

## **2018 UTCVM Research Day Faculty Abstracts**

### **BENCH TO STALLSIDE: TRANSLATION OF BASIC RESEARCH INTO CELL-BASED THERAPIES IN REGENERATIVE MEDICINE**

Madhu Dhar, David E. Anderson, Henry S. Adair, James Schumacher, Dennis Geiser

The Large Animal Regenerative Medicine Program, started in 2010 conducts research in the use of mesenchymal stem cells, biomaterials and other forms of cell-based therapies that will translate to both veterinary and human medicine. Our ultimate goal is to make basic discoveries and to expand these discoveries into the development of diagnostic modalities and treatment protocols to solve complex medical problems related to musculoskeletal, and nerve injuries. We carry out specific *in vitro* assays to evaluate cell adherence, proliferation, and potential for differentiation into osteocytes, chondrocytes, or neural-like progenitors. We then conduct controlled studies, using rodents, to confirm the biocompatibility and efficacy of mesenchymal cells used alone or in combination with biomaterials. Finally, we translate these findings into controlled, preclinical studies using large animals, including goats, sheep, pigs, and horses. We perform the *in vitro* and rodent studies to improve clinical outcomes for large animal and human patients.

### **DETECTION AND ANALYSIS OF TICK-BORNE INFECTIONS IN COMMUNAL DOGS OF ZIMBABWE**

Melissa Kennedy, Anna McRee, Riley Thompson, Canny Fung, Jessica Dawson, Roger Parry, Chris Foggin, Rebecca Trout-Fryxell, and Agricola Odoi

Tick-borne diseases pose a significant risk to humans and domestic animals, including dogs, as well as wildlife in sub-Saharan Africa. We investigated the seroprevalence of three bacterial agents carried by ticks (*Ehrlichia canis*, *Anaplasma phagocytophila*, and *Borrelia burgdorferi*) in 2012 and 2014 among 345 community dogs in Zimbabwe. In addition, detection of the agent of the most seroprevalent infection, *E. canis* was undertaken using PCR on whole blood of 241 dogs. Based on serologic testing 10%, 0%, and 73% of the dogs had been exposed to *Anaplasma*, *Borrelia*, and *Ehrlichia*, respectively. The overall prevalence of *Ehrlichia* based on the PCR results was 7.5% (18/241) all of which were *E. canis*. It is evident that, of the agents assessed, *E. canis* is the most prevalent among community dogs in Zimbabwe. This may have important implications for disease transmission among domestic as well as wild species.

Elizabeth Lennon

Inflammatory bowel disease (IBD) is a chronic, relapsing condition with no cure. IBD is a therapeutic challenge due to lack of response to therapy, medication side effects, and the need for abdominal surgery for bowel resection due to fibrosis. Our previous studies have demonstrated that mast cells are key players controlling inflammation in IBD. In particular, mast cells have anti-inflammatory functions in chronic colitis even though they are proinflammatory in acute colitis. We hypothesized that mast cells have unique anti-inflammatory mediators that are upregulated during chronic inflammation. We have identified the bone morphogenetic protein (BMP) signaling pathway to be a paracrine and autocrine pathway that is regulated by mast cells during inflammation. The aims of our laboratory's work are to 1) identify novel pathways regulated by mast cells in colitis; 2) demonstrate the signals that result in BMP7 production by mast cells, and 3) demonstrate autocrine and paracrine signaling effects of BMPs on mast cells and other immune cells. Based on RNA sequencing of colon from mice with colitis and mast cell deficiency, we found that mast cells regulate BMP and substance P signaling pathways. Based on in vitro assays, we also identified that mast cells are critical for upregulating BMP7 during inflammation. BMP7 has autocrine effects that dampen mast cells' production of TNF in response to inflammatory stimuli, and BMP7 can induce T-regulatory cell differentiation. Furthermore, we demonstrated the BMP7 intracellular signaling pathway in mast cells that has not been previously described. The mast cell-BMP7 pathway is an attractive therapeutic target in IBD, since there are no currently available medications that are both anti-inflammatory and anti-fibrotic.

**A COMPARISON BETWEEN BARBED AND NON-BARBED ABSORBABLE SUTURES FOR LONGITUDINAL THELIOTOMY CLOSURE IN AN EX-VIVO BOVINE MODEL**

Neshan Sarkisian, Pierre-Yves Mulon

**OBJECTIVE:** To determine the differences in suture time and bursting pressure on longitudinal theliotomy closures using barbed vs. smooth suture materials.

**METHODS:** Thelotomies were performed on 24 teats from freshly slaughtered beef cows divided in two groups of 12 teats: conventional suture using 3-0 polydioxanone, and sutures using 3-0 polydioxanone bidirectional barbed suture material. Time was recorded from start of the mucosal suture to the completion of the subcutaneous layer. Bursting pressure was measured by continuous distension with a colored solution using a teat cannula and pressure bag until leakage occurred.

**RESULTS:** Suturing using the barbed suture was significantly faster compared to the conventional technique. No significant difference was present in bursting pressure between the two groups.

**CONCLUSION:** Using a barbed suture material for theotomy closure on cows is a viable option given that it can appose tissue as efficiently as traditional monofilament suture in a shorter amount of time.

### **MECHANICAL EVALUATION OF CANNULATED ORTHOPEDIC SCREWS REINFORCED WITH ORTHOPEDIC CEMENT AND/OR 316L SS PINS TO ENHANCE RESISTANCE TO BENDING**

Michael Zarzosa, David P Harper, David E Anderson, Pierre-Yves Mulon

**Objective:** To improve the peak resistance to bending of cannulated bone screws.

**Methods:** 7.3-mm titanium cannulated screws (CS) were divided into 3 experimental groups: control (CS), CS/cement (CCS) and CS/cement/pins (CPCS). Screws were tested in 3-point bending to failure. Load at yield, load at failure, maximum load, displacement at failure, and modulus were calculated and recorded.

**Results:** Maximum load and break point were significantly greater for the CPCS compared with the CS and CCS. The modulus was greater for the CPCS compared with CCS and CS resulting in a significantly stiffer connector. Load at yield was greater for reinforced screws compared to CS.

**Conclusion:** Filling of orthopedic cannulated bone screws with bone cement, alone, enhanced the bending resistance of these screws in a single cycle to failure. The addition of a pin inserted after the cement produces a significantly stronger and stiffer implant.

### **ROLE OF GLUCOSE METABOLISM IN HERPES SIMPLEX ENCEPHALITIS**

Naveen K Rajasagi, Barry T Rouse

Herpes simplex virus-1 (HSV-1) is an important human pathogen without an effective vaccine. Following ocular infection the virus replicates in the epithelial tissues and is transported to the trigeminal ganglia (TG) where it establishes latency. Upon periodic reactivation, the virus multiplies in the TG and the replicating virus can reenter the cornea which could result in clinical consequences in many cases. Frequent recurrences can result in chronic inflammatory reactions in the corneal stroma which impairs vision and such recurrences can ultimately result in blindness. Although rare, the virus can spread to the brain and can cause serious complications such as encephalitis especially in immunocompromised individuals. The host immune responses, especially CD8 T cells play a crucial role in controlling virus replication in the TG and prevent spread to the brain. In mouse model of ocular infection, we found that blocking glucose metabolism using 2-deoxy glucose (2DG) resulted in increased virus spread to the brain. The majority of animals treated with 2DG succumbed to herpes simplex encephalitis (HSE). Our results demonstrated that 2DG treatment impacted the magnitude of immune responses

in the draining lymph nodes and TG. The data also showed that glucose uptake is essential for HSV specific T cell responses to be appropriately induced and function and suggest that manipulation of glucose metabolism may serve to enhance anti-viral T cell responses acting to more effectively control infection.

## **RECENT ADVANCES IN THE DEVELOPMENT OF INJECTABLE-BASED ANESTHETIC PROTOCOLS**

Reza Seddighi

Maintenance of anesthesia is commonly achieved by using inhalational anesthetics. However, despite the refinements in the pharmacodynamic characteristics of the modern inhalational agents, their use is frequently associated with moderate to severe cardiopulmonary adverse effects. These effects are more significant with the use of higher concentrations and in animals with compromised cardiopulmonary conditions and may collectively result in a substantial increase in anesthetic mortality. One of the strategies to reduce the adverse effects of inhalational anesthetics includes combining these drugs with injectable agents to decrease the concentration of inhalational anesthetics needed to maintain anesthesia. This method is known as partial intravenous anesthesia (PIVA). Another method to eliminate all potential adverse effects of inhalational anesthetics is to maintain anesthesia by solely using injectable agents, a technique that is known as total intravenous anesthesia (TIVA). A variety of injectable agents have been evaluated as a part of PIVA and TIVA protocols. In this presentation, some recent advances in the development of PIVA and TIVA combinations, with an emphasis on the results obtained in our research laboratory, will be discussed. Evidencebased clinical observations indicate a noticeable improvement in patient safety and comfort, and a decrease in anesthetic-associated morbidity and mortality with the use of such multidrug regimens.