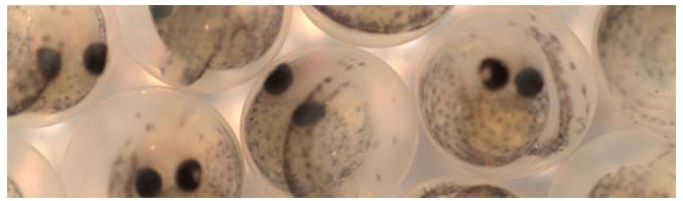


Cornell University
College of Veterinary Medicine



March 18, 2013



Clinical Investigator's Day





Cornell University

College of Veterinary Medicine

Welcome to the 2012/13 Clinical Investigators' Day sponsored by the Cornell University College of Veterinary Medicine. The primary goal of this forum is to provide an opportunity for residents and interns to showcase ongoing investigations carried out at Cornell University College of Veterinary Medicine. It is our hope that greater insights will be gained in the breadth and depth of clinical investigations conducted at the College and will serve as a catalyst to promote greater interactions among colleagues with clinical and basic science research interests.

Organizing Committee

Dr. Elizabeth Buckles, Co-Chair
Dr. Jonathan Cheetham
Dr. Gerald Duhamel
Dr. Ursula Krotscheck
Dr. Mary Martin, Co-Chair
Dr. Santiago Peralta
Dr. Tracy Stokol
Dr. Joseph Wakshlag, Co-Chair

Support Staff

Kim Eaton
Dave Frank
May Lovelace
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Judy Wood

Cover photo credits: Migrating cervical cancer cell stained for tissue transglutaminase, from Professor Richard Cerione's laboratory, fish eggs from the Aquatic Animal Health Program, Boxer dogs from Ms. Tammy Custer, remaining photos from Ms. Stephanie Specchio and communications.

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CLINICAL INVESTIGATORS' DAY

Lecture Hall I Monday, March 18, 2013 PROGRAM

8:00-8:30 **Continental Breakfast (Veterinary Education Center Atrium)**

8:35-8:45 **Welcome & Introductions – Elizabeth Buckles, Mary Martin, Joseph Wakshlag**

8:45-9:05 **Presentation – Key Note Speaker**

“STUDIES ON THE TRANSITION PERIOD IN DAIRY COWS”
Dr. Luciano Caixeta, Cornell Clinical Fellow
Department of Population Medicine and Diagnostic Sciences

9:05-10:20 **Resident Presentations**

9:05-9:20 THE EFFECTS OF SULFORAPHANE ON NEOPLASTIC CELL PROLIFERATION AND DEATH Pg.1

Vanessa Rizzo – Medical Oncology Resident

9:20-9:35 INVESTIGATION OF THE CHEMOPREVENTIVE EFFECTS OF DESLORELIN IN DOMESTIC CHICKENS WITH HIGH PREVALENCE OF OVARIAN CANCER Pg. 2

Brendan Noonan– Exotic Animal Medicine Resident

9:35-9:50 THE 5-LIPOXYGENASE INHIBITOR TEPOXALIN, INDUCES APOPTOSIS AND PTEN OXIDATIVE/ALKYLATION CHANGES IN CANINE OSTEOSARCOMA CELLS Pg.3

John Loftus – Rotating Intern

9:50-10:05 TISSUE FACTOR MEDIATES THROMBIN GENERATION IN CANINE CANCER CELLS Pg.4

Erika Gruber–Clinical Pathology Resident

10:05-10:20 TREATMENT OF NEUROPATHIC PAIN WITH MICROENCAPSULATED LIDOCAINE Pg. 5

Rohit Rajoria-Laboratory Animal Medicine Resident

10:20-10:35 **Break**

10:35-11:50

Resident Presentations

10:35-10:50 ORAL BIOAVAILABILITY, PHARMACOKINETICS AND PHARMACODYNAMICS OF SINGLE DOSE INTRAVENOUS AND ORAL TRAZODONE IN DOGS Pg. 6

Ariane Jay-Small Animal Surgery Resident

10:50-11:05 CHARACTERIZATION OF THE IMMUNE SYSTEM DURING EXPERIMENTAL REACTIVATION OF LATENT CANINE HERPESVIRUS-1 IN ADULT DOGS Pg. 7

Kay Kim-Comparative Ophthalmology Resident

11:05-11:20 The abstract of Dr. Fred Brewer has been withdrawn due to illness.

Fred Brewer IV-Cardiology Resident

11:20-11:35 DUCTAL PLATE MALFORMATION IN BOXER DOGS: CLINICAL AND HISTOPATHOLOGICAL CHARACTERISTICS Pg. 8

Smitha Pankajavally Somanathan Pillai-Anatomic Pathology Resident

11:35-11:50 MICE LACKING THE DNA DAMAGE RESPONSE GENE FANCD2 ARE HYPERSENSITIVE TO LIVER DISEASE FOLLOWING HIGH FAT DIET FEEDING Pg. 9

Elizabeth Moore-Laboratory Animal Medicine Resident

11:50-12:50

Lunch & Presentations

Career Opportunities in Research beyond Resident Training

“GRADUATE TRAINING PROGRAM IN COMPARATIVE MEDICINE”

Dr. John Parker

Associate Professor of Virology
Baker Institute for Animal Health

“RESEARCH AND TRAINING OPPORTUNITIES BEYOND YOUR RESIDENCY”

Dr. Joel Baines

James Law Professor of Virology
Associate Dean for Research and Graduate Education
Department of Microbiology and Immunology

“PANEL DISCUSSION ON CAREER PATHS”

Dr. Jon Cheetham, Dr. Erin Daugherty, and Dr. Joseph Wakshlag

Research Scientists, Clinical Veterinarian, Associate Professor of Clinical Nutrition

Key Note Speakers



Luciano Souza Caixeta, DVM, Cornell Clinical Fellow. After graduating from veterinary college at the Federal University Goiás, Brazil, Dr. Caixeta completed a residency in ambulatory and production medicine at Cornell University. As a Clinical Fellow, he is beginning his graduate studies under the mentorship of Dr. Nydam in the Department of Population Medicine and Diagnostic Sciences and Dr. Yves Boisclair in the Department of Animal Science. He is studying metabolic regulation and clinical nutritional management of transition dairy cows.

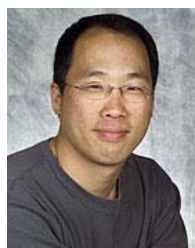


Kelly Hume, DVM, DACVIM (Oncology), Assistant Professor, Section of Oncology, Adjunct Assistant Professor, Department of Biomedical Sciences. Dr. Hume received her DVM, Cum Laude, in 2003 from Auburn University and received her Board Certification in Veterinary Internal Medicine, Specialty of Oncology, in 2008. She completed her three-year residency at North Carolina State University prior to receiving one of the first Cornell Clinical Fellows awards made in 2008. Dr. Hume's long term goals are to interact with clinician and basic scientists at all levels of cancer biology, recognizing the need to marry the two vital tracks. Mentoring and teaching undergraduate students, graduate students, and oncology residents in both clinical and molecular oncology is one of Dr. Hume's overarching career goals.

Moderators



Susan L. Fubini, DVM, Professor of Large Animal Surgery, Department of Clinical Sciences. Dr. Fubini received her DVM in 1980 from the University of Georgia and received her Board Certification in Veterinary Surgery in 1987. She completed her three-year intern and resident training at Cornell University prior to joining the College faculty. She is currently a member of the College of Veterinary Medicine's College Research Council and was recently named the Associate Chair for Promotion, Tenure, and Mentoring in the Department of Clinical Sciences. Dr. Fubini has mentored over 50 interns and residents since her tenure at the College and in 1990 received the Norden Distinguished Teacher of the Year award.



Dave Lin, Ph.D. Associate Professor of Neurobiology, Department of Biomedical Sciences. Professor Lin received his Ph.D. in 1994 from the University of California at Berkeley. He joined the college faculty in 2001 and also served as the Director of the Microarray Core from 2004-2010. Dr. Lin is the Director of Graduate Studies for Comparative Biomedical Sciences and of Genomics. He is a member of the following graduate fields: Molecular & Integrative Physiology; Pharmacology; Biochemistry, Molecular & Cell Biology; Genetics, Genomics and Development; Genomics; and Neurobiology & Behavior. Additionally, Dr. Lin is a member of the Dual Degree (DVM/PhD) Oversight Committee and Biological and Biomedical Sciences Graduate Program Oversight Committee. His laboratory focuses on the development of the nervous system using the mouse olfactory system as a model.

Moderators (Continued)



Carolyn S. Sevier, Ph.D. Assistant Professor, Department of Molecular

Medicine. Dr. Sevier received her Ph.D. in 1999 from Johns Hopkins School of Medicine. She completed her postdoctoral training at the Massachusetts Institute of Technology and was then subsequently appointed as a Research Scientist in 2004. During her postdoctoral training, Dr. Sevier was also awarded a three-year NIH National Research Service Award. Her research accomplishments center on elucidation of the fundamental molecular mechanisms used by cells to efficiently fold, process, and traffic proteins. She joined the faculty at the College of Veterinary Medicine in 2010.

Speakers



Joel Baines, VMD, Ph.D., James Law Professor Virology, Department of Microbiology and Immunology, and Associate Dean for Research and Graduate

Education. Dr. Baines received the VMD degree from the University of Pennsylvania in 1983. He then received his PhD from Cornell University in 1988, studying the molecular virology of feline coronaviruses. The Baines' laboratory is focusing on the molecular basis of herpesvirus assembly as it pertains to the discovery of antiviral targets. His work has been continuously supported by the NIH since 1995. He is also Director of the Veterinary Investigators Program (VIP) and the Cornell Clinical Fellows Program.



John S. Parker, BVMS, Ph.D., Associate Professor of Virology. Dr.

Parker received his veterinary degree from Glasgow University, Scotland, in 1983, and practiced clinical veterinary medicine for 11 years prior to pursuing a Ph.D. at Cornell University. He continued his postdoctoral training at Cornell and at the Harvard Medical School before returning to Cornell as faculty member of the Baker Institute for Animal Health. In 2005, Dr. Parker received the prestigious Burroughs Wellcome Fund award for “Investigators in Pathogenesis of Infectious Disease” and has had continuous grant support from sponsors such as the Cornell Feline Health Center, Morris Animal Foundation, NIH, and US-Israel Binational Agricultural Research Development Fund. Dr. Parker is an active teacher and strong mentor to veterinary students and veterinarians seeking advanced degree training. He is the Director of the Cornell University Leadership Program for Veterinary Students and Director of the Graduate Training Program in Comparative Medicine, both supported by the NIH and other sponsors.



Jon Cheetham, VetMB, MA, DipACVS, Ph.D. Research Scientist, Department of Clinical Sciences. Dr. Cheetham is a 1995 graduate of the Cambridge University

Veterinary School where he received his MA degree in Medical Sciences and a VetMB in Veterinary Medicine. His work focuses on restoring function in the larynx, nasopharynx and trachea using tissue engineering, reinnervation and functional electrical stimulation techniques. The lab's research is applied to both human and veterinary patients. Dr. Cheetham is board certified by the American College of Veterinary Surgeons and holds a Ph.D. from Cornell.

Speakers (Continued)



Erin Daugherty, DVM, Clinical Veterinarian, Cornell Center for Resources and Education. Dr. Daugherty graduated with a B.S in Animal Science from Cornell University in 1997. After spending two years working as a research associate at the University of Wisconsin-Madison, McArdle Laboratory for Cancer Research, she attended veterinary school at the University of Wisconsin-Madison and received her DVM in 2007. She then returned to Cornell University to complete a residency in laboratory animal medicine with the Center for Animal Resources and Education (CARE). As a resident, she joined the Robert Weiss Laboratory and completed a Clinical Fellowship in October 2012. Her research focuses on fatty liver disease and its progression to hepatocellular carcinoma. Dr. Daugherty is now a Clinical Veterinarian at Cornell, with continued work in the Weiss Lab.



Joseph Wakshlag, MS, DVM, Ph.D., Associate Professor of Clinical Nutrition, Department of Clinical Sciences. Dr. Wakshlag has been a member of the college faculty since 2006. He received his DVM at Cornell University and continued his residency training in Pathology and Nutrition at Cornell and subsequently received his Ph.D. in Pharmacology in 2005. Dr. Wakshlag is also the head of the nutrition and obesity management services in the college. He serves on a number of college and university committees, such as the Institutional Animal Care and Use Committee, Clinical Sciences Research Committee, College Research Council, serves as a mentor to trainees at all levels, including veterinary and graduate students, interns and residents, and postdoctoral fellows, and has an active clinical research program.

Judges



Bruce Akey, MS, DVM, Assistant Dean for Diagnostic Operations and Executive Director Animal Health Diagnostic Center College of Veterinary Medicine. Dr. Akey provides overall leadership and management of the Animal Health Diagnostic Center and the over 240 employees therein. The Center's clients span all 50 states as well as federal and international clients. Prior to joining the College of Veterinary Medicine in 2006, Dr. Akey served as the Assistant State Veterinarian of the New York State Department of Agriculture-Division of Animal Industry from 2003-2006 and from 1990-2003 he was Chief, Office of Laboratory Services Virginia Department of Agriculture and Consumer Services, Division of Animal Industry Services. He received his Masters of Science from the University of Florida in parasitology and his DVM from the University of Minnesota, in 1981 and 1987, respectively.



Kei Hayashi, DVM, PhD, Dipl.ACVS, Associate Professor, Department of Clinical Sciences. Dr. Hayashi joined the College faculty in February 2013 as a small animal orthopedic surgeon. Dr. Hayashi graduated from the University of Tokyo, Veterinary Medical Science in 1993 with a focus in small animal medicine and surgery and a post-doctoral degree in Veterinary Medical Science in 1997. Concurrently he also completed a post-doctoral degree in Comparative Biomedical Sciences at the University of Wisconsin. He then completed a fellowship in Small Animal Medicine and Surgery and a residency in Small Animal Surgery at the University of Wisconsin in 2003. His areas of expertise include all aspects of orthopedic surgery and minimally invasive surgery. Dr. Hayashi has numerous research publications, and has contributed to text book chapters in the field of small animal surgery.

Judges (Continued)



Sean McDonough, DVM, DipACVP, Ph.D., Associate Professor, Section of Anatomic Pathology, Department of Biomedical Sciences. Dr. McDonough obtained his DVM from Colorado State University in 1981 and engaged in small animal medicine in central Wyoming. Dr. McDonough entered the veterinary pathology residency program at the University of California, Davis in 1989 and achieved diplomate status in the American College of Veterinary Pathology in 1992. The Ph.D. in Comparative Pathology was awarded by the University of California, Davis in 1996. Dr. McDonough has been instrumental in leading the College's Residency Program in Anatomic Pathology. He has collaborated extensively with faculty and scientists throughout the world focusing on research of disease pathogenesis and gene function and genomics to help bridge the link between animal diagnostics and experimental biology. His personal research interests are to employ use of contemporary methods to explore immune function in spontaneous veterinary disease.



Bhupinder Singh, DVM, Board Certified in the American College of Laboratory Animal Medicine, Clinical Veterinarian, Cornell Center for Animal Resources and Education (CARE). Dr. Singh received his Master of Veterinary Science degree from Punjab Agricultural University in 1996, and his Educational Commission on Foreign Veterinary Graduates Certificate from Cornell in 2004. After a post-doctoral residency in Laboratory Animal Medicine at Yale, joined CARE in July 2007. He is a member of the American Society of Laboratory Animal Practitioners and American Association for Laboratory Animal Science.



David Way, Associate Director, Center for Teaching Excellence. Dr. Way has helped initiate college-wide graduate teaching development programs within the University, developed training and educational materials used throughout the university, and assisted colleges to redesign their student evaluation of teaching systems. He initiated and published the first university-wide newsletter on undergraduate education, has consulted with over 30 departments and academic fields on instructional and faculty development, and has been instrumental in the design and development of an annual faculty retreat on teaching and learning. Dr. Way teaches "Teaching in Higher Education" and is the author of the *Cornell Teaching Evaluation Handbook*. He has been involved in the University Self-Study Working Group on Assessment of Student Learning and on the Vice Provost for Undergraduate Education's Core Assessment Committee. Dr. Way is also the Center for Teaching Excellence Liaison for the College of Veterinary Medicine. He has facilitated several educational workshops and seminars on effective communications skills for students, residents, staff, and faculty in the College during his more than 30 year tenure at Cornell.

Name/Degrees: **Vanessa Rizzo, DVM**

Email: vlr33@cornell.edu



<u>Institution and location (Chronological)</u>	<u>Degree</u>	<u>Year</u>
Western University of Health Sciences, Pomona CA	DVM	2010
Cornell University, Ithaca NY	Residency	2011- present

Current Position: Resident, Medical Oncology - 2nd year

Abstract Title: THE EFFECTS OF SULFORAPHANE ON NEOPLASTIC CELL PROLIFERATION AND DEATH

Authors Names: Vanessa L. Rizzo, Cornell University; Joseph Wakshlag, Cornell University; Jessica Chandler, Cornell University

Project Mentor(s): Joseph Wakshlag, Department of Clinical Sciences (Mentor), Kelly Hume, Department of Clinical Sciences (Co-mentor), Robert Weiss, Department of Biomedical Sciences (Co-mentor)

Abstract:

Introduction: Recent evidence in human cancer patients and rodent models suggests that the nutraceutical sulforaphane (typically found in raw cruciferous vegetables) may have utility in prevention of cisplatin induced renal toxicity, however there is little examination on its effects on cancer cells with or without conjunctive chemotherapeutics.

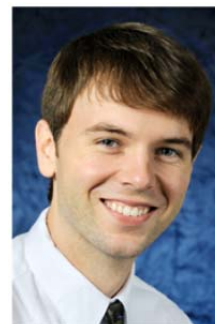
Methods: To examine the potential safety and effects on canine cancer cells three canine cell lines were treated with a serial dilution of sulforaphane (0-50 uM) for 48 hours and 6 day growth curve assays were performed using MTT assays. Apoptosis was examined using annexin V staining, or caspase 3 immunoblotting. Further viability assays were performed to examine sulforaphane treatment in conjunction with either palladia (mast cells) or doxorubicin (osteosarcoma). Statistical analysis was performed using analysis of variance with Tukey's post hoc analysis or Student's T test to determine significance.

Results: Results suggest that all cell lines have reduced cell viability in both the 48 hour MTT proliferation and the growth curve analysis at between 2 and 3 uM of sulforaphane ($p < 0.05$) with apoptosis occurring in two of the three cell lines (mast cells and osteosarcoma cells) at concentrations between 10-20 uM. Sulforaphane did not promote cell survival nor did it promote further cell death in the face of other chemotherapeutic insults in mast or osteosarcoma cells.

Conclusion: Further mechanisms for reduced cell viability are being examined, however sulforaphane does not confer a survival advantage for these cell lines making it a potential nutraceutical to investigate for chemotherapy-induced renal cytotoxicity.

Name/Degrees: **Brendan Noonan, DVM**

Email: bpn3@cornell.edu



<u>Institution and location (Chronological)</u>	<u>Degree</u>	<u>Year</u>
Cornell University, Ithaca NY	DVM	2009
Broward Avian and Exotic Animal Hospital, FL	Internship	2009-2010
Cornell University College of Veterinary Medicine	Residency	2011-present

Current Position: Resident, Exotic Animal Medicine – 3rd year

Abstract Title: INVESTIGATION OF THE CHEMOPREVENTIVE EFFECTS OF DESLORELIN IN DOMESTIC CHICKENS WITH HIGH PREVALENCE OF OVARIAN CANCER

Authors Names: Brandan Noonan,¹ Elizabeth Buckles,² Alexander Nikitin,² Patricia Johnson,³ Ricardo de Matos¹

¹Department of Clinical Sciences, College of Veterinary Medicine, Cornell University

²Department of Biomedical Sciences, College of Veterinary Medicine, Cornell University

³Department of Animal Sciences, College of Agriculture and Life Sciences, Cornell University

Project Mentors: Ricardo de Matos (mentor), Alexander Nikitin (co-mentor)

Abstract:

The domestic chicken is the only naturally occurring model of human ovarian cancer. The goals of the study were to: 1) evaluate safety and efficacy of deslorelin implants in inhibiting egg laying activity, and 2) evaluate cancer prevention properties of deslorelin implant in a strain of domestic chickens with high prevalence of ovarian cancer. Thirty actively laying 2 year old chickens were randomly assigned to 1 of 3 groups (10 birds per group): 1) placebo, 2) 4.7mg or 3) 9.4mg deslorelin implant. All birds were evaluated (weight, ultrasound examination of the reproductive tract) weekly for one month and once a month after for 12 months. Egg laying activity was recorded daily. Within two weeks of implant application, 100% of the birds with drug implant presented suppressed ovary activity. All placebo birds continued to lay eggs and presented normal follicular activity on ultrasound examination. The mean duration of inhibition was 180 days for the 4.7mg group and 319 days for the 9.4mg group. After 12 months, a second implant was placed in 50% of the remaining birds in each treatment group. Monitoring was as described above for an additional 10 months. Postmortem exam was performed in all birds euthanized or that died during the study period. After 22 months of observation, ovarian cancer incidence was 50% for the placebo group, 10% for the 4.7mg group and 0% for the 9.4mg group. This data suggests chemopreventive effect of deslorelin in a strain of domestic chickens with high incidence of ovarian cancer.

Name/Degrees: **John Loftus, DVM**

Email: jpl249@cornell.edu

Institution and location (Chronological)
University of Massachusetts, Boston MA
Cornell University, Ithaca, NY

<u>Degree</u>	<u>Year</u>
Ph.D.	2008
DVM	2012



Current Position: Rotating Intern

Abstract Title: THE 5-LIPOXYGENASE INHIBITOR TEPOXALIN, INDUCES APOPTOSIS AND PTEN OXIDATIVE/ALKYLATION CHANGES IN CANINE OSTEOSARCOMA CELLS

Authors Names: John Loftus, Derek Cavatorta, Carolyn Sevier, Joseph Wakshlag - Cornell University College of Veterinary Medicine, New York

Project Mentor: Joseph J Wakshlag, Department of Clinical Sciences

Abstract:

5-Lipoxygenase (5-LOX) inhibition has been shown to induce apoptosis in many epithelial cell lines; however, their utility in cancer has not been fully elucidated due to observed side effects in-vivo. Though various inhibitors of 5-LOX have been examined in epithelial cells, relatively little work has been performed on other cell lines including round cell or sarcoma cells. Considering the utility and common use of the 5-LOX inhibitor tepoxalin in veterinary medicine, we chose to examine the utility of this unique dual 5-LOX/COX inhibitor using canine osteosarcoma cell lines as a model to determine if tepoxalin was cytotoxic to three different canine osteosarcoma cell lines. Results suggest that tepoxalin, but not its COX inhibiting metabolite (RWJ20142), is cytotoxic and can induce apoptosis in all OSA cell lines examined between 1-10 μ M, with varying sensitivity as observed through caspase 3 activation and annexin staining. Interestingly, apoptosis is superseded by oxidative damage induced by tepoxalin as measured by activation of dihydrorhodamine 123 and mitosox, but not the COX inhibiting metabolite (RWJ20142). Additionally, 5-LOX inhibition by tepoxalin appears to allow phosphagen and tensin homolog (PTEN) activation by either altering alkylation or oxidation, which diminishes its ability to inactivate phosphoinositide-3-kinase thereby heightening activation of protein kinase B (AKT) phosphorylation prior to the apoptotic response, suggesting that oxidation is the major mechanism for tepoxalin's cytotoxic effects, while lipoxygenase inhibition might also play a role through protein alkylation changes.

Name/Degrees: **Erika Gruber, DVM**

Email: ejg33@cornell.edu

Institution and location (Chronological)

Cornell University, Ithaca, NY
Colorado State University, Ft. Collins, CO
Cornell University

Degree

DVM
Internship
Residency

Year

2006
2007
2013



Current Position: Resident, Clinical Pathology, 3rd year

Abstract Title: TISSUE FACTOR MEDIATES THROMBIN GENERATION IN CANINE CANCER CELLS

Authors Names: Erika Gruber, Cornell University; James Catalfamo, Cornell University; Tracy Stokol, Cornell University.

Project Mentor: Tracy Stokol, Department of Population Medicine and Diagnostic Sciences

Abstract: (\leq 250 words)

Hypercoagulability is a recognized paraneoplastic syndrome in dogs and humans. Tissue factor (TF), the main activator of coagulation, is upregulated in numerous human and canine cancers and may play a role in altered hemostasis in these disorders. Furthermore, TF and thrombin, a product in the coagulation cascade, both engage in cell signaling pathways that influence tumor growth and metastasis. We hypothesized that high-TF expressing cells from a canine mammary tumor (CMT25) would generate more thrombin than low-TF expressing cells from a canine osteosarcoma (HMPOS). Thrombin generation potential (TGP) of suspended cells was measured with a kinetic assay using microparticle-free canine or human plasma and a fluorogenic thrombin-specific substrate, with no additional trigger or phospholipid reagents. Compared with HMPOS, CMT25 cells had shorter lag time (average 3.1 versus 6.9 minutes, $p=0.045$; unpaired t test) and greater thrombin generation (average area under the curve, 3693 versus 809 nM*minutes, $p=0.009$). TGP of CMT25 cells was markedly reduced in human factor VII-deficient plasma compared to human control plasma. TGP of CMT25 cells was independent of contact activation since it was unaffected by corn trypsin inhibitor (CTI) or factor XII deficiency. In contrast, TGP of HMPOS cells was inhibited by CTI. We conclude that TGP is driven largely by TF expression in the two evaluated cancer cell lines. Since TF and thrombin have roles in cancer biology independent of thrombosis, characterization of their expression and activity in specific tumors may lead to the development of novel therapeutic agents targeting these proteins in canine cancer patients.

Name/Degrees: **Rohit Rajoria, DVM**

Email: rr427@cornell.edu

Institution and location (Chronological)

St. George's University, Grenada, West Indies
Cornell University, Ithaca New York

Degree

DVM
Residency

Year

2011
Current



Current Position: Resident, Laboratory Animal Medicine – 2nd year

Abstract Title: TREATMENT OF NEUROPATHIC PAIN WITH MICROENCAPSULATED LIDOCAINE

Authors Names: Rohit Rajoria¹, Bhupinder Singh¹, Teresa Southard², L Masinde³, Todd Pavek¹

¹Center for Animal Resources and Education (CARE), Cornell University, Ithaca, NY

²College of Veterinary Medicine: Biomedical Sciences, Cornell University, Ithaca, NY

³Capsulated Systems, Inc., Yellow Springs, OH

Project Mentor: Todd Pavek, DVM, DACLAM.

Abstract:

Neuropathic pain (NPP) is a type of chronic pain that can result from numerous medical conditions whether localized or systemic. NPP is characterized by exaggerated responses to painful (hyperalgesia) and non-painful stimuli (allodynia) that frequently becomes a chronic condition leading to progressive reduction in quality of life. The goal of this study is to assess effectiveness and duration of effect for locally and systemically administered lidocaine prepared in sustained release formulation (MicroEncapsulation; ME). The ME substance used to encapsulate the lidocaine is the primary component of commonly used absorbable sutures.

A commonly accepted model of NPP, known as Chronic Constrictive Injury (CCI), leads to a normal inflammatory process through constrictive ligature with chromic gut suture which acts as a potent irritant to the sciatic nerve of the rat. This peripheral neural irritation results in a reduced pain and mechanical irritation threshold for the dermatomes supplied by the sciatic nerve. Two common methods for objective measurement of NPP are: 1) pain threshold reduction (thermal withdrawal latency-TWL); and 2) presence of allodynia (Von Frey fiber apparatus- VFTS). Preliminary data (n=7) suggest that extended relief of NPP results from one intraoperative dose of ME lidocaine (MEL) at days 5, 7, and 10. However, systemic administration of MEL does not appear to provide relief of NPP at any time point so far. This study provides objective parameters to identify an appropriate method and dose for ME lidocaine that can provide adequate analgesia for a longer duration (vs. standard lidocaine) in cases of NPP.

Name/Degrees: **Ariane Jay, DVM**

Email Address: arj23@cornell.edu

Institution and location (Chronological)

Cornell University, Ithaca, NY

Cornell University, Ithaca, NY

Cornell University, Ithaca, NY

Degree

DVM 2010

Internship 2010-2011

Resident 2011-2014

Year



Current Position: Resident, Small Animal Surgery, 2nd year

Abstract Title: ORAL BIOAVAILABILITY, PHARMACOKINETICS AND PHARMACODYNAMICS OF SINGLE DOSE INTRAVENOUS AND ORAL TRAZODONE IN DOGS.

Author(s) Names: Ariane R. Jay, Ursula Krotscheck, Elizabeth Parsley, Lisa Terezakis, Ariel Kravitz, Abby Mulligan, Wayne S. Schwark

Cornell University, College of Veterinary Medicine

Project Mentor: Ursula Krotscheck, Department of Clinical Sciences

Abstract:

Objective: To determine absolute bioavailability(%F), pharmacokinetics, and pharmacodynamics of trazodone in healthy dogs following IV and oral administration.

Animals: 6 beagle dogs.

Procedures: Dogs received trazodone HCl at 8mg/kg orally and intravenously in a randomized controlled crossover design. Blood samples were collected prior to drug administration and at 5, 15, 30, 60, 120, 240, 480, 720, 1080, and 1440 minutes. Heart rate, blood pressure, anxiety score, and sedation score were obtained. Plasma trazodone concentrations were determined by ultra-high performance liquid chromatography. Data were subjected to non-compartmental analysis with area under the time-concentration curve calculated using the trapezoidal model. Additional variables determined were elimination half-life($t_{1/2}$), plasma total body clearance(CIT), apparent volume of distribution(Vd), mean residence time(MRT), maximum plasma concentration(Cmax), and time to maximum plasma concentration(Tmax).

Results: Following IV administration the mean \pm SD $t_{1/2}$, Vd, CIT were 169 \pm 53 min, 2.53 \pm 0.47 L/kg, and 11.15 \pm 3.56 ml/min/kg, respectively. Following oral administration the mean \pm SD $t_{1/2}$ and %F were 166 \pm 47 min, and 84.6 \pm 13.2%, respectively. Cmax following oral administration was 1.3 \pm 0.5 ug/ml, and Tmax was 445 \pm 271 min. After IV administration all dogs experienced immediate transient tachycardia (184.3 \pm 8.0 bpm), and 3/6 dogs experienced aggression. Increase in heart rate was significantly associated with increase in drug level following IV administration. Sedation and anxiety scores were not significantly correlated with drug level.

Clinical Relevance: Oral administration results in acceptable %F, though Tmax is highly variable. Individualized approaches in dosing intervals may be necessary for dogs receiving trazodone. Oral doses of 8mg/kg trazodone are well tolerated in dogs.

Name/Degrees: **Kay Kim, VMD**



Email: kk656@cornell.edu

<u>Institution and location (Chronological)</u>	<u>Degree</u>	<u>Year</u>
University of Pennsylvania, Philadelphia PA	VMD	2008
Michigan State University, East Lansing MI	Internship	2008-2009
Cornell University, Ithaca NY	Residency	2010-present

Current Position: Resident, Comparative Ophthalmology, 3rd year

Abstract Title: CHARACTERIZATION OF THE IMMUNE SYSTEM DURING EXPERIMENTAL REACTIVATION OF LATENT CANINE HERPESVIRUS-1 IN ADULT DOGS

Authors Names: Kay Kim, Julia Felipe, Eric Ledbetter, Cornell University, College of Veterinary Medicine, Ithaca -- New York

Project Mentor: Eric Ledbetter, Department of Clinical Sciences (Co-mentor)
M. Julia Felipe, Department of Clinical Sciences (Co-mentor)

Abstract:

Purpose. To characterize the immune status during canine herpesvirus-1 (CHV-1) reactivation in latently infected dogs.

Methods. Adult beagles with experimentally induced CHV-1 latent infections were administered a viral reactivation stimulus (prednisolone 3mg/kg orally once daily for 7 days). All dogs had complete ophthalmic examinations performed every 3 days for the duration of the 30 day study. Conjunctival swab and blood samples were collected at intervals for CHV-1 PCR, CHV-1 neutralizing antibody titers, complete blood counts, lymphocyte phenotyping and proliferation assays, and interferon gamma (IFN-gamma) production in vitro.

Results. Clinical examination revealed abnormalities consistent with recurrent CHV-1 ocular disease in all 10 dogs by study day 6. Ocular CHV-1 shedding was detected by PCR in three dogs (30%) between study days 9 and 15. CHV-1 neutralizing antibody titer elevations (1.5 to 4-fold) were detected in 7 dogs (70%) by study day 15. Median lymphocyte count did not vary during the study period. Proportion of lymphocytes expressing CD4, CD8, CD21, and MHC class I and II markers increased by study day 7, and returned to baseline values on study days 14 and 21. Lymphocyte proliferation index and IFN-gamma production in vitro were maintained during the study period.

Conclusions. Viral reactivation was achieved using immunosuppressive therapy; however, immunologic testing did not reveal an expected systemic immunosuppression. These findings contrast with previous publications that indicate a direct effect of prednisolone on lymphocyte number, distribution and function in dogs. It is possible that concomitant viral reactivation changes the systemic immunologic effect of the immunosuppressive agent.

Name/Degrees: **Smitha Pankajavally Somanathan Pillai, BVSc, MVSc, PhD**

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<u>Institution and location (Chronological)</u>	<u>Degree</u>	<u>Year</u>
Kerala Agricultural University	BVSc	2003
Kerala Agricultural University	MVSc	2005
The Ohio State University	Ph.D.	2009

Current Position: Resident, Anatomic Pathology

Abstract Title: DUCTAL PLATE MALFORMATION IN BOXER DOGS: CLINICAL AND HISTOPATHOLOGICAL CHARACTERISTICS

Authors Names: Smitha Pankajavally Somanathan Pillai, Sharon Center; Sean McDonough, Cornell University, College of Veterinary Medicine

Project Mentor: Sharon Center, Department of Clinical Sciences (Mentor); Sean McDonough, Department of Biomedical Sciences (Co-mentor)

Abstract:

Ductal plate malformations (DPM) reflect persistence of excess embryonic biliary structures and fibrosis in portal tracts. We suspected predisposition of Boxer dogs for DPM based on biopsy submissions to the Section of Anatomic Pathology.

Methods: Electronic databases (1996-2012, College of Veterinary Medicine) identified 110 Boxers; n=10 with DPM. Digitally scanned slides stained with H&E and Masson's trichrome were used to quantify portal expansion and fibrillar collagen; DPM dogs were compared to age-matched Boxer controls (n=5, Wilcoxon rank sum test, P<0.05). Immunohistochemical analyses used antibodies against Cytokeratin 19 (CK19) and collagen IV.

Results: Incidence was 9.1%, without gender predisposition, presenting age was 1.0 (0.3-1.7) and survival was 6.5 (0->10) years. Clinical features included gastrointestinal signs, weight loss, and increased liver enzymes. Most livers were grossly normal or finely nodular. Portal tracts were markedly expanded/bridged with collagen with intact limiting plates. Numerous bizarre dilated bile ducts, hyperplastic arterioles, and occasional inflammatory infiltrates were present in portal tracts. DPM portal tract area (9.8% [5.2-17.8]) was significantly higher than controls (3.7% [3.0-5.2]), P=0.05. Fibrillar collagen was increased (not significantly, P=0.09). Ductular epithelium was normal and well differentiated having strong CK19 immunoreactivity. Portal tracts exhibited strong type IV collagen immunoreactivity.

Conclusion: DPM Boxers present early (<2 yrs), have vague gastrointestinal signs or increased liver enzymes, and may survive >10 years. Histopathological features recapitulate those described in humans including: >2.5-fold expansion of portal tracts, increased type I and IV collagens, strong CK19 immunoreactivity (well differentiated biliary epithelium) and type IV collagen (fetal collagen) in portal tracts.

Name/Degrees: **Elizabeth Moore, DVM**

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<u>Institution and location (Chronological)</u>	<u>Degree</u>	<u>Year</u>
Cornell University, Ithaca, NY	DVM	2012
Cornell University, Ithaca, NY	Residency	2012-2015

Current Position: Laboratory Animal Medicine Resident, Center for Animal Resources & Education- 1st Year

Abstract Title: MICE LACKING THE DNA DAMAGE RESPONSE GENE FANCD2 ARE HYPERSENSITIVE TO LIVER DISEASE FOLLOWING HIGH FAT DIET FEEDING

Authors Names: Elizabeth Moore*[^], Erin Daugherty*, Gabriel Balmus[^], Teresa Southard[^], Robert Weiss[^] *Cornell University, Center for Animal Resources and Education, Ithaca, NY
[^]Cornell University, Department of Biomedical Sciences, Ithaca, NY

Project Mentor: Robert Weiss, Biomedical Sciences (mentor); Erin Daugherty, CARE (co-mentor)

Abstract:

Introduction: Fanconi anemia (FA) is a phenotypically and genetically heterogeneous genomic instability disease affecting 1 in 131,000 people in the United States, with 1 in 181 people being heterozygous at an FA locus. The FA pathway consists of at least 15 genes and responds to polymerase blocking lesions. FA phenotypes include developmental defects, cancer predisposition, and increased susceptibility to genetic stress. The endogenous sources of DNA damage to which FA-deficient cells are sensitive are poorly understood. We employed a *Fancd2*^{-/-} mouse model to test the hypothesis that lipid oxidation products are a source of endogenous damage repaired by the FA pathway.

Methods: *Fancd2*^{-/-} and control mice were placed on a standard diet (SD) or a high fat diet (HFD) at weaning for 8 or 12 weeks. Complete blood counts, serum chemistries, and liver and body weight were analyzed. Histological sections were scored for cellular and nuclear atypia, fibrosis, vesiculation, and bile duct hyperplasia. TUNEL was utilized to quantify apoptosis, and hepatic expression of DNA damage response genes was quantified by qPCR.

Results: HFD fed *Fancd2*^{-/-} mice had elevated liver enzymes, increased bile duct hyperplasia, elevated hepatic apoptosis, and increased expression of the DNA damage response gene p21 compared to HFD fed *Fancd2*^{+/+} controls.

Conclusion: *Fancd2*^{-/-} mice have more severe HFD-induced hepatic pathology, and increased expression of DNA damage response genes compared to controls. These results suggest that *Fancd2*^{-/-} mice are deficient in repairing HFD induced damage and have important implications for dietary management of FA patients.

Name/Degrees: **Kate Breyer, DVM**

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<u>Institution and location (Chronological)</u>	<u>Degree</u>	<u>Year</u>
University of Illinois, Urbana-Champaign IL	DVM	2010
Cornell University, Ithaca, NY	Residency	2010-present

Current Position: Resident, Laboratory Animal Medicine, 3rd year

Abstract Title: EVALUATING THE EFFICACY OF A LOW-DOSE GARLIC COMPOUND AGAINST AEROMONAS SALMONICIDA IN RAINBOW TROUT

Authors Names: Kate E. Breyer¹, Rod Getchell², Greg Wooster², George Ketola,³ Paul Bowser¹

¹Cornell University, Center for Animal Resources and Education

²Cornell University, Department of Microbiology and Immunology, Aquatic Animal Health Program,

³ Tunison Laboratory of Aquatic Science, Great Lakes Science Center, U.S. Geological Survey, Cortland NY

Project Mentor: Paul Bowser, Department of Microbiology and Immunology; Kirk Maurer (formally of Cornell University's Center for Animal Resources and Education)

Abstract:

Nutritional supplements have long been used to increase immunity and thereby decrease rates of disease in many species; this may be especially important in aquatic medicine, where antibiotic usage is limited. Allicin, the active component in garlic, has proven antimicrobial activity against many pathogens and may upregulate non-specific immune defenses. The purpose of this study was to determine if allicin is a safe and effective feed supplement to promote immunity and survival among young rainbow trout (*Oncorhynchus mykiss*) challenged with a modified LD50 dose of *Aeromonas salmonicida* (furunculosis). Hypotheses were 1) fish fed allicin would have increased survivability against challenge with *A. salmonicida*, and 2) those fed the highest allicin dose would have the best survivability. Fish were fed diets containing 0%, 0.5%, 1.0% and 2.0% allicin for 14 days prior to bacterial challenge and were then monitored for morbidity and mortality for 28 days post-infection. Significant ($p < 0.05$) increases in survival were noted in the 0.5% and 1.0% groups with decreased survival in the 2.0% group. Quantitative PCR sampling, to determine if systemic bacterial loads varied with allicin dose, will be performed in the future. Though the mechanism is not yet well understood, it appears that a low-dose (0.5%) supplementation with allicin may promote survivability in fish challenged with *A. salmonicida* and may be a useful feed additive to promote immunity in intensive aquaculture settings.

Name/Degrees: **Marina McConkey, DVM BSc**

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<u>Institution and location (Chronological)</u>	<u>Degree</u>	<u>Year</u>
Western College of Veterinary Medicine, Saskatoon	DVM	2011
Cornell University, Ithaca NY	Intern	2012
Cornell University, Ithaca NY	Resident	2012-present

Current Position: Resident, Small Animal Surgery, 1st year

Abstract Title: EFFECT OF A PROXIMAL ABDUCTING ULNAR OSTECTOMY ON INTRA-ARTICULAR PRESSURES OF THE CANINE ELBOW EX VIVO

Authors Names: Marina McConkey¹, Ursula Krotscheck¹, Dominick Valenzano¹, Alexander Wei,² Ting Li,² Marjolein van der Meulen, Swanson Professor of Biomedical Engineering²

¹Cornell University, College of Veterinary Medicine, Ithaca NY

²Mechanical and Aerospace Engineering, Cornell University, Ithaca NY

Project Mentor: Ursula Krotscheck

Abstract:

Introduction: The ALPS (Advanced Locking Plate System) Proximal Abducting Ulnar Osteotomy (PAUL) plate was developed to treat medial compartment disease (MCD) by unloading the medial compartment of the elbow joint. Intra-articular pressure distributions in incongruent (short radius) canine elbows were measured after placement of a PAUL plate. We hypothesized the PAUL plate would reduce pressure in the medial compartment.

Methods: The medial and lateral elbow compartments of cadaveric limbs were instrumented with thin-film sensors (n=6). A 200N cyclic force with a 20 second hold was applied to each limb. Contact area (CA), mean contact pressure (mCP), and peak contact pressure (pCP) were then determined at this point, after shortening the radius 1.5mm, and after sequential placement of 2 and 3mm PAUL plates. Paired t-tests were used to compare the treatment to normal with a bonferroni correction (p<0.017 was significant)

Results: The creation of an incongruent elbow decreased the CA and increased the mCP in the medial compartment of the elbow joint (p=0.010, p=0.008). The placement of the 2mm PAUL plate decreased CA and pCP in the medial compartment (p=0.002, p=0.016) while the 3mm PAUL plate decreased CA, mCP, and pCP in the medial elbow compartment (p=0.002, p=0.001, p=0.006).

Conclusion: An incongruent canine elbow has decreased medial contact area and increased medial contact pressure compared to the normal elbow. The PAUL plate significantly decreases contact area, and mean and peak contact pressure in the medial elbow compartment and may be an effective treatment for MCD.

Acknowledgements: Supported by a Canine Health Foundation ACORN grant. All implants provided by KYON Pharma Inc.

Name/Degrees: **Whitney Knauer, VMD**

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<u>Institution and location (Chronological)</u>	<u>Degree</u>	<u>Year</u>
University of Pennsylvania	VMD	2010
Cornell University, Ithaca NY	Internship	2010-2011
Cornell University, Ithaca NY	Residency	2011-2013

Current Position: Resident, Ambulatory and Production Medicine, 2nd year

Abstract Title: THE HERITABILITY OF TONGUE LOLLING IN DAIRY CATTLE

Authors Names: Whitney Knauer, Charles Guard III, Cornell University, College of Veterinary Medicine, Ithaca NY

Project Mentor: Charles Guard III, Department of Population Medicine & Diagnostic Sciences

Abstract:

Introduction:

The most common stereotypy in dairy cattle is tongue lolling. It can develop in calves as early as ten days old. Restraint, feed restriction and isolation all have been shown to contribute to its development in heifers and lactating dairy cattle. Given the same environment, it still remains unclear why some animals develop tongue lolling behavior and others do not. The goal of this study was to investigate the heritability of oral stereotypy behavior in adult dairy cattle.

Materials and Methods:

Over a year time period during routine visits to one large predominantly Holstein dairy, animals that were observed to be tongue lolling were recorded. Sire information was retrieved from computer records.

Results:

A total of 96 cows were identified as positive for tongue lolling of which 93 had their sire recorded. A chi square test of independence between sire and tongue lolling indicated lack of independence ($p < .001$). A further analysis was performed by including the sire of the sire ($n=59$) which also indicated lack of independence with grandsire ($p < .001$).

Discussion:

The conventional wisdom holds that tongue lolling is familial. Our study clearly demonstrated that there is a genetic basis for the behavior but does not address potential environmental modifiers. Our method of identifying positive cows was specific but not sensitive as not all cows were observed.

If tongue lolling is heritable, then environment may not be the sole cause for development of the behavior.

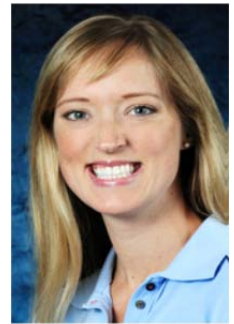
Name/Degrees: **SallyAnne Ness, DVM**

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Institution and location (Chronological)

Oregon State College of Veterinary Medicine, Corvallis
Cornell University, Ithaca, NY

<u>Degree</u>	<u>Year</u>
DVM	2008
Residency	2010-present



Current Position: Resident, Large Animal Internal Medicine, 3rd year

Abstract Title: CLINICAL AND SEROLOGIC DIAGNOSIS OF BESNOITIOSIS IN DONKEYS

Authors Names: SallyAnne Ness¹, Gereon Schares², Jeanine Peters¹, Linda Mittel¹, Jitender Dubey; Dwight Bowman¹, Hussni Mohammed¹, Thomas Divers¹

¹Cornell University, Ithaca, New York

²Friedrich-Loeffler-Institut, Federal Research Institute for Animal Health, Wusterhausen, Germany

³Animal Parasitic Diseases Laboratory, USDA, Beltsville, Maryland

Project Mentor: Thomas J. Divers, Cornell University Department of Clinical Sciences

Abstract: (\leq 250 words)

Introduction: Besnoitiosis is an emerging infectious disease of donkeys in the United States caused by infection with the protozoan parasite *Besnoitia bennetti*. Clinical disease is characterized by miliary dermatitis with parasitic cysts in the skin, nares, and sclera. Currently the only method of diagnosis is histopathologic identification of *Besnoitia* organisms within tissues.

Objective: The purpose of this study was to evaluate the utility of clinical examination and three serologic assays for the diagnosis of besnoitiosis in donkeys.

Methods: A prospective study of 416 donkeys in 6 states was performed. Donkeys were examined for clinical lesions suggestive of besnoitiosis and evaluated for antibodies against *B. bennetti* using an immunofluorescent antibody (IFA) test and 2 immunoblot assays specific for bradyzoite and tachyzoite antigens, respectively. Donkeys confirmed to be infected with *B. bennetti* by histopathology (cases; n=32) were compared to those with no clinical signs of besnoitiosis (controls; n=384).

Results: Identifying clinical lesions in 2 or more locations correctly identified infected donkeys 80% of the time. Donkeys with besnoitiosis had significantly higher IFA titers ($P < .001$) and numbers of bradyzoite ($P < .001$) and tachyzoite ($P < .001$) immunoblot bands than control donkeys. The sensitivity and specificity of the serologic assays for detecting besnoitiosis was 88% and 100% for IFA, 81% and 96% for bradyzoite immunoblot, and 90% and 100% for tachyzoite immunoblot, respectively.

Discussion: Immunofluorescent antibody and immunoblot assays are effective at identifying donkeys with besnoitiosis and provide a more efficient and less invasive diagnostic alternative to histopathology.

Name/Degrees: **Samantha Nelson, DVM, MA**

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<u>Institution and location (Chronological)</u>	<u>Degree</u>	<u>Year</u>
Whitman College, Walla Walla WA	BA	1999
University at Buffalo, Buffalo NY	MA	2001
Cornell University, Ithaca NY	DVM	2009
Cornell University, Ithaca NY	Residency	2010-present

Current Position: Resident, Small Animal Surgery, 3rd year

Abstract Title: LONG-TERM FUNCTIONAL OUTCOME OF TPLO VERSUS EXTRACAPSULAR REPAIR IN A HETEROGENEOUS POPULATION OF DOGS

Authors Names: Samantha Nelson¹, Ursula Krotscheck¹, Jeremy Rawlinson¹, Rory Todhunter¹, Zhiwu Zhang², Hussni Mohammed¹

¹Cornell University, College of Veterinary Medicine,

²Cornell University, Institute for Genomic Diversity

Project Mentor: Ursula Krotscheck, Department of Clinical Sciences (Mentor); Rory Todhunter, Department of Clinical Sciences (Co-mentor)

Abstract:

Objective: To compare the long-term outcome of tibial plateau leveling osteotomy (TPLO) and extracapsular repair (ECR) for treatment of a ruptured cranial cruciate ligament (RCCL).

Study Design: Prospective clinical trial.

Animals: Normal adult dogs (control, n = 79); dogs with unilateral CCL disease (n = 38).

Methods: Dogs had TPLO (n = 15) or ECR (n = 23) for treatment of RCCL. Force plate gait analysis was performed for the control group at one time point and for treatment groups at serial points up to one year post-operatively. Symmetry indices (SIs) were calculated between pelvic limbs for ground reaction forces (GRFs), including peak vertical force (PVF), contact time (CT), and vertical impulse (VI). GRFs of the treatment and control groups were compared using a general linear model and Kaplan–Meier survival analysis.

Results: At 8 weeks, for PVF and VI, the TPLO group had more symmetric limb loading than the ECR group at the walk and trot. SIs of the TPLO group were not different from the control group by 6 months to 1 year postoperatively. SIs for the ECR group were less symmetrical than the control group at all time periods. Using survival analysis, median time to normal function was no different at the walk between groups, but was shorter for the TPLO group for VI and PVF at the trot.

Conclusions: Dogs achieved normal limb loading faster after TPLO than ECR. TPLO resulted in operated limb function that was indistinguishable from the control population by 1 year.