College of Health Sciences
Faculty of Medicine & Dentistry
Anesthesiology & Pain Medicine

UNIVERSITY OF ALBERTA

13th ANNUAL GELFAN AND BELL

ANESTHESIOLOGY CONTINUING EDUCATION AND RESEARCH SYMPOSIUM

Friday May 10, 2024
Maple Leaf Room - Lister Centre

This event is an Accredited Group Learning Activity (Section 1) as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada, and approved by the University of Calgary Office of Continuing Medical Education and Professional Development.
You may claim a maximum of [3.5] hours (credits are automatically calculated)

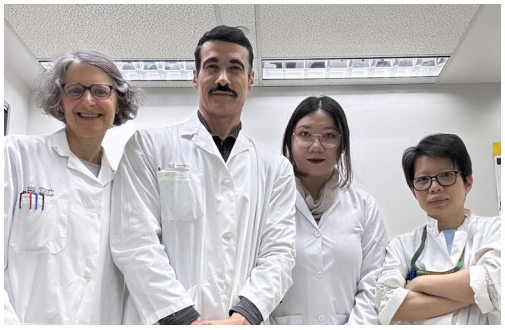
Update from the Labs

Dr. Michael Zaugg

Research in the Zaugg Lab seeks to understand the signaling networks involved in the stress response related to ischemia-reperfusion injury in mammalian cells and tissues, with the goal of translating this knowledge into potential therapies aiming at improving perioperative patient care and outcomes. In addition, we strive to understand the role of metabolic stress and of inflammatory pathways in conditions relevant to perioperative medicine such as major trauma (surgery), transplantation, cardiovascular, and thoracic surgery. Finally, we understand that the enhancement and optimization of nutritional support in surgical and critically ill patients is of great importance at a time of major stress with synthesis of key blood/tissue components and necessary for proper wound healing and recovery (regeneration).

Collaborations are always welcome and we very much support research contributing to the understanding of physiological changes (e.g. genetic, metabolome- or microbiome-related) in response to anesthesia and/or to surgical stress in patients.

The Zaugg Lab



Additional funding has been secured from

1) **Crohn's and Colitis Canada: "Protecting the gut and boosting healthy immunity during oral nutrition deprivation: role of lipid mediators and interleukin-10".** Exclusive enteral nutrition therapy (EEN, where patients receive all calories needed through formula and do not eat regular food) is used in children with inflammatory bowel disease (IBD) to induce and maintain remission by reducing inflammation of the gut and improving nutrition. It can be also used in adults with IBD, specifically frail elderly IBD patients suffering from additional diseases such as diabetes, heart failure or cancer, where the administration of strong medications with adverse side-effects needs to be minimized as much as possible. In this proposal, Dr. Zaugg's team will study a novel EEN formula containing a specific mixture of fatty acids that they developed in the past five years in their laboratories. It has unique properties, namely strong anti-inflammatory effects combined with beneficial effects on both sugar and fat metabolism in the whole body. It also boosts the immune system to efficiently counteract potentially dangerous infections. It is their hope that this novel treatment will induce remission in IBD patients more quickly and will result in a more sustained maintenance of remission. The unique mixture of fatty acids will be tested in a mouse model where they use chemicals to induce acute inflammation of the bowel mimicking IBD conditions. In these studies, they will measure gut inflammation and leakiness and also identify very specific bioactive metabolites of the administered fatty acids collectively called oxylipins and test their causal role in eliciting the beneficial effects. As some patients with severe IBD develop intestinal failure and are ultimately dependent on intravenous nutrition (total parenteral nutrition, TPN), they will further test the unique mixture of fatty acids in an intravenous nutrition mouse model where they compare their formula with a commercially available standard one. These studies will serve as proof-of-concept that the unique mixture of fatty acids is indeed beneficial in IBD and superior to currently available standard therapies (EEN and TPN). The data collected will provide the scientific evidence necessary to initiate clinical studies in IBD patients. Dr. Zaugg's team involves collaborations with pediatric gastroenterology and immunology.
2) **Canadian Institutes of Health, commercialization grant: Vegaven, a novel lipid emulsion with unique superior biological actions designed for parenteral nutrition.** Millions of patients worldwide, namely patients (including infants) with intestinal failure, critically ill, and cancer patients are dependent on life-saving parenteral nutrition (PN). Currently available. PN therapies involving intravenous administration

of a combination of fatty acids from lipid emulsions, amino acids, glucose, vitamins, and supplements often cause lipid-induced adverse immune and metabolic effects in these already vulnerable patients. Motivated by the unsatisfactory clinical outcomes such as liver toxicity with potential organ failure, diabetes-like metabolic conditions, and immunosuppression-associated infection risk in patients reliant on PN using currently available lipid emulsions, we developed a novel lipid emulsion (Vegaven) for nutritional therapy. Unlike clinically used lipid emulsions, Vegaven is rich in α-linolenic acid (ALA, C18:3 n-3) and stearidonic acid (SDA, C18:4 n-3). So far, it has been tested in vivo using a murine PN model. The published results provide clear evidence that Vegaven has unique superior biological actions. Vegaven leads to systemic upregulation of the immune-regulatory cytokine interleukin-10, promotes insulin signaling, and displays immunity-enhancing effects by generating beneficial ALA/SDA-derived oxylipins. The proposed experiments with highly relevant preclinical models (piglets, human biopsies) provide a path to Vegaven's successful clinical application and commercialization.

Selected Recent Publications

Wawrzyniak P, Hubeli B, Wawrzyniak M, Noureddine N, Walberg A, Scharl S, Turina M, Scharl M, Zaugg M, Krämer SD, Rogler G, Hersberger M. Crosstalk within peripheral blood mononuclear cells mediates anti-inflammatory effects of n-3 PUFA-rich lipid emulsions in parenteral nutrition. Clin Nutr. 2023 Dec;42(12):2422-2433. doi: 10.1016/j.clnu.2023.10.016. Epub 2023 Oct 17. PMID: 37871483

Lucchinetti E, Lou PH, Holtzhauer G, Noureddine N, Wawrzyniak P, Hartling I, Lee M, Strachan E, Clemente-Casares X, Tsai S, Rogler G, Krämer SD, Hersberger M, Zaugg M. Novel lipid emulsion for total parenteral nutrition based on 18-carbon n-3 fatty acids elicits a superior immunometabolic phenotype in the murine model compared to standard lipid emulsions. Am J Clin Nutr. 2022 ;116(6):1805-1819. PMID: 36166844

Noureddine N, Hartling I, Wawrzyniak P, Srikanthan P, Lou PH, Lucchinetti E, Krämer SD, Rogler G, Zaugg M, Hersberger M. Lipid emulsion rich in n-3 polyunsaturated fatty acids elicits a pro-resolution lipid mediator profile in mouse tissues and in human immune cells. Am J Clin Nutr. 2022;116(3):786-797. PMID: 35849016

Lucchinetti E, Lou PH, Lemal P, Bestmann L, Hersberger M, Rogler G, Krämer SD, Zaugg M. Gut microbiome and circulating bacterial DNA ("blood microbiome") in a mouse model of total parenteral nutrition: Evidence of two distinct separate microbiotic compartments. Clin Nutr ESPEN. 2022 Jun;49:278-288. PMID: 35623826

Lou PH, Lucchinetti E, Wawrzyniak P, Morsy Y, Wawrzyniak M, Scharl M, Krämer SD, Rogler G, Hersberger M, Zaugg M. Choice of Lipid Emulsion Determines Inflammation of the Gut-Liver Axis, Incretin Profile, and Insulin Signaling in a Murine Model of Total Parenteral Nutrition. Mol Nutr Food Res. 2021; 65(5): e2000412. PMID:32729969.

Dr. Bradley Kerr

Overview: Research in the Kerr lab is focusing on the neuro-immune contributions to chronic pain states arising from injury or disease in the nervous system. We have a primary focus on pain in auto-immune disorders such as MS but are also interested in pain that arises after traumatic nerve injury to a peripheral nerve. The lab employs a variety of behavioral assays to assess pain and nociception in rodents and we also use cell and molecular techniques to understand the underlying mechanisms generating chronic pain in these disorders.

The Neuroimmunology and Pain Lab is located on the 5th floor of HMRC. It is a shared research space with the lab of Dr. Jason Plemel (Dept. of Medicine). We currently have a collaborative project examining macrophage phenotypes after peripheral nerve injury and chronic inflammation that includes contributions from the UofA Multidisciplinary Pain Clinic and Dr. Bruce Dick (Dept. of Anesthesiology). Other collaborations involve members of the Dept. of Pharmacology (Dr. Anna Taylor and Dr. Harley Kurata) as well as a project with George Washington University (Lab of Dr. John Bethea) examining TNF, ER stress and the effects on neural plasticity on pain.

The Neuroimmunology and Pain Lab

Funding: The lab is currently funded by two CIHR Project Grants “Understanding the contribution of the peripheral nervous system to central neuropathic pain” and “Deciphering macrophage phenotypes in neuropathic pain”. We are also funded by an Operating Grant from the MS Society of Canada, “Examining inflammatory processes in the DRG as a driver of neuropathic pain in MS”

Dr. Stephane Bourque

The Bourque laboratory is located on the 3rd floor of the Katz Centre for Pharmacy and Health Research. My research group uses various rodent models and employs integrative and molecular approaches to investigate two broad areas of cardiovascular physiology. The first focuses on elucidating the mechanisms by which stressors (iron deficiency, sepsis) during gestation and early infancy affect growth and development of the fetus/neonate, and in turn predispose the offspring to lifelong health complications. The second focuses on identifying mechanisms underpinning the development of sepsis-induced cardiomyopathy and acute kidney injury. These projects are currently funded by grants from CIHR and WCHRI.

My research group is also actively involved in the National Preclinical Sepsis Platform of Sepsis Canada. The NPSP is a collaborative network of basic science researchers with a collective goal of conducting multi-laboratory preclinical studies on sepsis. Through an iterative process, members of the NPSP have successfully developed and characterized a standardized murine model of sepsis to harmonize study outcomes and improve data sharing. With a model in-hand, members of the NPSP are poised to conduct our first multi-centre preclinical study. This work is currently funded by grants from CIHR and Sepsis Canada.

Selected references

1. Kibalnyk Y et al. Ankrd11, a chromatin regulator and a KBG syndrome risk gene, is a critical regulator of cardiac neural crest cell biology and heart development. In press at Nat Comm. (IF: 17.69) Apr 2023.

2. Martens MD et al. Reactive Oxygen Species Modulator (ROMO1) plays an obligate role in cardiomyocyte hypertrophy. Circ Res. (IF: 23.22) 2024 Jan 5;134(1):114-116.

3. Noble RMN et al. Use of photoacoustic imaging to study the effects of anemia on placental oxygen saturation in normoxic and hypoxic conditions. In press at Reprod Sci. (IF: 2.92) Oct 2023. Manuscript selected as the most outstanding paper published in Reprod. Sci in 2023.

4. Chatterjee P et al. Sex-specific effects of prenatal hypoxia and a placental antioxidant treatment on cardiac mitochondrial function in the adult offspring. Int J Mol Sci. (IF:6.21). 2023 Sep;24(17):13624.

5. Alavi P et al. Aging is associated with organ-specific alterations in level and expression pattern of von Willebrand factor. In press at Arterioscl Thromb Vasc Biol. (IF: 10.51) 2023 Nov; 43(11):2183-2196.

6. Noble RM*, Holody CD* et al. Perinatal iron restriction is associated with changes in neonatal cardiac function and structure in a sex-dependent manner. Clin Sci (London) (IF: 6.88). 2023 Aug;137(15):1115-1130.

7. Sharma N et al. for the National Preclinical Sepsis Platform and Sepsis Canada. Development and characterization of a fecal-induced peritonitis model of murine sepsis: results from a multi-laboratory study and iterative modification of experimental conditions. Intensive Care Med Exp. (IF: 3.5) 2023 Jul;11(1):45.

8. Ssewanyana D et al. Hepcidin across pregnancy and its correlation with maternal markers of iron and inflammation, maternal body weight outcomes and offspring neurodevelopmental outcomes: A systematic review and meta-analysis. AJOG Glob Rep. 2023 May;3(3):100222.

9. Zhang M et al. Canadian Critical Care Translational Biology Group, the Sepsis Canada National Preclinical Sepsis Platform. Sex-based analysis of treatment responses in animal models of sepsis: a preclinical systematic review protocol. Syst Rev. (IF: 4.80) 2023 Mar 21;12(1):50.

10. Salim SY et al. Oncostatin M Receptor Type II knockout mitigates inflammation and improves survival from sepsis in mice. Biomedicines. (IF: 4.7) 2023 Feb 8;11(2):483.

11. Woodman AG et al. Perinatal iron deficiency causes sex-dependent alterations in renal retinoic acid signaling and nephrogenesis. J Nutr Biochemistry. (IF: 5.94) 2023 Feb;112:109227.

The Bourque Lab at Rosso

Recent Trainee Awards

In 2023-24, trainees from our research group were awarded 33 scholarships and travel awards totalling >$350,000. A few notable awards include:

1. Heart and Stroke Foundation of Canada Doctoral Personnel Awards to Ibrahim Khodabocus and Jad Julian Rachid.

2. CIHR Canadian Graduate Scholarship (MSc) to Si Ning Liu.

3. FoMD 75th Anniversary and Delnor Award to Alyssa Wiedemeyer.

4. Summer Studentships from WCHRI (to Navdeep Badhan), NSERC (to Ben Magalnick), Alberta Innovates (to Anson Wong) and URI (to Avery Noppers).