and were decreased in the hypothermic limbs (vs. AMB limbs, $p<0.05$) in the OG1 group; no change in CD163(+) cell numbers was noted.

This study demonstrated that hypothermia of the distal limbs instituted early in the disease process in the horse at risk of SRL significantly attenuates the increase of MAC387(+) leukocytes in the digital lamellae, but has minimal effect on increases in lamellar concentrations of CD163(+) mononuclear cells.

Keywords: Laminitis, sepsis, hypothermia, CD163, MAC387, oligofructose

IMID - 6

CX3CR1 IN COTTON RATS IS THE RECEPTOR FOR RESPIRATORY SYNCYTIAL VIRUS AS IT IS IN HUMANS. G Green[1], S. Johnson[2], A. Oomens[4], M. Teng[3], M. Peeples[2], S. Niewiesk[1]
[1]Department of Veterinary Biosciences, The Ohio State University, Columbus, Ohio; [2]Center for Vaccines and Immunity, The Research Institute at Nationwide Children's Hospital, Columbus, Ohio; [3]Division of Allergy and Immunology, Department of Internal Medicine, Morsani College of Medicine, University of South Florida, Tampa, Florida; [4]Department of Veterinary Pathobiology, Oklahoma State University, Stillwater, Oklahoma.

Respiratory syncytial virus (RSV) is a leading cause of death among infants worldwide. Despite this, there are no effective vaccines or antivirals available. A recent publication by SM Johnson et. al. [(2015) RSV Uses CX3CR1 as a Receptor on Primary Human Airway Epithelial Cultures. PLoS Pathog 11(12):e1005318], has demonstrated that RSV uses CX3CR1 rather than heparan sulfate as a receptor on primary human airway epithelial cell cultures, a more physiologically relevant model than immortalized cell lines, which express heparan sulfate as a receptor. RSV replicates in the upper and lower respiratory tract of cotton rats in a manner similar to humans. Sequencing and cloning of cotton rat CX3CR1 revealed 82% shared amino acid sequence identity with humans. RSV binds to CX3CR1 via its attachment glycoprotein or G protein. In order to understand the interaction of RSV with its receptor molecule in vivo, we used G protein mutated in the CX3CR1 binding site and measured viral replication in the lungs of cotton rats following intranasal inoculation. All virus mutants grew well in cell culture on immortalized cell lines, but in contrast to wild-type virus, the G protein mutants were not detectable at 4 days post-infection in the lung. Wild-type RSV was recovered at a titer of $10^{4.3}$ $TCID_{50}$/gram lung tissue. In a similar experiment, RSV was incubated with an antibody directed against the CX3CR1 binding site of G protein to block G protein binding to CX3CR1. Subsequent intranasal inoculation into cotton rats resulted in undetectable levels of RSV in the lungs 4 days post-infection. If RSV was incubated with heparan sulfate before intranasal inoculation into cotton rats, viral growth was not affected. So far, these results indicate that CX3CR1 functions as the receptor for RSV in cotton rats. Experiments are in progress to formally prove this role of CX3CR1.

Keywords: Respiratory Syncytial Virus, Viral entry, Receptor, Cotton rat

IMID - 7

EVALUATION OF THE VIRULENCE OF A PORCINE EPIDEMIC DIARRHEA VIRUS WITH A 197 AMINO ACID-DELETION IN THE SPIKE PROTEIN

Y. Hou, C.M Lin, X. Gao, Z. Lu, X. Liu, Y. Qin, L. J. Saif and Q. Wang
Food Animal Health Research Program, Ohio Agricultural Research and Development Center, College of Food, Agricultural and Environmental Sciences, Department of Veterinary Preventive Medicine, The Ohio State University, Wooster, Ohio, USA

Porcine epidemic diarrhea virus (PEDV) belongs to the *Alphacoronavirus* genus within the *Coronaviridae family*. It is a highly contagious and lethal enteric pathogen in piglets. A mutant PEDV strain PC177 shares a similar backbone to the highly virulent original US PEDV strain PC22A, but has a 197 amino acid (aa)-deletion in the N-terminal domain (NTD) of the S1 region of the spike (S) protein. For the alphacoronavirus transmissible gastroenteritis virus (TGEV), a 224 aa-deletion in the NTD of S1 reduced its virulence and changed its tissue tropism from intestinal to respiratory [subsequently designated porcine respiratory coronavirus (PRCV)]. We hypothesized that the 197 aa deletion of PC177 may alter its virulence and tissue tropism. To test this hypothesis, 4-day-old cesarean-derived colostrum-deprived (CDCD) piglets were inoculated orally with PC177 (n=6), PC22A (n=5), or mock (n=4). Within 7 days post-inoculation (DPI), no mock pigs had diarrhea, but 100% PC22A- and 50% PC177-inoculated piglets had diarrhea. However, PC177-inoculated piglets showed milder diarrhea and lower fecal PEDV RNA shedding titers compared with PC22A-inoculated piglets. Mortality rates were 0% and 100% in PC177- and PC22A-inoculated piglets, respectively. Immunohistochemistry (IHC) staining of PEDV N protein at the acute phase of infection showed that both PC177- and PC22A-antigens were detected in the small intestinal epithelial cells, but not in the bronchial epithelial cells and lungs. In addition, milder villous atrophy and lower antigen scores were observed in PC177-inoculated piglets. In a recent report, no mortality occurred in 7-day-old field suckling piglets (n=120) infected with a Japanese PEDV strain (Tottori2/2014) with a 194 aa-deletion (Δ23-216 aa) in the S1 NTD, similar to that of PC177 (Δ 34-230 aa). Both findings suggest that the large deletion in the NTD of S1 may be responsible for the reduced virulence.

Keywords: porcine epidemic diarrhea virus, spike, pathogenesis

IMID - 8

CATHEPSIN K INHIBITION RENDERS EQUINE BONE MARROW NUCLEATED PROGENITOR CELLS HYPO-RESPONSIVE TO LPS AND UNMETHYLATED CPG STIMULATION *IN VITRO.* H. Hussein[1], P. Boyaka[2], J. Dulin[1], A. Bertone[1, 2]. [1].Dept. of Veterinary Clinical Sciences. [2]. Dept. of Veterinary Biosciences. College of Veterinary Medicine, The Ohio State University, Columbus, OH, USA.

Cathepsin K (CatK) is an important enzyme regulating bone degradation and immune response. Cathepsin K inhibition has been proposed as a therapeutic for equine osteo-inflammatory conditions. Bone marrow is the body's resource for progenitor cells of osteoblastic and osteoclastic cell lines responsible for bone formation and turnover, and for the lymphoid cell lines as well. Our study aimed to investigate the effect of CatK inhibition on Toll like receptor (TLR) 4 and TLR9 signaling pathways in equine whole bone marrow nucleated cells (BMNCs). This cellular fraction was chosen to include both the lymphoid and non-lymphoid cells (myeloid progenitors, mesenchymal stem and other progenitor cells) since equine immune (myeloid and lymphoid) and non-immune cells, such as chondrocytes and synovial fibroblast-like cells showed significant inflammatory response when stimulated with Lipopolysaccharides (LPS) *in vitro.* Equine BMNCs were isolated and exposed to VEL-0230, a highly selective CatK inhibitor, at a concentration of 0, 1, and 10 µM in cell culture media with and without LPS (1 µg/ml) and unmethylated CpG (5 µg/ml). Subsequent analyses of cell viability, cytokine secretion by stimulated BMNCs; specifically IL-1β, IL-6, and TNF-α, and BMNCs surface markers' expression and Major histocompatibility (MHC) II molecule were performed. Cathepsin K inhibition promoted BMNCs viability and reduced cell apoptosis. Moreover, CatK inhibition significantly decreased cytokine secretion and MHC II molecules expression of either naïve or stimulated BMNCs. In conclusion, CatK inhibition in horses did affect BMNCs other than mature osteoclasts rendering them hypo-responsive to both TLR4- and TLR9-induced inflammation, predicting a proteolytic activity for CatK within the MyD88 pathway and/or the following proteolytic events required for the cytokines secretion.

Keywords: immune, cytokine, inflammation, Toll like receptor, Cathepsin K, VEL-0230.

IMID - 9

ANTIMICROBIAL USE AND RESISTANCE IN ZOONOTIC BACTERIA RECOVERED FROM NONHUMAN PRIMATES. J. Kim, The Ohio State University, College of Veterinary Medicine, Department of Veterinary Preventive Medicine, College of Public Health, Columbus, Ohio, United States of America; D. J. Coble, The Ohio State University, College of Veterinary Medicine, Department of Veterinary Preventive Medicine, University of Laboratory Animal Resources, Columbus, Ohio, United States of America; G. W. Salyards, University of California, Davis, California National Primate Research Center, Davis, California, United States of America; W. Rinaldi, Alpha Genesis Incorporated, Yemassee, South Carolina, United States of America; G. Plauche, University of California, Davis, California National Primate Research Center, Davis, California, United States of America; G. H. Habing, The Ohio State University, College of Veterinary Medicine, Department of Veterinary Preventive Medicine, Columbus, Ohio, United States of America

Antimicrobial resistance (AMR) has become a central topic as it is a growing threat in human and animal health. Major surveillance systems, such as the National Antimicrobial Resistance Monitoring System (NARMS), are now established to monitor AMR. However, there appears to be a lack of comprehensive literature on AMR among nonhuman primates (NHP) used in biomedical research. *Shigella flexneri, Yersinia enterocolitica, Y. pseudotuberculosis,* and *Campylobacter jejuni* are zoonotic enteric bacteria common among NHPs, and AMR strains may lead to serious mortality and morbidity in both NHP patients in staff. This study aims to provide data on current antimicrobial use strategies and the prevalence of AMR in zoonotic bacteria recovered from NHPs within biomedical research institutions. Fifteen veterinarians, seven biomedical institutions, and four diagnostic laboratories participated, providing data on antimicrobial practices and susceptibility test results across three years (1/2012 – 4/2015). Participating veterinarians also identified a threshold prevalence of AMR (TP-AMR), where if exceeded by the true prevalence of AMR, would cause the veterinarians to change their antimicrobial use strategies. We hypothesized that the prevalence of AMR among the above bacteria will exceed participating veterinarians' TP-AMRs. Participating veterinarians primarily treated cases caused by *S. flexneri, Y. enterocolitica,* and *Y. pseudotuberculosis* with enrofloxacin, but treated *C. jejuni* cases with azithromycin and tylosin. High proportions of AMR were observed to other antimicrobials, but all isolates were susceptible to their associated primary antimicrobials. Notably, resistance patterns were not shared between this study's NHP isolates and human isolates presented by NARMS. The presented study demonstrates that zoonotic bacteria recovered from NHP diagnostic samples are broadly susceptible to the antimicrobials used to treat the clinical infections. These results can help veterinarians ensure effective antimicrobial therapy and consequently, protect staff by minimizing occupational risk.

Keywords: *Shigella flexneri*; *Yersinia enterocolitica*; *Yersinia pseudotuberculosis*; *Campylobacter jejuni*; antimicrobial resistance (AMR); nonhuman primates (NHP); threshold prevalence of AMR (TP-AMR); National Antimicrobial Resistance Monitoring System (NARMS)

IMID - 10

EPITHELIAL CELL IKKβ REGULATES EOSINOPHIL LEVELS IN THE INTESTINE AND SEVERITY OF ALLERGIC RESPONSES TO INGESTED ALLERGENS E. Kim, M. M. Lembert, T. L. Martin, J. C. Rowe, H. E. Steiner, E. Cormet-Boyaka, P. N. Boyaka. Depts. of Veterinary Biosciences

Allergic sensitization to food allergens has subsequent potential to developing allergic responses in the gastrointestinal tract, and also to skin or lung. Our previous study showed that lack of IKKβ in intestinal epithelial cells regulates favors IgA responses to ingested allergen, which in turn limits the severity of allergic responses in the airway. In this study we investigated whether intestinal epithelial IKKβ also regulated allergic responses to oral antigens. Wild-type C57BL/6 and IKKβ$^{\Delta IEC}$ mice, which lack IKKβ in intestinal epithelial cells, were orally sensitized to a food antigen in the presence of cholera toxin. Allergen-specific serum IgE responses and fecal IgA responses were similar between the groups. However, after oral allergen-challenge, IKKβ$^{\Delta IEC}$ mice only developed minimal clinical and histological signs of allergy, including drop in body temperature and mucus in small intestinal villi and crypts. Interestingly, IKKβ$^{\Delta IEC}$ mice expressed lower levels of CCL11 (eotaxin) and eosinophils than control wild-type mice and their levels were only weakly increased after oral allergen sensitization and challenge. In summary, this study reveals a new role of intestinal epithelial cells in the regulation of allergy in the GI tract through a NF-κB – CCL11 axis.

Keywords: Allergy, Intestinal epithelium, IKKβ, Eosinophil, CCL11

IMID - 11

DEVELOPING A CRYOPRESERVATION METHOD THAT PRESERVES FUNCTION OF CANINE AND FELINE PERIPHERAL BLOOD MONONUCLEAR CELLS. Y. Lin, R. Vicetti Miguel, N. Quispe Calla, K. Henschel, and T. Cherpes. Depts. of Microbial Infection and Immunity and Obstetrics and Gynecology

Adequate cryopreservation methods for canine and feline peripheral blood mononuclear cells (PBMC) do not exist. Herein, we compared viability and function of canine and feline PBMC using the current gold standard for human PBMC cryopreservation (i.e., 90% fetal bovine serum (FBS) and 10% dimethyl sulfoxide (DMSO)) vs. a serum-free medium (i.e., RPMI supplemented with 12.5% bovine serum albumin (BSA) fraction V and 10% DMSO). Though FBS-based media consistently preserved the number and viability of cryopreserved canine PBMC (i.e., 90% cell recovery after thaw), recovered cells were less responsive than fresh cells to polyclonal immune activators. Conversely, serum-free media allowed 80% recovery of cryopreserved canine PBMC, but better conserved responsiveness to immune activation. To directly define capacity of the serum-free medium to preserve immune function of cryopreserved vs. fresh PBMC, we isolated fresh feline PBMC and stimulated them with polyclonal immune activators, and also cryopreserved an aliquot of these same PBMC in serum-free media. One week later, frozen PBMC were recovered and stimulated identically as the fresh PBMC. Comparing these responses, we newly demonstrate that serum-free medium preserves immune function of feline PBMC. Our optimization of methodology that preserves immune function of canine and feline PBMC is likely to significantly impact immunological studies in comparative oncology, infectious disease pathogenesis in preclinical models of human disease, and companion animal vaccine development.

Keywords: PBMC, peripheral blood mononuclear cells, cryopreservation, serum-free, immune function, canine, feline

IMID - 12

EXPERIMENTAL MODELING OF THE NONSPECIFIC PROTECTIVE EFFECTS WITH MEASLES VIRUS VACCINATION. S. C. Linn, D. Huey, and S. Niewiesk.Department of Veterinary Biosciences, College of Veterinary Medicine, The Ohio State University

The administration of a vaccine can have non-specific effects that are protective against unrelated pathogens in an infant patient and can, therefore, be protective against viruses for which currently no vaccines exist. Respiratory syncytial virus (RSV) is one of the most common causes of lower respiratory tract infections in infants with 3.4 million cases leading to hospitalization in children under 5 years of age. A recent study in Denmark, however, observed that children whose most recent vaccine was the live measles-mumps-rubella vaccine had a lower rate of RSV hospitalization compared to children who had inactivated DTaP-IPV-Hib3 as their most recent vaccine. The aim of this study is to provide the experimental basis for the nonspecific protective effects of measles virus immunization in the presence or absence of maternal antibodies against infection with RSV. We established three groups of animals: cotton rats immunized with measles virus in the presence or absence of measles virus specific maternal antibodies and unvaccinated controls. From these groups, we measured viral titers of RSV in lung and nasal turbinate homogenates and measured the antibody response against measles virus and RSV. We have analyzed RSV viral titers from 1, 3, and 5 weeks post vaccination with measles along with 5 weeks post-measles vaccination in the presence of maternal antibodies. For the three timepoints observed, there was no correlation between measles virus immunization and RSV infection in cotton rats.

Keywords: cotton rat, Respiratory Syncytial Virus, measles virus

IMID - 13

3’3’-CGAMP INDUCES A BALANCED TH1 AND TH2 CYTOKINE PROFILE FOLLOWING SUBLINGUAL IMMUNIZATION. T. Martin, E. Kim, J. Jee, H.E. Steiner, and P.N. Boyaka. Dept. of Veterinary Biosciences

Mucosal immunization confers systemic immunity as well as immunity in mucosal compartments. This mucosal protection occurs through induction of secretory IgA antibodies (SIgA.) Intranasal immunization is a well-established route of mucosal immunization in both humans and animals, however adverse effects have been associated with this route. Facial nerve paralysis is reported in humans immunized with vaccines containing the adjuvants cholera toxin (CT) or heat-labile toxin from *Eschericia coli* (LT.) Mucosal immunization via the sublingual route could obviate this risk while effectively inducing SIgA, but currently approved adjuvants such as alum do not effectively induce SIgA following sublingual immunization. 3’3’-cyclic guanosine monophosphate-adenosine monophosphate (3’3’-cGAMP) is a cyclic dinucleotide of bacterial origin that elicits innate immune responses by binding to stimulator of interferon gamma genes (STING) on the endoplasmic reticulum. To examine the effectiveness of 3’3’-cGAMP as an adjuvant for sublingual immunization, C57BL/6J mice were immunized with recombinant *Bacillus anthracis* protective antigen (PA) in the presence of 3’3’-cGAMP. Sublingual immunization with 3’3’-cGAMP elicited a balanced Th1 and Th2 immune response, as evidenced by the ratio of serum IgG2a:IgG1. This response was further evidenced by the cytokine profile elicited by 3’3’-cGAMP immunization, which included elevations in both pro- and anti-inflammatory cytokines , but did not lead to elevations in production of Th2 or th17 cytokines associated with allergies.. Combined with previous data showing that immunization with 3’3’-cGAMP encourages SIgA production in the respiratory tract, this data indicates that 3’3’-cGAMP could be both a safe and effective adjuvant for sublingual immunization against respiratory pathogens such as *Bacillus anthracis.*

Keywords: sublingual, mucosal, immunization, adjuvant, Immunoglobulin A , IgA, cGAMP

IMID - 14

MATERNAL ANTIBODY TRANSFER IN THE COTTON RAT PLACENTA

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Respiratory syncytial virus (RSV) is the leading cause of bronchiolitis and viral pneumonia in infants and young children worldwide, and a significant cause of respiratory disease in the elderly. There is no vaccine or antiviral therapy to prevent or treat RSV infection, but virus neutralizing monoclonal antibodies can be given prophylactically emphasizing the protective potential of antibodies. One concept of RSV vaccinology is the immunization of mothers to induce high antibody titers, which will lead to the transfer of high levels of maternal antibodies. Currently, there are clinical trials investigating the benefit of maternal immunization for RSV to induce protective passive immunity in infants. Cotton rats are the best small animal model for RSV infection and are used to test maternal immunization. In cotton rats, maternal IgG antibodies is transferred via the placenta in utero and postnatally via intestinal absorption from colostrum. To further develop the cotton rat model, we characterized the cotton rat placenta and Fc receptor localization. Placentas from cotton rats at mid-gestation (~ day 14) and late gestation (~ day 27), as well as neonatal (<1 week) gastrointestinal tracts were collected for light microscopy, immunohistochemistry and electron microscopsy. The cotton rat placenta is hemotrichorial, and has 5 distinct layers: decidua, junctional zone, labyrinth, chorionic plate, and yolk sac. Consistent with the transfer of maternal antibodies, the majority of the Fc receptors were present in the yolk sac endoderm, as well as the chorionic plate fetal capillary endothelium, and 10% of the fetal capillary endothelium within the labyrinth. Fc receptors were also present in the duodenal and jejunal enterocytes, similar to humans, mice, and rats. Therefore, the cotton rat is an animal model that can be used to investigate maternal antibody transfer after maternal immunization to prevent RSV infection in infants.

Keywords: Cotton rat, Placenta, Fc receptor, Passive transfer

IMID - 15

EFFECT OF NF-κB PATHWAY IN INTESTINAL EPITHELIAL CELLS DURING INGESTION OF LOW DOSES OF CADMIUM. J. Rowe, E. Kim, H. Steiner, E. Cormet-Boyaka, and P. Boyaka. Dept. Veterinary Biosciences

Chronic gastrointestinal inflammation is a great concern to human medicine, veterinary medicine, and food animal production. Minor disruptions to the homeostatic equilibrium of the intestinal tract can lead to Inflammatory Bowel Disease (IBD), Crohn's disease, and ulcerative colitis, which affect approximately 1.4 million people in the United States. Further, prolonged bouts of inflammation could similarly cause IBD in dogs and are contributing factors to colic in horses and depressed production of food animals. Low levels of cadmium are commonly found in water runoff and accumulation can occur in plants, seafood, and soft tissues of mammalians. This heavy metal is now listed 7th in the priority list of hazardous substances and is believed to promote inflammation. This study explored the role of intestinal epithelial cells (IECs), and more specifically the canonical NF-κB pathway of these cells, in host mucosal responses to repeated ingestion of cadmium. Control wild-type C57BL/6 and IKKβ$^{\Delta IEC}$ mice, which lack IKKβ in IECs, were maintained in conventional SPF housing (n=5 per group) and provided cadmium as CdCl2 (10 uM or 2 ppm) in drinking water for 14 days. Analysis of total sIgA in fecal samples collected on days 0, 7, and 14 showed that cadmium treatment reduces sIgA levels in both groups of mice. We also found that repeated ingestion of cadmium differentially affected the frequency of lymphocyte subsets in mesenteric lymph nodes (MLNs) of IKKβ$^{\Delta IEC}$ and control wild-type mice and increased percentage of B cells while reducing the percentage of T cells in IKKβ$^{\Delta IEC}$ mice. Furthermore, cadmium treatment enhanced gut TGFβ and TNFα mRNA responses to the bacterial product cholera toxin in IKKβ$^{\Delta IEC}$ mice. Taken together, our data suggest that the canonical NF-κB in intestinal epithelial cells plays a key role in host response to environmental pollutants and subsequent inflammatory status in the gastrointestinal tract.

Keywords: NF-κB, Intestinal Epithelium, Cadmium

IMID - 16

EXAGGERATED PRO-INFLAMMATORY INNATE IMMUNE RESPONSE OF CYSTIC FIBROSIS AIRWAY EPITHELIA CELLS TO H1N1 INFLUENZA A INFECTION. S. YOUNG[1], P. Woods[1], M. Peeples[2], and I. Davis[1]. [1]The Ohio State University College of Veterinary Medicine; [2]Nationwide Children's Hospital Medical Center

Cystic Fibrosis (CF) is an autosomal recessive genetic disorder resulting from mutations in the cystic fibrosis transmembrane conductance regulator gene (*cftr*). CF is characterized by a progressive decline in lung function, often as a result of repeated pulmonary exacerbations. Relative to normal subjects, respiratory epithelial cells from CF patients release higher amounts of pro-inflammatory cytokines and chemokines following infection with bacterial pathogens such as *Pseudomonas aeruginosa*, which results in significant damage to the respiratory tract. This damage leaves the lung susceptible to further bacterial colonization, resulting in a vicious cycle of bacterial colonization, inflammation, and lunch damage. Infection with influenza A viruses is associated with severe symptom exacerbations, which contribute to increased CF patient morbidity, bacterial colonization, and disease progression. While influenza infection rates do not differ between CF and non-CF patients, disease is more severe in those with CF. Human airway epithelial cells (HAECs) isolated from normal and CF patient donor lungs, were grown at an air-liquid interface to generate influence to generate confluent, highly-differentiated monolayers of similar cellular composition to normal airways. HAEC cultures were then mock-infected or infected *in vitro* with influenza A/WSN/33 (H1N1) at a multiplicity-of-infection of 1. mRNA was isolated and analyzed by qRT-PCR. Following infection for 24 hours, expression of pro-inflammatory cytokines IFN-α, IL-6, IL-8, and TNF-α, was higher in CF than non-CF HAECs. CF HAECs also expressed higher levels of viral toll-like receptors TLR-3 and TLR-7. These findings show that the innate immune response of CF HAECs to *in vitro* influenza A virus infection is abnormal, which suggests that an excessive respiratory epithelial cell inflammatory response to infection contributes to the severity of symptom exacerbations in influenza-infected CF patients.

Keywords: Cystic Fibrosis, HAECs, symptom exacerbations, Influenza A (H1N1), TLRs

MIR-155 IMPACTS T CELL MIGRATION IN ACUTE GRAFT-VERSUS-HOST-DISEASE (AGVHD). N.C. Zitzer[1], P.A. Taylor[2], A. Ngankeu[1], Y.A. Efebera[1], S.M. Devine[1], B.R. Blazar[2], R. Garzon[1], P. Ranganathan[1]. [1]Comprehensive Cancer Center, The Ohio State University, Columbus, OH; [2]Blood and Marrow Transplantation, Division of Pediatrics, Department of Medicine, University of Minnesota, Minneapolis, MN

We reported that miR-155 expression is upregulated in donor T cells during aGVHD and mice receiving miR-155 knock-out (KO) donor splenocytes do not exhibit lethal GVHD and have improved survival as compared to mice receiving wild type (WT) splenocytes. Here, we investigate the impact of miR-155 expression in T cell migration and elucidate the T cell population responsible for miR-155-mediated modulation of aGVHD. There was dramatic decrease in T cell infiltration of peripheral organs in recipients of miR-155-KO T cells as compared to WT T cells as evidenced by confocal microscopy of GFP-labeled donor cells. There was a significant decrease in chemokine receptor CCR5 mRNA and protein expression in miR-155-KO versus WT donor T cells in recipient mice with clinical aGVHD. Allo-activated miR-155 KO T cells show significantly reduced migration towards CCR5 ligands RANTES and MIP-1a using *in vitro* transwell migration assays, with an average migration index (MI) of 1.08, compared to the average MI of WT T cells of 4.52 ($p<0.005$). We performed a B6 into F1 transplant using only CD4+ donor T cells. Median survival of recipients of WT CD4+ T cells (n=13) was 42 days, compared to 100% survival of recipient mice of miR-155 KO CD4+ T cells (n=12) on day 100, ($p<0.0001$). Recipients of miR-155 KO CD4+ T cells also exhibited significantly lower aGVHD clinical ($p<0.01$) and pathological scores ($p<0.01$) than WT recipients. Our data suggest that miR-155 exerts its modulating effects in aGVHD by affecting T cell migration and indicates that the CD4+ T cells plays an important role in miR-155 regulation of aGVHD. Future experiments are underway to determine the role of miR-155 in regulatory and CD8+ T cell subsets in the modulation of aGVHD and evaluate the role of miR-155 in modulating T cell migration through other chemokine receptors.

Keywords: aGVHD, graft-versus-host-disease, T cell migration, microRNA-155

IMID – 18

INHIBITION OF LUNG TISSUE NON-SPECIFIC ALKALINE PHOSPHATASE ATTENUATES INFLUENZA-INDUCED ACUTE LUNG. P. S. Woods[1,2], L. Doolittle[1,2], and I. C. Davis[1] Department of Veterinary Biosciences[1], The Ohio State University
The Ohio State School of Medicine[2], The Ohio State University

Influenza A viruses are readily transmissible respiratory pathogens that remain a significant threat to human health. However, available vaccines and antiviral drugs have limited efficacy. Our limited understanding of influenza pathogenesis remains a major obstacle in improving influenza therapeutics. Extracellular nucleotides and nucleosides regulate fluid balance within the lung and can serve as leukocyte chemoattractants. We have previously shown that influenza infection of mice leads to increased ATP and adenosine accumulation in the airway lumen. Moreover, we demonstrated that A1-adenosine receptor activation contributes significantly to influenza-induced acute lung injury (ALI). Extracellular adenosine levels are regulated by cell surface enzymes that metabolize ATP to adenosine. Ecto-5'-nucleotidase (CD73) is a high-affinity, low-capacity enzyme that converts AMP to adenosine. It has been proposed that CD73 regulates extracellular adenosine concentrations under steady-state conditions within the lung. Tissue non-specific alkaline phosphatase (TNAP) is a low-affinity, high-capacity enzyme that catabolizes nucleotides in a non-specific manner. TNAP is therefore likely to play a more significant role in nucleotide breakdown in situations of robust nucleotide release, such as influenza infection. We found that influenza-induced ALI was not attenuated in CD73-knockout mice or by treatment of infected mice with a CD73 inhibitor (DPCPX). Hence, we hypothesized that TNAP mediates adenosine generation in influenza-infected mice and that inhibition of TNAP will attenuate influenza-induced ALI. To test our hypothesis, C57BL/6 mice were inoculated with 10,000 pfu/mouse of influenza A/WSN/33 (H1N1). Preliminary data suggest that influenza infection upregulates TNAP gene and protein expression and enzymatic activity as early as 2 days post infection (d.p.i.). Treatment of infected mice at 2 and 4 d.p.i. with 50µl of 10µM TNAP inhibitor or vehicle (DMSO) intranasally significantly attenuated hypoxemia, pulmonary edema, and immune cell infiltration. These data suggest that TNAP inhibition attenuates influenza-induced ALI, most likely by reducing inflammation and fluid accumulation within the lung.

Key Words: Influenza, Acute Lung Injury, Nucleotide Signaling

MOLECULAR
AND
CELLULAR BIOLOGY

IDENTIFYING THE ROLE OF NOVEL TAX-1 INTERACTING PROTEIN SNX27 IN HTLV-1 INFECTION.

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Human T-cell Leukemia Virus Type-1 (HTLV-1) is a complex retrovirus infecting 15-20 million people worldwide, and is the etiological agent of an aggressive malignancy of CD4+ T-cells termed Adult T-Cell Leukemia. By contrast, HTLV-2 is non-pathogenic in humans. Both HTLV-1 and HTLV-2 express related Tax proteins termed Tax-1 and Tax-2, respectively. Studies have revealed that Tax-1 contains a C-terminal post synaptic density protein (PDZ) binding motif (PBM) which is absent in Tax-2. We aim to determine whether this domain in Tax-1 is required for protein-protein interactions. These could prove crucial for differences in pathogenesis of the two viruses. Using Tax-1 mutants lacking the PBM we identified several candidates via a mass spectrometry based proteomic screen. One candidate was Sorting Nexin 27 (SNX27), a member of the sorting nexin family of proteins which are involved in endocytosis and protein trafficking. SNX27 is a unique member of the sorting nexin family in that it contains a PDZ domain. Published literature has shown that SNX27 is involved in GLUT1 recycling from lysosomes to the plasma membrane, and without SNX27 GLUT1 is internalized and degraded. We propose that Tax-1 interaction with SNX27 may alter this SNX27 regulation of GLUT1, which is the receptor molecule for HTLV-1. This modulation could prove beneficial to HTLV-1 since plasma membrane bound receptor molecules have been shown to interfere with virion release and infectivity in other retroviruses, including HIV. We confirmed that Tax-1 interacts with SNX27 through the PDZ. We also demonstrated that SNX27 overexpression does not affect Tax-1 transactivation, but resulted in decreased p19 release into the supernatant. Our future work will determine the mechanistic role of the SNX27 and Tax-1 interaction in modulation of GLUT1. These studies will further our knowledge on HTLV-1 virus release and infectivity, and may potentially lead to new therapies to prevent infection.

Keywords: HTLV-1, ATL, SNX27, GLUT1

MCB - 2

SALMON POISONING DISEASE: CANINE IMMUNE RECOGNITION OF *NEORICKETTSIA HELMINTHOECA*. K. Bachman, M. Lin, Y. Rikihisa.
Department of Veterinary Biosciences, College of Veterinary Medicine,
The Ohio State University

Neorickettsia helminthoeca, the causative agent of Salmon Poisoning Disease (SPD), is an obligate helminth-borne intracellular bacteria that infects reticuloendothelial cells of wild and domestic canids. Endemic to the Pacific Coast, dogs acquire SPD by ingesting salmonid fish infested with *N. helminthoeca*-infected trematode. The current definitive diagnostic test - PCR, takes time and requires trained personnel and special equipment. Due to the high mortality rate of SPD (>90%), there is a need for a more rapid serodiagnostic test. We have previously identified, cloned, and purified 5 antigenic, surface exposed, recombinant outer membrane proteins (OMPs) of *N. helminthoeca*: P51, NSP-1/2/3, and SSA. The aim of this study was to determine (1) if these recombinant OMPs will be detected by experimentally infected and clinical SPD sera, and (2) which of these recombinant OMPs, if any, will react most strongly. Preliminary Western blotting data using both experimental and naturally infected dog sera showed seroreactivity to P51, SSA, NSP1, and NSP2 but not NSP3. Both sera reacted most strongly to SSA, followed by NSP2. Future research will focus on obtaining more clinical SPD samples to perform Western blotting to support or refute this preliminary data. Furthermore, highly antigenic, surface exposed oligopeptide domains within these *N. helminthoeca* OMPs will be determined by ELISA to examine the sensitivity and specificity compared to other closely related members like *N. risticii* (the agent of Potomac Horse Fever) and *N. sennetsu* (the agent of Sennetsu Ehrlichiosis in humans). Applications of this research include development of a more rapid, sensitive, and specific immunodiagnostic test and of a vaccine for SPD.

Keywords: *Neorickettsia helminthoeca*, Salmon Poisoning Disease, Diagnosis, Molecule cloning, Bacterial Outer Membrane Proteins, Recombinant Proteins, Trematode, Western Blotting

MCB - 3

IMPROVING EFFICIENCY IN SAUGEYE PRODUCTION USING CRYOPRESERVED MILT. B.Blawut[1], M. Krcmarik[1], B. Wolfe[3], M.C. da Silva[2], R. D. Zweifel[4], D. Sweet[4], & S.Hale[4]

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Periodically, saugeye (Sander canadensis x S. vitreous) production goals have been compromised by weather-related alterations in broodstock collection seasons. Sperm cryopreservation can be used to store excess milt for long term use. Recently, hypertonic extenders have been shown to increase post-thaw motility, viability and fertility of ram (Ovis aires) sperm. The objective of this study was to assess the effect of three different extenders on cryopreserved sauger milt post-thaw motility and viability. Ejaculates from twenty males were divided into three aliquots and diluted in Rathbun (Moore 1987) extender at different osmolarities (350, 500, or 750 mosm/kg) to one billion sperm per milliliter. Samples were then diluted 1:1 with 10% dimethyl sulfoxide, distributed into 0.25 ml straws and cooled in liquid nitrogen (LN2) vapor for ten minutes prior to submersion in LN2. After cryopreservation, straws were thawed in a 21°C water bath for 30 seconds and post-thaw motility and plasma membrane integrity were assessed. Post-thaw motility and viability were significantly different ($p < 0.05$) in samples cryopreserved at different osmolalities. These methods will be further developed for scaling of cryopreservation protocols to provide fry production security during unfavorable weather conditions.

Keywords: Cryopreservation, Sperm, Wildlife

MCB - 4

THE EFFECT OF TRYPAN BLUE ON POSTERIOR CAPSULE OPACIFICATION IN AN EX VIVO CANINE MODEL BM Brash, DA Wilkie, AJ Gemensky-Metzler, HL Chandler, Department of Veterinary Clinical Sciences, The Ohio State University

Purpose. To determine if trypan blue (TB) reduces lens epithelial (LEC) or corneal endothelial cell viability. **Methods.** Tissue was harvested from canine cadavers. Cultured LECs were treated with TB at 0, 0.05, 0.1, 0.2, or 0.3% for 30, 60, or 120 seconds. Cell morphology was evaluated and an LDH viability assay performed. Cultured LECs were treated with 0 and 0.3% TB for 120 seconds and an apoptosis assay was performed to assess caspase-3 activity. To evaluate the effects of TB on *ex vivo* PCO, following mock cataract surgery, lens capsules were treated with 0 and 0.3% TB at the above times and maintained in culture for two weeks. Capsules were monitored for changes in cell density and morphology; histology was performed at experimental completion. Corneal endothelial cells were treated with 0 and 0.3% TB for 120 seconds and an LDH viability assay performed. **Results.** TB did not significantly reduce LEC density. While TB-treated LECs demonstrate higher rates of cell death compared to vehicle control, the difference was not significant. Induction of apoptotic signaling was found in TB-treated LEC cultures. *Ex vivo* PCO formation was not significantly different in any treatment group. Endothelial cells treated with TB or vehicle showed no significant differences in cell death. **Conclusions.** TB induced low levels of LEC death via apoptotic signaling cascades but was not effective at reducing *ex vivo* PCO formation. TB did not induce endothelial cell death. Funded by ACVO Vision for Animals Foundation grant (VAF2014-01). Trypan blue provided by Acrivet.

Keywords: canine, lens, cataract surgery, posterior capsule opacification, trypan blue

MCB - 5

ANTITUMOR ACTIVITY OF SELECTED CHEMOTHERAPY AGENTS ON A FELINE BRONCHIOLOALVEOLAR LUNG CARCINOMA CELL LINE. D. L. Burroughs, S. Roy, and G. Lorch. Department of Veterinary Clinical Sciences.

The prognosis for feline advanced lung cancer remains poor and new treatments are needed. Cell culture models provide a framework for identification of the most important biochemical pathways involved in tumorigenesis. Evaluation of gene and protein expression levels in biospecimens aids in the identification of molecular targets expressed in the tumor. Aberrant signaling of epidermal growth factor receptor (ERBB or EGFR) and its family members are known to be overexpressed in human non-small cell lung cancer. We hypothesized that EGFR gene amplification and protein overexpression would be present in feline bronchioloalveolar lung carcinoma (BAC). The objectives of this study were to investigate the biologic activity of cytotoxic chemotherapeutics and EGFR small molecule inhibitors on a feline BAC cell line, and evaluate EGFR gene expression and protein levels in primary BACs and associated digit metastases from two cats. Relative viability and the half-maximal inhibitory concentrations (ICs_{50}) were determined after 72 hr exposure to vinorelbine, docetaxel, paclitaxel and EGFR inhibitors, sapitinib and poziotinib. With respect to currently used cytotoxic chemotherapeutics, treatment with paclitaxel achieved the lowest IC_{50} (6.9 nM). Quantitative real-time PCR identified EGFR, EGFRvar1 and HER2 mRNA expression in all primary tumors and digit metastases. mRNA expression levels of ERBB members differed between primary lung tumors and digit tumors. Determination and quantification of tumor ERBB protein levels are being optimized. Differing expression levels of ERBB members in primary tumors *vs.* metastases suggests a pan-EGFR inhibitor might offer an effective therapeutic opportunity to manage the feline lung cancer patient.

Keywords: Feline, Lung, Cancer, Chemotherapy

MCB - 6

CANINE MODEL OF PROSTATE CANCER AND THE ROLE OF THE GASTRIN-RELEASING PEPTIDE RECEPTOR (GRPR). R. Y. Camiener, S. M. Elshafae, W. P. Dirksen, and T. J. Rosol, Department of Veterinary Biosciences, College of Veterinary Medicine, The Ohio State University, Columbus, OH, USA.

Spontaneous prostate cancer occurs in only two species: humans and dogs. The cancer has similar characteristics in both species, and canine prostate cancer can serve as an effective model for developing novel diagnostic tests and therapy. In early-stage prostate cancer (PrC), the GRPR is overexpressed, which makes GRPR a desirable molecular target. We have shown that human GRPR signaling promoted prostate cancer cell proliferation and enhanced their migration and invasion *in vitro*. Additionally, bombesin, a GRPR agonist, increased the growth of canine prostate cancer cells (Ace-1) in nude mice, forming larger tumors. However, the effects of canine GRPR and its activity in canine prostate cancer cells are not yet known. Using quantitative RT-PCR we will measure GRPR mRNA expression in canine PrC cell lines (n=5) and spontaneous tumors (n=4). We found that a subset of spontaneous canine prostate cancers had high levels of GRPR. Concurrently, we cloned canine GRPR cDNA and stably transduced an expression vector of canine GRPR into the canine prostate cancer cell, Ace-1. Our lab developed Ace-1 cells from a primary prostatic carcinoma of an eight-year-old male castrated Labrador retriever. The Ace-1 cells can be successfully transplanted to the prostate glands of cyclosporine (CYA)-treated dogs to form focal tumors. We transduced human GRPR into Ace-1 cells and injected them into canine subjects, but found that CYA-treated dogs rejected the cells. We expect to avoid an intense immunological reaction in canine subjects by using Ace-1 cells transduced with canine GRPR. This will enable us to enhance the canine PrC model to better understand the disease and develop improved diagnostics and treatments.

Keywords: Prostate, Cancer, GRPR, Canine

MCB - 7

TOPOGRAPHY INFLUENCES GLIAL AND NEURONAL MIGRATION UNDER INFLUENCE OF LAMININ IN VITRO. J Cronin[1,2]; C Czeisler, PhD[1,3]; A Short, PhD[1,4]; J Winter, PhD[1,4]; JJ Otero, MD, PhD[1,3]
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The interaction between topography and chemical substrates within the CNS has been poorly characterized with regard to CNS migration, an essential function in embryonic brain development and pathologically migrating gliomas across species. We sought to determine the contribution of scaffold topography to the migration of CNS cells by modeling different scaffolds in vitro. We mimicked two types of CNS scaffolds encountered by neural stem cells during development by constructing different diameter electrospun polycaprolactone (PCL) fiber mats, a substrate that is topographically similar to aligned brain scaffolds. We compared the effects of 10um fibers (large diameter fibers made to mimic blood vessels) with those of 800nm diameter fibers (small diameter fibers made to mimic radial glial processes) on the migration of glia and neurons. We demonstrate that glial and neuronal migration on 10um fibers is improved by laminin coating. Without laminin coating, little to no cell migration occurs on the 10um fibers. By contrast, 800nm fibers induce some degree of glial and neuronal migration without laminin, and this effect is potentiated by the presence of laminin. We also show that neurons on 10um fibers follow the migration of glia, while neurons on 800nm fibers are capable of migrating independently of glia. We propose that the physical structure of distinct scaffolds, in combination with key chemical substrates such as laminin, induces unique signaling cascades that regulate the migration of glia and neurons distinctly. These findings may have broad implications to understanding the response of CNS cells to combined topographical and chemical cues.

Keywords: CNS migration, Topography, Laminin, Embryonic brain development, Pathologically migrating gliomas

MCB - 8

ANALYSIS OF FAS-MEDIATED APOPTOSIS IN CANINE CERVICAL SPONDYLOMYELOPATHY. E. Curtis, R.C. da Costa. Department of Veterinary Clinical Sciences

Cervical spondylomyelopathy (CSM), or Wobbler Syndrome, is a common neurological disease affecting the cervical spine of large and giant breed dogs. Despite the multitude of surgical and conservative treatment options, the long-term survival of CSM-affected dogs remains unchanged. The reasons for this short-term survival are not known but may involve adjacent segment disease and apoptosis. The close proximity of the spinal cord with cerebrospinal fluid (CSF) allows us to look for biomarkers to better understand the apoptotic mechanism. We know that detection is possible via the CSF from previous work in our laboratory. Evidence in both human and animal models suggest involvement of Fas-medicated apoptosis, which led us to a working hypothesis that pro-apoptotic biomarkers caspase-3 and soluble Fas will be increased in the CSF of CSM-affected dogs compared to dogs without CSM, and will correlate with severity of neurological deficits and spinal cord compression. CSF was collected from 24 Great Dane dogs, 13 CSM-affected dogs (confirmed with magnetic resonance imaging) and 11 control dogs. A canine-specific solid-phase sandwich ELISA was sued for the quantitative determination of canine caspase-3 and soluble Fas in the CSF samples. Based on previous studies in rodents and people with traumatic brain injuries, both caspase-3 and soluble Fas were expected to have significantly increased concentrations in the CSF of CSM-affected dogs affected by CSM as compared to the control group. Neither assay showed statistically significant differences between the CSM-affected dogs and the control dogs. The lack of results could indicate a true negative result, or it may be a consequence of poor sensitivity of the assays. Discovering the detailed mechanism of apoptosis is extremely important for finding a successful treatment. Once the exact pathogenesis is discovered, the use of anti-apoptotic drugs can be evaluated in the treatment of dogs with CSM.

Keywords: Cervical Spondylomyelopathy, Wobbler Syndrome, Apoptosis, Spinal Cord

MCB - 9

THE EFFECT OF HYPOTHERMIA ON INFLAMMATORY AND GROWTH FACTOR SIGNALING PATHWAYS IN ACUTE LAMINITIS. K. Dern, M. Watts, A. van Eps, J. Belknap. Dept of Veterinary Clinical Sciences

Recent work in sepsis-related laminitis (SRL) has revealed that not only does an initial injury result in similar cytoskeletal and structural changes in the laminar epithelium as reported for equine metabolic syndrome associated laminitis (EMSAL), but that the only therapy proven to mitigate laminar damage in SRL is continuous digital hypothermia (CDH). Although early reports indicated that CDH is effective via inhibition of inflammatory signaling, we have not found this effect of CDH in late stage laminitis. Due to recent work demonstrating insulin-induced activation of laminar mTORC1/RPS6 signaling (characteristic of growth factor-related signaling) in EMSAL, we hypothesized that the same signaling is induced by STAT3 activation in SRL and that CDH blocks this signaling. We assessed laminar concentrations of activated/phosphorylated proteins of interest in Standardbred horses (n=16) administered either oligofructose (n=8) or water (n=8) in the OF model of SRL, with one forelimb maintained at ambient temperature and one limb placed in ice water (CDH) for 24h starting 12 h after OF/water administration. Laminar tissue was harvested from both forelimbs 24h after initiation of CDH. Immunoblotting revealed increased ($P<0.05$) lamellar concentrations of phosphorylated/activate forms of STAT3, p70S6K, and RPS6 in the ambient limb; CDH inhibited the activation of p70S6K and RPS6. Real time quantitative PCR assessment of laminar mRNA concentrations of pro-inflammatory cytokines, chemokines, endothelial adhesion molecules, and COX-2 revealed that CDH did not significantly decrease lamellar mRNA concentration of any of the assessed inflammatory mediators. These results confirm that similar mTORC1-related signaling occurs in the laminae in SRL as previously reported for EMSAL, and establishes an association between the protection conferred by CDH and a profound decrease in the activation of the growth factor-related signaling proteins, mTORC1 and RPS6.

Keywords: laminitis, hypothermia, mTORC1, RPS6, inflammation, sepsis-related laminitis

MCB - 10

TRACKING TRANSCRIPTOME MODIFICATIONS RESPONSIVE TO THE ESTROUS CYCLE IN THE MOUSE UTERUS. A Diedrich, C Koivisto, G Leone. College of Veterinary Medicine (Diedrich, Koivisto), School of Biological Sciences-Molecular Virology, Immunology and Molecular Genetics, College of Medicine (Leone) The Ohio State University

Endometrial cancer is the most common malignancy of the female reproductive tract. Between 80-85% are classified as type I endometrial carcinoma (EMC). One known risk factor for EMC is the persistent exposure to estrogen. We have created a reproducible mouse model of EMC (100% incidence of disease) by conditionally deleting the tumor suppressor protein Pten specifically in uterine epithelium. Based on this, we hypothesize that 1) Pten exerts is tumor suppressor effects in EMC by regulating multiple sex hormone signaling pathways and 2) hormonal changes during the normal estrous cycle plays a significant role in Pten function. To address these questions, we are collecting whole transcriptome data from wild-type FVB mice from each estrous cycle stage. This will be used to evaluate which pathways associated with Pten are responsive to hormonal signaling. These pathways will then be evaluated in heterozygous knockout Pten mice to elucidate, or rule out, their potential role(s) in the progression of type 1 EMC. We expect to find that the transcriptome of the endometrium is highly variable between stages of the estrous cycle. Along with the goal of describing the progression of type 1 EMC, we expect this data will demonstrate the critical importance of the reproductive cycle's fluctuations in the progression of other cancers.

Keywords: Endometrial Carcinoma, Pten, Estrous Cycle

MCB - 11

THE EFFECT OF HDACI (AR-42) ON CANINE PROSTATE CANCER METASTASIS. S. Elshafae[1], N. Kohart[1], L. Altstadt[1], W. Dirksen[1] and T. Rosol[1]. Department of Veterinary Biosciences[1], The Ohio State University, Columbus, OH, USA.

Canine prostate cancer (PCa) is an excellent preclinical model for human PCa. AR-42 is a novel histone deacetylase inhibitor (HDACi) developed at Ohio State University that inhibits proliferation of multiple myeloma and lung and hepatocellular cancer. We investigated whether AR-42 would prevent or decrease metastasis of PCa to bone. We measured the proliferation, cell viability, invasion, and metastasis of a canine prostate cancer cell line (Ace-1) after treatment with AR-42, and measured the expression of EMT, stem cell-related markers and anoikis resistance genes in Ace-1-treated cells. We investigated the efficacy of AR-42 to prevention PCa metastases in nude mice injected in the left cardiac ventricle with Ace-1 cells. The results showed that AR-42 inhibited proliferation of Ace-1 cells in a time and dose-dependent manner. The IC50 concentration of AR-42 for Ace-1 cells was 0.42 µM after 24 hr of treatment. AR-24 induced apoptosis and decreased the migration potential and stem cell properties of Ace-1 cells in vitro. AR-42 downregulated E-cadherin, N-cadherin, TWIST, Myoferlin, and anoikis resistance and osteomimicry genes while it upregulated Snail, PTEN, FAK and ZEB1 in Ace-1 cells. Interestingly, AR-42 decreased the number of bone metastases in nude mice and induced apoptosis and morphological changes in the metastases. These data demonstrated that AR-42 decreased the progression of PCa bone metastasis, induced apoptosis in cancer cells established in bone and diminished the effect of PCa cells on bone cells by downregulation of osteomimicry genes. Future studies will evaluate the effect of AR-42 on the PCa bone microenvironment.

Keywords; Prostate cancer, AR-42, HDACi, Metastasis

MCB - 12

INSULIN-RELATED GROWTH FACTOR SIGNALING EVENTS IN THE EQUINE LAMINAE USING A MODEL OF EQUINE METABOLIC SYNDROME. O. Hegedus, M. Watts, P. Weber, K. Woltman, J. Belknap. Dept. of Veterinary Clinical Sciences, College of Veterinary Medicine, Ohio State University, Columbus, OH (Hegedus, Watts, Balknap). Dept. of Large Animal Clinical Sciences, College of Veterinary Medicine, Michigan State University, East Lansing, MI (Weber and Woltman).

Equine metabolic syndrome associated laminitis (EMSAL) is the most common presentation of laminitis in equine practice with limited pharmaceutical options for treatment. Equine metabolic syndrome (EMS) is defined by a set of physical and pathophysiologic traits, which include regional or general adiposity and insulin dysregulation. A recently established model of EMSAL is a euglycemic hyperinsulinemic clamp (EHC) model which results in manifestations of laminitis (both clinical and histopathologic laminar changes) in approximately 48 hours. We hypothesized that insulin activates RPS6 (a protein associated with epithelial cell dysregulation in human cancers) via activation of growth factor-related signaling pathways MEK/ERK and PI3K/Akt/mTORC1, resulting in dysregulation of the laminar basal epithelial cells and thus laminar failure. In the current study, 16 healthy Standardbred horses were randomly placed either 1) on the protocol previously reported to induce laminitis in which a EHC was instituted for 48 H (or until signs of lameness, n=8), or 2) administered saline for 48 H (CON, n=8). Upon Western blot analysis of laminar samples, EHC samples have significantly increased ($p<0.05$) concentrations of phosphorylated forms of RPS6 at both Ser 240/244 and Ser 235/236 moieties (vs. controls). Additionally, EHC samples also have increased ($p<0.05$) concentrations of phosphorylated forms of signaling proteins upstream of RPS6 including p70S6K, p90RSK, Akt, and ERK 1/2. These findings provide a basis for the evaluation of potential therapeutic avenues to control signaling pathways resulting in the activation of RPS6 in an effort to prevent progression to laminar failure in horses with EMS

Keywords: Equine metabolic syndrome, laminitis, ribosomal protein S6, insulin

MCB - 13

DOWNREGULATION OF SAMHD1 EXPRESSION CORRELATES WITH INCREASED MICRORNA-181 LEVELS IN SÉZARY SYNDROME PATIENT CD4+ T-CELLS. R. Kohnken[1], K.M. Kodigepalli[1], A. Mishra[2,3], P. Porcu[2,3,4] and L. Wu[1,2,5]

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Sézary syndrome (SS) is a rare subtype of human cutaneous T-cell lymphoma (CTCL) that is characterized by aggressive spread of neoplastic CD4+ T-cells from the skin into the bloodstream with metastasis to visceral organs. The deoxynucleoside triphosphohydrolase SAMHD1 is highly expressed in normal human CD4+ T-cells, while its expression is down-regulated in CD4+ T-cells from SS patients. MicroRNA (miR) dysregulation is an important epigenetic mechanism in the pathogenesis and progression of SS. MiR-181 has been shown to inhibit SAMHD1 expression in human lymphoma and leukemia cell lines and was recently identified as an important prognostic biomarker in CTCL. However, whether SAMHD1 is down-regulated by miR-181 in primary neoplastic CD4+ T-cells from SS patients is unknown. Compared to normal CD4+ T-cells, SAMHD1 protein expression is significantly reduced in CD4+ T-cell lines derived from lymphoma or leukemia patients and primary CD4+ T-cells from SS patients, which inversely correlates with increased miR-181 levels in these cells. Over-expression of miR-181b in primary CD4+ T-cells from healthy donors significantly decreased SAMHD1 protein level, but not mRNA level. In contrast, inhibition of miR-181b in a CD4+ T-cell line increased the level of SAMHD1 protein expression. Our results demonstrate that miR-181 is an important regulator of SAMHD1 protein expression in neoplastic CD4+ T-cells, likely through a mechanism of translational inhibition.

Keywords: Sèzary Syndrome, SAMHD1, microRNA

MCB - 14

INDUCIBLE CRE-MEDIATED ABLATION OF E2F7 AND E2F8 IN THE MOUSE SMALL INTESTINE. M. Maglaty[1], M. Cuitino[2], J. Rakijas[2], and G. Leone[2]. [1]College of Veterinary Medicine; [2]Department of Molecular Virology, Immunology, and Medical Genetics, College of Medicine, The Ohio State University.

The E2fs are transcription factors that act as master regulators of cell proliferation. *In vivo* studies have shown that the atypical repressors E2f7 and E2f8 play a crucial role in the control of proliferation and apoptosis during embryonic development; their ablation leads to embryonic death by E11.5. Further studies have demonstrated their involvement in the regulation of endocycles in trophoblast cells and hepatocytes. However, their role in other tissues and the molecular pathways they regulate remain unknown. To explore how the atypical E2f repressors control proliferation *in vivo*, an inducible intestinal-specific cre transgene (Ah-cre) and conditional knockout alleles of E2f7/8 generated in the Leone lab were used. We hypothesized that ablation of E2f7/8 in the small intestine could lead to altered proliferation and disruption of the tissue architecture and function. Two-month old mice were administered β-naphthoflavone to induce Ah-cre expression and harvested 4 and 14 days later. Duodenum and jejunum were collected for histology and immunostaining of proliferation and apoptosis markers. The deletion of E2f7/8 was confirmed by PCR genotyping of DNA from isolated duodenal epithelium. No changes in intestinal histology were observed. Markers of DNA synthesis, mitosis and apoptosis are being used to quantify changes in the cell cycle and cell death. Future directions include mRNA isolation from intestinal epithelium to look for changes in expression of E2F7/8 transcriptional targets by RT-qPCR. Gaining insight into the normal functions of E2f7 and E2f8 *in vivo* will contribute to a better understanding of their implications in the pathogenesis of human disease.

Keywords: E2F7, E2F8, apoptosis, proliferation, embryonic development, cell cycle control, transcription factors, cre transgene, conditional knockout

MCB – 15

PLATFORM PRESENTATION

PRMT5 IS UPREGULATED IN HTLV-1-MEDIATED T-CELL TRANSFORMATION AND SELECTIVE INHIBITION ALTERS VIRAL GENE EXPRESSION AND INFECTED CELL SURVIVAL. A. Panfil, J. Al-Saleem, C. Howard, J. Mates, J. Kwiek, R. Baiocchi, and P. Green. Depts. of Veterinary Biosciences

Human T-cell leukemia virus type-1 (HTLV-1) is a tumorigenic retrovirus responsible for development of adult T-cell leukemia/lymphoma (ATLL). This disease manifests after a long clinical latency period of up to 2-3 decades. Two viral gene products, Tax and HBZ, have transforming properties and play a role in the pathogenic process. Genetic and epigenetic cellular changes also occur in HTLV-1-infected cells, which contribute to transformation and disease development. However, the role of cellular factors in transformation is not completely understood. Herein, we examined the role of protein arginine methyltransferase 5 (PRMT5) on HTLV-1-mediated cellular transformation and viral gene expression. We found PRMT5 expression was upregulated during HTLV-1-mediated T-cell transformation, as well as in established lymphocytic leukemia/lymphoma cell lines and ATLL patient PBMCs. shRNA-mediated reduction in PRMT5 protein levels or its inhibition by a small molecule inhibitor (PRMT5i) in HTLV-1-infected lymphocytes resulted in increased viral gene expression and decreased cellular proliferation. PRMT5i also had selective toxicity in HTLV-1-transformed T-cells. Finally, we demonstrated that PRMT5 and the HTLV-1 p30 protein had an additive inhibitory effect on HTLV-1 gene expression. Our study provides evidence for PRMT5 as a host cell factor important in HTLV-1-mediated T-cell transformation, and a potential target for ATLL treatment.

Keywords: ATLL; HBZ; HTLV-1; PRMT5; Tax; lymphoma; transformation

MCB - 16

CHARACTERIZATION OF LIVING SYNOVIAL EXTRACELLULAR MATRIX SCAFFOLDS FOR GENE DELIVERY. N. Reisbig, H. Hussein, E. Pinnell, A. Bertone. Department of Veterinary Clinical Sciences. College of Veterinary Medicine, The Ohio State University, Columbus, OH, USA.

Cartilage injury and degeneration is a leading cause of disability in humans and horses. There is currently no treatment to reverse the loss of chondrocyte function. However, regenerative cells, including synovial mesenchymal stromal cells (SMSCs) and anabolic agents, combined with scaffolds for targeted delivery is a promising option. The synovium offers the advantage of containing highly metabolic cells that readily proliferate and have been shown to secrete joint restorative substances. Synovial cells can also be genetically engineered to secrete growth factors. Our hypothesis was that decellularized synovium (synECM) seeded with synoviocytes genetically modified with Bone morphogenetic protein 2 (BMP2-SMSCs) would show enhanced scaffold migration, engraftment, and living cell counts while producing significant levels of BMP-2. Synovium from equine stifles was harvested and decellularized. Synoviocytes, from digested synovium, were either transduced with Ad-BMP-2/Green fluorescence protein (SMSCSs-BMP2/GFP) for tracking and documentation of gene delivery potential of the living scaffolds, or left as control cells (SMSCs). The synECM was seeded and incubated using a 30% fetal bovine serum gradient. The explants were examined for cell growth, CD-90 expression, viability, and morphology on day 3, 7 and 14, and the supernatant were analyzed for BMP-2, hyaluronic acid (HA) and proteoglycan (PG) secretions. Increased cell counts, cell migration into the scaffold and evidence of cell differentiation support that synECM seeded with SMSCs or BMP2-SMSCs produced a living synovial scaffold. Significant levels of BMP-2 concentrations were produced by the BMP2/GFP-SMSCs, followed by an increase in both HA and PG indicating gene production and enhanced synovial function. The results of this study suggest that synECM seeded with normal and genetically altered SMSCs may have potential for treatment of cartilage injuries.

Keywords: synovium, Bone morphogenetic protein 2, cartilage, synoviocytes, extracellular matrix scaffold.

MCB - 17

MICRORNA AS A HOST DETERMINANT OF SEVERITY IN INFLUENZA A VIRUS INFECTION. L.D. Schermerhorn*, P. Woods*, S.P. Nana-Sinkam[&]. I.C. Davis*
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[&]Division of Pulmonary, Allergy, Critical Care, and Sleep Medicine, The Ohio State University College of Medicine

As the 8th leading cause of attributable annual mortality in the USA, influenza A viruses are a significant public health concern. Severe primary influenza can result in acute lung injury (ALI), which is characterized by hypoxemia, pulmonary edema, and impaired lung function. Currently, there are few therapeutic options for patients with influenza A virus-induced ALI, especially with onset of acute respiratory distress syndrome (ARDS). MicroRNAs (miRs) are short, endogenous, non-coding RNA's that regulate expression of multiple genes simultaneously at the post-transcriptional level. miRs regulate host immunity and cell survival, and altered miR expression may contribute to the pathogenesis of other forms of ALI. Influenza A virus infection has been shown to alter miR expression at the whole lung level. We infected C57BL/6-congenic *adora1*-KO and F508del CFTR-heterozygous mice with 10,000 pfu/mouse influenza A/WSN/33 (H1N1) virus, and performed primary isolation of alveolar type-2 epithelial cells (ATII cells) as described previously. Total RNA isolation with preservation of small RNA's (<25 nucleotides) was performed. Using probes specific for *miR-155-5p*, we quantified ATII cell derived *miR-155-5p* expression in our experimental groups, finding strain-specific differences in expression and other clinical parameters. Other studies in our lab show *miR-155* induction is STAT-1 dependent, and an overall reduction of inflammatory phenotype manifests in global *miR-155*-knockout (155-KO^{G}) mice in response to infection. Further work indicates ARDS attenuation is dependent on 155-KO^{G} stromal cells, not myeloid cells, suggesting specific ATII cell dependency for the pathogenesis of ALI and ARDS. Furthermore, novel experiments in selective antagonism and inhibition of ATII cell STAT-1 phosphorylation have resulted in subsequent improvement in clinical prognostic parameters that are analogous to those used in human patients. These findings strongly suggest that *miR-155* is a previously unidentified host determinant of influenza severity, and is a valuable target for therapeutic development and intervention.

Keywords: Influenza, microRNA, acute lung injury, ARDS, qRT-PCR

MCB - 18

WNT SIGNALING IN PROSTATE CANCER GROWTH AND BONE METASTASIS.

W. Supsavhad, W. Dirksen, S. Elshafae, B. Hassan, N. Kohart, L. Altstadt and T. Rosol. Department of Veterinary Biosciences, College of Veterinary Medicine, Ohio State University

Prostate cancer is the second most common cancer in men worldwide and fatal bone metastasis occurs in 17% of patients. Ace-1-Dkk-1, a canine prostate cancer overexpressing human Dkk-1 was used in this study to investigate whether enhanced Wnt/JNK signaling could alter tumor growth, metastasis and the bone microenvironment. Evidence has shown in prostate cancer that Dkk-1 up-regulated the non-canonical Wnt/JNK pathway resulting in downstream alterations in gene expression important in bone formation, cell proliferation and epithelial to mesenchymal transformation (EMT) of tumor cells. Inhibition of non-canonical Wnt/JNK signaling using a JNK inhibitor (SP600125) significantly increased the mRNA expression of genes that induce bone formation as well as decreased bone lysis in vitro. Dkk-1 increased tumor volume in mice. When mice were injected subcutaneously with Ace-1-Dkk1, treatment with SP600125 significantly reduced tumor size and altered tumor cell morphology. However, treatment with SP600125 did not alter tumor size in mice that were injected intra-tibially with Ace-1-DKK1 cells. Inhibiting non-canonical Wnt/JNK signaling using SP600125 resulted in decreased tumor volume but did not alter tumor size in bone.

Keywords: Wnt signaling, prostate cancer, bone metastasis

MCB - 19

ROLE OF STAT3 IN PROSTATE INVOLUTION AND CANCER CELL DEATH

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Signal transducer and activator of transcription 3 (STAT3) is a transcription factor that, when activated by phosphorylation, is involved in a variety of pathways including proliferation and survival. In normal epithelial cells, STAT3 induces a pro-apoptotic response. This is also true for the mammary gland, a hormone dependent gland that involutes after the loss of hormonal signaling after lactation which displayed delayed involution in a STAT3 knockdown mouse model. Previous studies in our laboratory have shown STAT3 signaling in the prostate, another hormone dependent gland, after androgen withdrawal or castration. In prostate cancer, the common treatment involves anti-androgen drug therapy to induce involution of the gland and cancer cells. Interestingly, the role of STAT3 in prostate cancer cells is anti-apoptotic and prolongs the cancer's survival. Thus, we hypothesized that STAT3 knockout prostates would have delayed involution and decreased apoptotic markers after castration while STAT3 knockdown cancer cell lines would have increased apoptosis after androgen withdrawal. To investigate the role of STAT3 in normal prostate involution, PBCre STAT3 F/F knockout and B6 wild type (WT) control mice were castrated and harvested at either 4 or 6 days. The prostates were weighed and analyzed by immunohistochemistry and western blot for P-STAT3 and apoptotic markers. To investigate STAT3 in prostate cancer, 2 cell lines, LNCAP and LAPC4 with shRNA knockdowns for STAT3, were subject to androgen withdrawal with the growth/death measured and western blot preformed for apoptotic markers. It is important to understand the role of STAT3 in normal and cancer tissue and optimize biomedical research models to understand this potential target in cancer cell therapy.

Keywords: STAT3, castration, prostate cancer, apoptosis, androgens

STRUCTURE/FUNCTION

INTRAVENOUS ADMINISTRATION OF COBALT CHLORIDE IS ASSOCIATED WITH HEMODYNAMIC ALTERATIONS IN HORSES. Burns TA, Dembek K, Kamr A, Dooley B, Dunbar LK, Brewington S, Aarnes TK, Bednarski KS, O'Brien C, Lakritz J, Toribio RE.

Cobalt is a substance of abuse in humans and animals performing in strenuous athletic competitions. When administered at pharmacologic doses, it has been associated with induction of erythropoietin release, increased hematopoiesis, which is thought to confer competitive advantage. Cobalt chloride ($CoCl_2$) is reportedly given to racehorses to enhance performance, and recently, allowable limits for cobalt have been set by several racing jurisdictions for post-race illicit substance testing of blood and urine. While preliminary single-dose pharmacokinetic data have been published for $CoCl_2$ in horses, information regarding the effects of repeated dosing (which is how the substance is reportedly used illicitly in performance horses) is unavailable. Even fewer data have been published describing the pharmacodynamic effects of $CoCl_2$ administration in horses, particularly at high doses. The purpose of this pilot study was to describe the physiologic and biochemical effects of weekly intravenous doses of $CoCl_2$ to Standardbred horses. This report describes the hemodynamic effects of $CoCl_2$ in a dose escalation study.

Five Standardbred mares (12-13 years-old; 460-530 kg) were randomly assigned to receive one of 5 doses of $CoCl_2$ (4, 2, 1, 0.5, or 0.25 mg/kg) as an intravenous bolus (infused over 1 minute) once weekly for 5 weeks. Prior to each dose, animals were instrumented with pulmonary artery and right atrial catheters, a transverse facial artery catheter, two external jugular venous catheters, an indwelling urinary catheter, and electrocardiography leads. Physical examination parameters, blood pressure (systolic arterial pressure [SAP], diastolic arterial pressure [DAP], and mean arterial pressure [MAP]), cardiac output, and qualitative ECG assessment were evaluated every 5-10 minutes for 4 hours immediately after administration of the first and fifth weekly doses of $CoCl_2$.

All mares were subjectively anxious (nostril flaring, muscular tremor/fasciculation, pawing, straining) by 5 minutes following the $CoCl_2$ infusion; this persisted for ~60 minutes in mares receiving higher doses (4, 2, and 1 mg/kg). Mares receiving 4, 2, or 1 mg/kg doses developed tachycardia immediately after dosing (HR 60-126 bpm), but this was not observed in mares receiving 0.5 or 0.25 mg/kg (HR 36-52). Paroxysmal ventricular tachycardia was noted in the first 10 minutes post-administration in the mare receiving the 4 mg/kg dose. Elevations in SAP, DAP, and MAP were noted following drug administration at most doses; while profound hypertension was observed at 4 mg/kg (SAP/DAP, MAP [mmHg] = 291-300/163-213, 218-279), all mares became hypertensive in the 30-45 minutes following $CoCl_2$ administration. Mares receiving 4 and 2 mg/kg developed conspicuous oral mucous membrane congestion that persisted for 20 minutes post-dosing and subsequently resolved. At all doses, cardiovascular parameters returned to baseline by 1-2 hours post-administration.

Results of this preliminary study document significant, repeatable hemodynamic alterations associated with intravenous $CoCl_2$ administration to horses. Further, the degree of hypertension observed following infusion raises humane and human safety concerns if doses of >1 mg/kg are used.

Keywords: Cobalt, Horses, Cardiovascular, Hypertension, Pharmacodynamics
Performance enhancement

COR - 1

RESEARCH PATHOLOGY SUPPORT FOR EXPERIMENTAL ANIMAL MODELS PROVIDED BY THE COMPARATIVE PATHOLOGY & MOUSE PHENOTYPING SHARED RESOURCE. K. La Perle, S. Knoblaugh, J. Bolon, A. Flechtner, F. Jaynes, J. Rectenwald, A. Saulsbery, J. Sneddon. Department of Veterinary Biosciences.

The Comparative Pathology & Mouse Phenotyping Shared Resource (CPMPSR) at The Ohio State University supplies readily available, affordable, expert experimental pathology support to investigators utilizing animal models of human and veterinary disease. The CPMPSR comparative pathologists are familiar with the normal anatomy, physiology, and pathology of many animal species, including the potential impact of confounding factors such as age- and strain-related background lesions, pathogens, and husbandry practices on study outcomes. Primary research interests for the CPMPSR pathologists encompass cancer biology, developmental pathology, endocrine disease, immune-mediated conditions, neurobiology, and toxicologic pathology. However, translational research based on any animal model is supported. The CPMPSR offers a full array of pathology services, and can tailor its support to the needs of a client. Routine procedures include comprehensive macroscopic and microscopic examinations with an emphasis on phenotype characterization of newly produced lines of genetically engineered mice as well as pre-clinical efficacy and toxicity studies. Other common methods include clinical chemistry, hematology, radiography, whole slide digitization (Aperio) and quantification, frozen and paraffin slide preparation, transmission electronic micrograph grid and tissue microarray preparation, and many special histochemical and immunohistochemical staining techniques. The CPMPSR pathologists and staff are valuable collaborators for all facets of animal model development including study design, optimal sample collection, data analysis and interpretation, and communication. The CPMPSR was created to serve the experimental pathology needs of investigators at The Ohio State University, especially those in the seven health-related schools and the Comprehensive Cancer Center. However, the CPMPSR also functions as a referral service for experienced biomedical scientists at many other institutions (academic, government, and industrial).

Keywords: animal model, genetically engineered mice, histology, pathology, pre-clinical