Clinical Investigators’ Day 2020
Welcome to the 2020 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.

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The organizing committee thanks the following individuals who contributed to the success of the Day:

Mr. Dave Frank

Cover and CVM Images: Drew Kirby

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For more information or to participate contact:

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Program Schedule

Friday, November 6, 2020

9:00 am  Welcome & Introductions – Erin Daugherity, DVM, MS, DACLAM; Co-chair, Clinical Investigator’s Day Organizing Committee

9:00 am – 10:15 am  Resident Presentations – Moderated by Sabine Mann, VMD, PhD

- Pre-Operative CTA Underestimates Final Portal Vein Diameter in Dogs with Extra-Hepatic Portosystemic Shunts
  Denaé Campanale, DVM, MPH – Diagnostic Imaging  Pg. 1

- Assay Variability and Storage Stability of The Myeloperoxidase Index from the ADVIA® 2120i Analyzer in Canine And Equine Whole Blood Samples
  Shelley A. Chu, DVM – Clinical Pathology  Pg. 2

- Effect of Temperature and Volume Alterations on Accuracy and Trending of Transpulmonary Ultrasound Dilution Measurements
  Stephanie A. Hon, DVM – Anesthesia and Pain Medicine  Pg. 3

- Investigation of Inflammatory Proteins as Novel Diagnostic Biomarkers for Endometritis in the Mare
  Jennine Lection, DVM – Theriogenology  Pg. 4

- Identification of Synovium Secretome Factors That Protect Articular Cartilage from Catabolism For Prevention of Osteoarthritis.
  Santiago Mejia Hernandez, MVZ – Large Animal Surgery  Pg. 5

10:15 am – 10:30 am  Break

10:30 am – 11:45 am  Resident Presentations – Moderated by Elizabeth Moore, DVM

- Effects of Cisapride, Buprenorphine, and Their Combination on Gastrointestinal Transit in New Zealand White Rabbits
  Erica Feldman, DVM – Laboratory Animal Medicine  Pg. 6

- Recommendations for Administering Infraorbital and Maxillary Nerve Blocks in Cats to Minimize the Risk of Iatrogenic Trauma
  Shanna Landy, DVM – Dentistry and Oral Surgery  Pg. 7

- Fungal Flora of Rosette Quills in the North American Porcupine (Erethizon Dorsatum)
  Sara J. Sokolik, DVM – Zoological Medicine  Pg. 9
Schedule (cont.)

- *Equine Gammaherpesviruses and Equine Gastric Ulcer Syndrome — Is There a Link?*
  
  **Rachelle N. Thompson, DVM** – Large Animal Internal Medicine  
  *Pg. 10*

- *Influence of Extracellular Matrix Hydrogel Direct Injection On Tibial Nerve Regeneration*
  
  **Rebecca C. McOnie, DVM** – Equine & Farm Animal Medicine  
  *Pg. 11*

**11:45 am – 12:00 pm**  
**Lunch**

**12:00 pm – 12:30 pm**  
**Keynote Address**

*Racehorse Fetlock Fractures: Morphology, Mechanics and Maladaptation*

**Heidi Reesink, DVM; Assistant Professor, Large Animal Surgery**

**12:30 pm**  
**Award Presentations**

**Robert Weiss, DVM, PhD; Associate Dean for Graduation Education**
Keynote Speaker

Heidi Reesink, DVM, PhD, DACVP

Harry M. Zweig Assistant Professor in Equine Health, Section of Large Animal Surgery, Department of Clinical Sciences, Cornell University

Moderators

Elizabeth S. Moore, DVM, PhD

NYSTEM Post-doc Fellow, Department of Biomedical Engineering, Cornell University

Joy Tomlinson, DVM, DACVIM (LAIM)

Lecturer, Section of Large Animal Internal Medicine, Department of Clinical Sciences and Post-doc, Baker Institute for Animal Health.
2020 Judges

**Philippe Baneux, DVM, Diplomate ECLAM**
Attending Veterinarian and Director, Center for Animal Resources and Education (CARE), Cornell University

**Dr. Thomas Divers, DVM, DACVIM, DACVECC**
Rudolph J. and Katharine L. Steffen Professor of Veterinary Medicine, Department of Clinical Sciences, Cornell University

**Dr. Elisha Frye, DVM**
Extension Associate, Veterinary Support Services, Department of Population Medicine and Diagnostic Sciences and the Animal Health Diagnostic Center (AHDC), Cornell University

**Dr. John Parker, BVMS, PhD**
Associate Professor of Virology, Department of Microbiology and Immunology and the Baker Institute for Animal Health, Cornell University
Abstract Title:
Pre-Operative CTA Underestimates Final Portal Vein Diameter in Dogs With Extra-Hepatic Portosystemic Shunts

Authors Names:
Denaé N. Campanale, Julia Sumner, Mark Rishniw, Philippa J. Johnson. Department of Clinical Sciences, Cornell University, Ithaca, New York.

Project Mentor:
Mentor: Julia P. Sumner, BVSc MANZCVSc DACVS, Department of Clinical Sciences, js Sumner@cornell.edu
Co-Mentor: Phillipa J. Johnson, BVSc, CertVDI, DipECVDI, MSc, MARCVS, Department of Clinical Sciences, pjj43@cornell.edu

Abstract:
Extra-hepatic portosystemic shunts are the most commonly encountered congenital abdominal vascular anomaly of dogs and are often characterized as having varying degrees of hypoplasia of the portal vein cranial to the shunting vessel. Accurately assessing the degree of this hypoplasia is paramount for surgical planning, as it is considered an indication of the ability to completely ligate the shunting vessel without inducing potentially fatal portal hypertension. Computed tomography angiography (CTA) is often performed for pre-operative assessment of the portal vein and the portosystemic shunt. Our hypothesis was that pre-operative CTA underestimated the final diameter of the portal vein cranial to the shunting vessel, and that ligation of the shunting vessel would result in a significantly larger portal vein diameter, notably in the segment cranial to the shunt. Portal vein diameters cranial and caudal to the shunting vessel, as well as the diameter of the shunting vessel were measured using pre-operative CTA and intra-operative portovenography. The measured diameters of the shunting vessel prior to ligation were correlated on CTA and portovenography, allowing for direct comparison of the modalities. The diameter of the portal vein segment cranial to the shunting vessel was compared from pre-operative CTA and post-ligation portovenograms performed intra-operatively.

All dogs had measurable cranial portal vein segments on pre-operative CTA. Portal vein diameters cranial to the shunting vessel increased by 1-2mm (P=0.0001) following ligation of the shunting vessel. Pre-operative CTA does not provide an accurate assessment of potential portal vein diameter following ligation of the shunting vessel.
Abstract Title:
Assay Variability and Storage Stability of the Myeloperoxidase Index from the ADVIA® 2120i Analyzer in Canine and Equine Whole Blood Samples

Authors Names:
Shelley Ann Ash Chu, Tracy Stokol; Department of Population Medicine and Diagnostic Sciences, Cornell University, Ithaca, New York

Project Mentor(s):
Tracy Stokol BVSc PhD DACVP, Department of Population Medicine and Diagnostic Science, ts23@cornell.edu

Abstract:
Background
The myeloperoxidase index (MPXI) provided by ADVIA® hematology analyzers reflects the mean neutrophil myeloperoxidase staining. It is used as a marker of inflammation in animals and people, but assay variability or storage stability are unknown.

Objective
Determine MPXI precision and refrigerated storage stability in canine and equine EDTA-anticoagulated blood and compare MPXI results between two ADVIA® 2120i analyzers.

Methods
Blood from 14-16 dogs and 26 horses with various MPXI levels were assayed 4-10 times within one day for intra-assay variability. Inter-assay variability was determined from 3 human-based controls assayed over the same 20 days. Blood from 10-12 dogs and 10-11 horses were analyzed after collection and 24, 48 and 72 hours of refrigerated storage. Single run results from 18 dogs and 26 horses were compared between analyzers. Non-parametric statistics were used to compare medians.

Results
Intra-assay coefficient of variation (CV) ranged from 0.6-64% for dogs and 3-350% for horses. Inter-assay CV ranged from 10.7-15.9% and 6.2-9.8% for each analyzer. Median MPXI significantly decreased with storage in canine blood with both analyzers, whereas equine values were more variable. The two analyzers yielded significantly different results, which was influenced by calibration-associated changes in gain settings.

Conclusion
The MPXI has high variability in equine samples with less variability in canine samples. Results change randomly and unpredictably with repeat analysis over 72 hours. Equivalent results may not be obtained between analyzers. MPXI measurements are not recommended for use in clinical patients but may be useful in controlled research settings.
Abstract Title:
Effect of Temperature and Volume Alterations on Accuracy and Trending of Transpulmonary Ultrasound Dilution Measurements

Authors Names:
Stephanie Hon1, Perry Koehler1, Nikolai Krivitski2, Robin Gleed1, Manuel Martin-Flores1

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Project Mentor(s):
Manuel Martin-Flores, MV, DACVAA, Department of Clinical Sciences, mm459@cornell.edu

Abstract:
Transpulmonary ultrasound dilution (TPUD) measures cardiac output (CO) using Stewart-Hamilton principles, and conventionally employs 1mL/kg of isotonic saline at 37oC as the indicator. There are practical benefits to minimizing indicator volume and to using a room temperature indicator.

In 8 anesthetized male Yorkshire piglets, CO was measured simultaneously by pulmonary artery flow probe (PAFP; gold-standard) and TPUD. The standard TUPD indicator (1mL/kg 37oC saline) was compared with 0.5mL/kg saline at 37oC, and with 1mL/kg saline at 20oC. Cardiac output was altered pharmacologically, and by changing blood volume. Bias, limits of agreement (LOA), and percentage error (PE) were measured with Bland-Altman plots. Trending ability, that is, the accuracy for measuring changes in CO, was compared using concordance, angular bias, and radial LOA.

A negligible bias was found with all indicators, however, the LOA and PE increased from 22% to 27% and 38% when the volume of the indicator was smaller or the indicator was at 20oC, respectively. Concordance was >94% with all indicators, suggesting an unaltered trending ability with the modified indicators.

Reducing the volume of the saline indicator, or using room temperature saline, results in increased error with TPUD measurements. However, the ability of the monitor to track directional changes in CO is not affected by these alterations.
Abstract Title:
Investigation of Inflammatory Proteins as Novel Diagnostic Biomarkers for Endometritis in the Mare

Authors Names:
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1Department of Clinical Sciences, Cornell University, Ithaca, New York
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3Department of Biomedical Sciences, Cornell University, Ithaca, New York

Project Mentor(s):
Mariana Diel de Amorim, DVSc DACT DVM, Department of Clinical Sciences, md649@cornell.edu

Abstract:
Equine endometritis is a prevalent, challenging disease for practitioners to diagnose. Currently, the gold standard diagnostic is endometrial biopsy; however, the time to receive results can be lengthy. Our objective was to test for validated equine inflammatory biomarkers, in uterine low-volume lavage (LVL) fluid to work toward a rapid diagnostic. We hypothesized these inflammatory biomarkers would be increased in LVL fluid of mares with evidence of endometritis or poor biopsy grade. Thirty mares had LVL followed by endometrial biopsy. Endometrial cytology was performed from LVL pellets. Biopsies were graded by a board-certified veterinary pathologist. Mares were assigned to acute endometritis (n=3) (endometrial cytology > 1% PMNs), chronic endometritis (n=9) (poor endometrial biopsy (IIB/III)), or healthy (n=18). LVL fluid was utilized in a multiplex bead assay (Luminex Corp. Austin, TX) to quantify the levels of the following biomarkers: IFN-γ, IL-1β,IL-10,IL-17, sCD14, TNF-α, chemokine (C-C motif) ligand 2 (CCL2), CCL3, CCL5, and CCL11. Statistical analysis was performed with STATA (College Station, TX). Since the data was not normally distributed, a Mann-Whitney U test was performed to compare the levels of markers between the groups, with significance set at P-value <0.05. The following inflammatory markers were significantly increased in LVL from mares with acute and chronic endometritis as compared to healthy mares: IFN-γ (p=0.0262), CCL2 (p=0.0482) and CCL3 (p=0.0299). These three biomarkers are all pro-inflammatory cytokines, which orchestrate the response of leukocytes to endometrial changes. This study demonstrates that these pro-inflammatory markers may serve as potential diagnostic markers for equine endometritis.
**Abstract Title:**
Identification of Synovium Secretome Factors That Protect Articular Cartilage from Catabolism for Prevention of Osteoarthritis

**Authors Names:**
Santiago Mejia Hernandez, Laura E. Keller, Laila Begum, Lisa A Fortier Fortier Laboratory, Department of Clinical Sciences, Cornell University, Ithaca, New York

**Project Mentor(s):**
Lisa A Fortier, DVM, PhD, Department of Clinical Sciences, laf4@cornell.edu

**Abstract:**
Osteoarthritis (OA) is a debilitating disease resulting in morbidity and expensive treatments in human and animal patients. Current therapies for OA are palliative and do not address the underlying disease process. Our laboratory has shown that the catabolic effects of interleukin-1β (IL-1β) on cartilage are significantly reduced when cartilage is co-cultured with synoviocytes. This has led to our hypothesis that synovium secretome factor/s can be identified as novel approaches for a drug that could truly alter the disease course of OA.

Methods and Results in progress: Cartilage and synovium were collected from the femoropatellar joints of 4 horses (3-7 years old). Three groups were established: cartilage, synoviocytes, and cartilage+synoviocyte co-cultures, and +/- IL-1β was applied to each group. The catabolic effect of IL-1β on cartilage was verified by measuring matrix glycosaminoglycan (GAG) released from cartilage into the medium. Residual media containing cell secretomes was saved for proteomic analysis. Cartilage GAG in cartilage will be verified with safranin-O histochemistry. Synoviocyte matrixmetalloproteinase-3 (MMP-3) expression will be measured by qPCR where we expect IL-1β – induced MMP-3 to be decreased in synoviocytes in co-culture compared to synoviocytes alone. Samples where co-cultures protect cartilage from catabolism (retained GAG in cartilage and decreased MMP-3 in synoviocytes) will be included in proteomic analysis. We anticipate that quantitative comparative proteomics will identify proteins secreted in co-cultures that are not present in cartilage/IL-1β cultures, and that one or more of these proteins that can be further explored as disease modifying OA drugs.
Abstract Title:
Effects of Cisapride, Buprenorphine, and Their Combination on Gastrointestinal Transit in New Zealand White Rabbits

Authors Names:
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²Cornell University College of Veterinary Medicine, Cornell University, Ithaca, New York
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Project Mentor(s):
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Co-mentor(s): Bhupinder Singh, BVSc & AH, MVSc, DACLAM, Center for Animal Resources and Education, bs256@cornell.edu
Manuel Martin-Flores, MV, DACVAA, Department of Clinical Sciences, mm459@cornell.edu

Abstract:
Deleterious gastrointestinal (GI) effects of opioids include reduced GI motility, reduced fecal output, and reduced food and water consumption in rabbits. These effects can lead to GI stasis, discouraging the use of opioids in rabbits in both the research and clinical setting. Gastroprokinetic agents like cisapride are effective in promoting gastric emptying in many species, but it’s unknown if cisapride is efficacious in rabbits. Efficacy of cisapride in rabbits was assessed by measuring GI transit times, fecal output, daily body weight, and food and water intake when administered as a single agent, and in combination with buprenorphine. Ten adult New Zealand White rabbits were studied on four occasions in a crossover, randomized design, and received four treatments: oil suspension vehicle and buprenorphine, cisapride and saline, cisapride and buprenorphine, or a vehicle and saline control every eight hours for two days. GI transit time was measured by administering barium-filled spheres via orogastric tube, and monitoring feces via radiography for detection of spheres. GI transit time was significantly longer for buprenorphine groups than control groups, regardless of cisapride treatment. Fecal output, and food and water intake were lower for buprenorphine groups than control groups. Cisapride did not significantly affect GI transit, fecal output, or food and water intake. Treatment group did not significantly affect body weight. In conclusion, treatment with three times daily buprenorphine increased GI transit time, and decreased fecal output, and food and water consumption. Administration of cisapride with buprenorphine, and cisapride alone did not appear to affect GI motility.
Abstract Title:
Recommendations for Administering Infraorbital and Maxillary Nerve Blocks in Cats to Minimize the Risk of Iatrogenic Trauma

Authors Names:
Shanna K. Landy1, Aaron J. Percival1, Ian Porter1, Santiago Peralta1, Nadine Fiani1

1Department of Clinical Sciences, Cornell University, Ithaca, New York

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Co-mentor(s): Ian Porter, DVM, DACVR, Department of Clinical Sciences, irp5@cornell.edu
Santiago Peralta, DVM, AVDC, FF-AVDC-OMFS, Department of Clinical Sciences, sp888@cornell.edu

Abstract:
Oral surgery in cats is indicated to treat a variety of clinically relevant diseases and conditions such as periodontitis, tooth resorption, chronic gingivostomatitis, and traumatic maxillomandibular and dentoalveolar injuries, among others. Adjunctive analgesia provided by locoregional nerve blocks mitigates surgically induced pain and decreases systemic anesthetic requirements. However, penetrating trauma may occur to the globe or periorcular structures during nerve block administration. While uncommon, this complication can have devastating consequences including pain, hemorrhage, and endophthalmitis leading to vision loss, enucleation, or even euthanasia. In cats, this risk is exacerbated by a relatively large globe located in close proximity to the oral cavity and needle insertion sites for infraorbital and maxillary nerve blocks. To date, morphometric analysis of feline skulls has not been used to provide precise recommendations for safe administration.

The goals of this study are 1) to describe the regional anatomy associated with infraorbital and maxillary nerve blocks in cats, and 2) to develop recommendations for needle size and insertion technique to minimize the risk of iatrogenic trauma during administration of these blocks.

Morphometric data will be collected retrospectively on computed tomography scans of heads from feline patients at the Cornell University College of Veterinary Medicine. Assessment parameters include skull index, dimensions of the infraorbital canal, distances between the infraorbital canal, caudal maxilla, dentition, and globe, and the angle between the palate, infraorbital foramen, and the orbital rim. These measurements will be used to develop recommendations for safer nerve block administration in the maxillae of cats.
Abstract Title:
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Authors Names:
Shanna K. Landy¹, Aaron J. Percival¹, Ian Porter¹, Santiago Peralta¹, Nadine Fiani¹

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Abstract:
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Abstract Title:
Fungal Flora of Rosette Quills in the North American Porcupine (Erethizon dorsatum)

Authors Names:
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Project Mentor(s):
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Abstract:
The North American porcupine is a unique rodent with quills on the dorsal surface of the body which serve as a defense mechanism commonly being exposed to predators. Despite being a contaminated foreign object, porcupine quills rarely cause infection when embedded in animals or humans, however fungal endocarditis due to Lodderomyces elongisporus secondary to porcupine quill migration has been reported in a dog (Costa, 2014). L. elongisporus was recently identified as a cause of lumbosacral (rosette) dermatitis in a wild porcupine (Childs-Sanford, unpublished data). The objective was to characterize the fungal flora of rosette quills in wild NA porcupines in the northeastern US, and determine if L. elongisporus is part of this normal flora.

Quills were collected from the rosette of 11 wild adult NA porcupines that had been recently admitted to wildlife rehabilitators in NY, CT, and ME. Quills were cultured for fungal organisms, and molecular techniques were used to further differentiate Lodderomyces from Candida. All samples grew at least one fungal organism, with up to 9 fungal organisms identified, including Trichoderma sp. (n=1), Candida famata (n=1), Candida albicans (n=1), unidentifiable Candida sp. (n=1), Verticillium sp. (n=1), Penicillium sp. (n=2), Rhodotorula muciladinosa (n=1), Mucor sp. (n=1) and Lodderomyces elongisporus (n=6). L. elongisporus was isolated from 55% of samples, indicating this organism is a common inhabitant of quills in this region. Fungal organisms, especially L. elongisporus, should be considered as a possible infection risk in animals or humans that have been impaled with porcupine quills.
Abstract Title:
Equine Gammaherpesviruses and Equine Gastric Ulcer Syndrome – Is There a Link?

Authors Names:
Rachelle N. Thompson¹, Gillian A. Perkins¹, Gerlinde R. Van de Walle², Joy E. Tomlinson²

¹Department of Clinical Sciences, Cornell University, Ithaca, New York
²Baker Institute for Animal Health, Cornell University, Ithaca, New York

Project Mentor(s):
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Co-mentor(s): Gerlinde R. Van de Walle, DVM, PhD, Baker Institute for Animal Health, grv23@cornell.edu
Joy E. Tomlinson, DVM, DACVIM, Baker Institute for Animal Health, jet37@cornell.edu

Abstract:
Background: Equine gastric ulcer syndrome (EGUS) encompasses equine squamous gastric ulcer syndrome (ESGUS) and equine glandular gastric ulcer syndrome (EGGUS). The pathogenesis of ESGUS is well described by previous literature. The pathogenesis of EGGUS, however, remains poorly understood. Humans have glandular gastric mucosa as well, and gammaherpesvirus infections have been linked with gastric ulcers.

Hypothesis and Scientific Design: We hypothesize that infection of the gastric mucosa with the equine gammaherpesviruses EHV-2 and/or EHV-5 can promote ulcer development. Gastric mucosa samples from normal and ulcerated tissue are being collected from horses during gastroscopy or postmortem exam. They will be studied at a macroscopic, microscopic, and molecular, level using gross necropsy or gastroscopy exam, in situ hybridization assay, and qPCR, respectively. We will use Pearson chi-squared test at alpha = 0.05 to test whether EHV2 and EHV5 infections are more prevalent in horses with ulcers compared to horses with a normal stomach. In horses with virus-positive ulcers, we will subsequently determine whether the virus is present in an active or latent state at the ulcer site, and we will evaluate additional samples from the same horse at normal sites as well. The McNemar's test will be used to analyze these results.

Expected Outcomes: We predict EHV-2 and EHV-5 are i) more prevalent in horses with ESGUS and EGGUS than normal horses, ii) more prevalent within ulcerated tissue than normal tissue within the same horse, and iii) in an active state in the ulcerated tissue.
Abstract Title:
Influence of Extracellular Matrix Hydrogel Direct Injection on Tibial Nerve Regeneration

Authors Names:
Rebecca McOnie¹, Ethan Blum², Mike Sledziona¹, Jonathan Cheetham¹

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²Department of Biomedical Engineering, Cornell University, Ithaca, New York

Project Mentor(s):
Jonathan Cheetham, VetMB, PhD, DACVS, Department of Clinical Sciences, jc485@cornell.edu

Abstract:
Post-traumatic peripheral nerve regeneration yields fractional and untimely nerve recovery and regrowth, leading to unsatisfactory functional outcomes. A nerve-specific extracellular matrix has been effective in modulating the local microenvironment at the site of nerve injury to improve functional recovery. The peripheral nerve matrix (PNM) has been studied in a conduit model that could be replaced with a practical, direct injection technique at the site of nerve coaptation. The functional indices for evaluating gait during peripheral nerve regeneration remain labor intensive.

Direct injection of PNM at the site of nerve injury will result in superior speed and extent of nerve regeneration that can be monitored by a center of mass gait marker. In this prospective, double-blinded study, tibial nerve regeneration will be evaluated over 12 weeks in a Lewis rat model (n=30). Three groups will be compared: transection with anastomosis +/- PNM injection and crush injury. Positive and negative control groups will be established. Video of constant speed treadmill runs will be acquired to track hock angle and a center of mass marker. Gastrocnemius compound muscle action potential, peak tetanic force, and muscle weight will provide further evaluation of nerve regeneration.

During treadmill running, the magnitude of hock angle change is expected to be reflected in the center of mass oscillation amplitude. Crush injury will result in the most profound and shortest recovery. The greatest degree and duration of functional deficit is anticipated with nerve transection and anastomosis; the speed and extent of recovery will be improved with PNM injection.