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

UNIVERSITY OF ALBERTA

12th ANNUAL GELFAN AND BELL ANESTHESIA CONTINUING EDUCATION AND RESEARCH SYMPOSIUM

Friday May 12, 2023

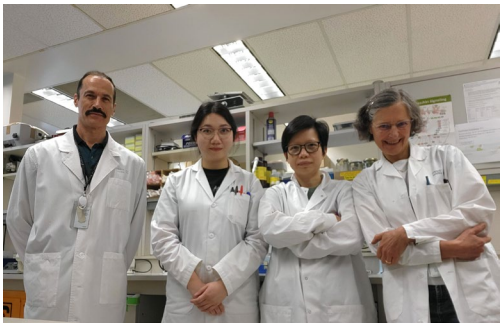
This event is an Accredited Group Learning Activity (Section 1) as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada, and approved by the University of Calgary Office of Continuing Medical Education and Professional Development. You may claim a maximum of 3.25 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).

The Zaugg Lab



We have currently two major areas of investigation:

1. *Conditioning of the heart in cardiac surgery and cardiac transplantation with the aim at reducing reperfusion injury*. We are currently testing multi-drug conditioning therapies in a large animal (porcine) model of Cardiac Donation after Circulatory Death (DCD). The porcine DCD heart transplant model is a unique model to study cardiac resuscitation in general, but also has a great potential of expanding the donor pool for cardiac transplants by successfully resuscitating hearts after circulatory arrest. Resuscitated hearts are perfused ex vivo for hours in a more natural protective beating state as opposed to preservation with cardioplegia, and can be tested whether they are suitable for transplantation.

Our current trainee on the project, Fulin Wang (Department of Pharmacology, University of Alberta), successfully passed her reclassification exam to PhD program in July 2022 and is expected to complete her degree in 2025. Fulin was awarded the Faculty of Medicine & Dentistry 2022/23 Graduate Studentship in Cardiac Sciences. She also won the prize for Best Oral Presentation at the Cardiovascular Research Institute Research Day held on June 17, 2022.

2. *Immuno-metabolism*: we are studying the potential to beneficially modulate the activity of the immune system by nutritional interventions with specific metabolic compounds such as lipid mediators (resolvins, maresins) involved in the resolution of the inflammatory state using a mouse model of total parenteral nutrition (TPN). The final goal is to understand the adverse effects underlying TPN and to ultimately improve the immunometabolic management of critically ill patients due to sepsis and organ failure.

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.

Selected Recent Publications

1. 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
2. Gueguen E, Morsy Y, Scharl M, Krämer SD, Zaugg M, Hersberger M, Rogler G, Wawrzyniak M. Endothelial Barrier Disruption by Lipid Emulsions Containing a High Amount of N3 Fatty Acids (Omegaven) but Not N6 Fatty Acids (Intralipid). Cells. 2022;11(14):2202. PMID: 35883643

3. 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

4. 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

5. Devereaux PJ and POISE-3 Investigators. Tranexamic Acid in Patients Undergoing Noncardiac Surgery.N Engl J Med. 2022;386(21):1986-1997. PMID: 35363452

6. Hartling I, Cremonesi A, Osuna E, Lou PH, Lucchinetti E, Zaugg M, Hersberger M. Quantitative profiling of inflammatory and pro-resolving lipid mediators in human adolescents and mouse plasma using UHPLC-MS/MS. Clin Chem Lab Med. 2021; 59(11): 1811-1823. PMID: 34243224

7. 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. Brad 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's 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 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 Drexel University (Lab of Dr. John Bethea) examining TNF, ER stress and the effects on neural plasticity.

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".

The Neuroimmunology and Pain Lab

Selected Recent Publications

1. Maguire, A.D., Fiedman, T.F., Villarreal, D., Haq, F., Dunn, J., Pfeifle, K., Tenorio, G., Buro, K., Plemel, J.R., Kerr, B.J. (2022). Sex differences in the inflammatory response of the mouse DRG and its connection to pain in experimental autoimmune encephalomyelitis. Scientific Reports 12, 20995 (2022). https://doi.org/10.1083/s41598-022025295-y

2. Zia, S., Hammond, B.P., Zirbgible, M., Sizov, A., Baaklini, C.S., Panda, S., Ho, M.F.S., Lee, K.V., Mainnali, A., Burr, M.K., Williams, S., Caprariello, A.V., Power, C., Simmen, T., Kerr, B.J., Plemel, J.R. (2022) Single-cell microglia transcriptomics during demyelination defines a microglial state required for lytic carcass clearance. Molecular Neurodeneration (accepted, in press)

3. Samtleben, S., Mina, L., Yap, M.C., Branton, W.G.,Yousuf, M.S., Tenorio, G., Ballanyi, K., Giuliani, F., Kerr, B.J., Power, C and Simmen, T. (2022) Astrocytes Show Increased Levels of Ero1a in Multiple Sclerosis (MS) and its Experimental Autoimmune Encephalomyelitis (EAE) Animal Model. European Journal of Neuroscience (accepted, in press)

4. Dworsky-Fried, Z., Faig, C.A., Vogel, H.A., Kerr, B.J.and Taylor, A.M.W. (2022) Central amygdala inflammation drives pain hypersensitivity and attenuates morphine analgesia in experimental autoimmune encephalomyelitis. Pain 163(1): 49-61

5. Yousuf, M.S., Samtleben, S., Lamothe, S., Friedman, T., Catuneanu, A., Thorburn, K., Desai, M., Tenorio, G., Schenk, G.J., Ballanyi, K., Kurata, H.T., Simmen, T. and Kerr, B.J. (2020). Endoplasmic reticulum stress in the dorsal root ganglia regulates large-conductance potassium channels and contributes to pain in a model of multiple sclerosis. FASEB 34 (9): 12577-12598

6. Yousuf, M.S, Maguire, A.D, Simmen, T and Kerr, B.J (2020) ER-mitochondria interplay in chronic pain: The calcium connection. Molecular Pain Jan-Dec 2020;16:1744806920946889

7. Dworsky-Fried, Z., Kerr, B.J. and Taylor, A. (2020) Microbes, microglia, and pain. Neurobiology of Pain. Jan 29;7:100045. doi: 10.1016/j.ynpai.2020.100045

8. Plemel, J.R., Stratton, J., Michaels, N.J., Rawji, K.S., Zhang, E., Sinha, S., Baaklini, C.S., Dong, Y., Ho, M., Thorburn, K., Friedman, T.N.,Jawad, S., Silva, C., Caprariello, A.V., Hoghooghi, V., Yue, J., Jaffer, A., Lee, K., Kerr, B.J., Midha, R., Stys, P.S., Biernaskie, J., Yong V.W. (2020) Microglia response following acute demyelination is heterogenous and limits infiltrating macrophage dispersion. Science Advances. Jan 15;6(3):eaay6324. doi:10.1126/sciadv.aay6324

Dr. Stephane Bourque

My research program focuses on understanding the mechanisms by which stressors (iron deficiency, sepsis) during critical periods of development affect growth and development of the fetus/neonate, and in turn predispose the offspring to lifelong health complications. In the past year, we've made progress in several research areas, but a few notable updates are summarized below.

ID is the most common nutritional deficiency worldwide; 25-30% of pregnant women in developed countries (23% in Canada), and a staggering 50-80% of women in developing countries have ID. ID during development can affect long-term health of the offspring, putting these individuals at increased risk for chronic diseases throughout life. Unfortunately, detecting ID in the fetus is difficult, and iron supplementation strategies rarely improve pregnancy outcomes. Our recent work has identified disparities between maternal and fetal biomarkers for ID (1-3), and we are currently conducting a clinical study to developing better diagnostic tools for fetal and neonatal ID and anemia. This clinical study was recently funded by a WCHRI Innovation Grant ($60,000; 2022-2025). In addition, we continue to study the effects of ID on offspring organ development (4), as well as long-term consequences on chronic disease risk using established animal models (5). In the past few years, we have invested heavily in "-omics"-based approaches (6), which provide unparalleled insights into the pathophysiology of ID, and continue to provide clues for novel therapeutic targets. Funding for this work was recently renewed by CIHR ($918,000; 2022-2027).

We've also recruited a number of excellent trainees in the past year. These include Ibrahim Khodabocus (PhD program), Si Ning Liu (MSc program), Rohini Roy Roshimi (MatCH program), Brandon Truong (undergraduate thesis program, summer research program), Avery Noppers (summer research program), Navdeep Badhan (summer research program), Ben Magalnick (summer research program), and Reid Collins (summer research program). Finally, two of our trainees have completed their training programs in my laboratory; Dr. Forough Jahandideh completed her postdoctoral fellowship, and accepted a position as Research Coordinator with

Sepsis Canada at the Ottawa Health Research Institute. Kimberly successfully defended her PhD dissertation in December 2022, and is currently running an independent research program in the Department of Critical Care Medicine.

Selected references

1. Woodman AG, Care AS, Mansour Y, Cherak S, Panahi S, Gragasin FS, BOURQUE SL. Modest and severe maternal iron deficiency in pregnancy are associated with fetal anaemia and hypoxia in rats. Sci Rep. 2017 Apr;7:46573. (2017 IF: 4.122)

2. Sanni OB, Chambers T, Li J, Rowe S, Woodman AG, Ospina MB, BOURQUE SL. A systematic review and meta-analysis of the correlation between maternal and neonatal iron status and hematologic indices. EClinicalMedicine. 2020 Oct 8;27:100555. (IF: 17.033)

3. Gragasin FS, Ospina MB, Serrano-Lomelin J, Kim SH, Kokotilo M, Woodman AG, Renaud SJ, BOURQUE SL. Maternal and cord blood hemoglobin as determinants of placental weight and efficiency: a cross-sectional study. J Clin Med. 2021 Mar; 10(5):997. (IF: 4.964)

4. Woodman AG, Mah RL, Kinney S, Holody CH, Wiedemeyer AR, Noble RMN, Clugston RD, BOURQUE SL. Perinatal iron deficiency causes sex-dependent alterations in renal retinoic acid signaling and nephrogenesis. J Nutr Biochemistry. 2022. In Press. (IF: 6.117)

5. BOURQUE SL, Davidge ST. Developmental programming of cardiovascular function: a translational perspective. Clin Sci (Lond). 2020 Nov 27;134(22):3023-3046. (IF: 6.876)

6. Roberts H, Woodman AG, Baines KJ, Jeyarajah MJ, BOURQUE SL, Renaud SJ. The effects of maternal iron deficiency on placental development and function. Endocrinology. 2021 Dec; 162:bqab215. (IF: 5.051)

The Bourque Lab at Rosso

Recent Trainee Awards

1. Jad Julian Rachid (MSc student) was awarded a Motyl Scholarship in Cardiac Sciences

2. Si Ning Liu (MSc student) was awarded a Maternal and Child Heart (MatCH) Scholarship

3. Claudia Holody (MSc student) was awarded a DOHaD international Travel Award (only 2 awards were available to be won)

4. Jad Julian Rachid (MSc student) and Si Ning Liu (MSc program) were awarded the Mary Louise Imrie Graduate Student Award.

5. Ibrahim Khodabocus (PhD student) and Si Ning Liu (Msc program) were awarded Medical Sciences Graduate Program Scholarships

6. Dr. Forough Jahandideh (postdoctoral fellow) and Kimberly Tworek (summer research program) were awarded travel awards from the Canadian Critical Care Translational Biology Group

7. Kimberly Tworek (summer student) received 2nd place for oral presentation at the 27th Annual Meeting of the ASICP