Developmental Origins
of Health and Disease

4th Annual Canadian DOHaD Society Meeting

Febuary 11-12, 2020

Banff, Alberta

Program Guide

Message from the Program Chairs:

On behalf of DOHaD Canada Leadership, it is with great pleasure that we welcome you to the 4th Annual Canadian DOHaD Society meeting (DOHaD Canada 2020) in the beautiful Canadian Rockies. This year, the DOHaD Canada scientific program will address new challenges for DOHaD in today's environment. The meeting will provide an important venue for information exchange and dissemination among Canadian DOHaD researchers, trainees, clinicians and policy leaders and a framework for translating and communicating the latest knowledge on early development to improve the immediate and long-term health of Canadians.

An event such as DOHaD Canada 2020 would not be possible without the commitment of the individuals who volunteered their time and expertise. We appreciate the wisdom of DOHaD Canada leadership, Dr. Stephen Matthews (President) and Dr. Tim Regnault (Treasurer). Thank you also to Victoria De Luca, administrative coordinator of DOHaD Canada for your assistance and efforts to arrange this scientific meeting.

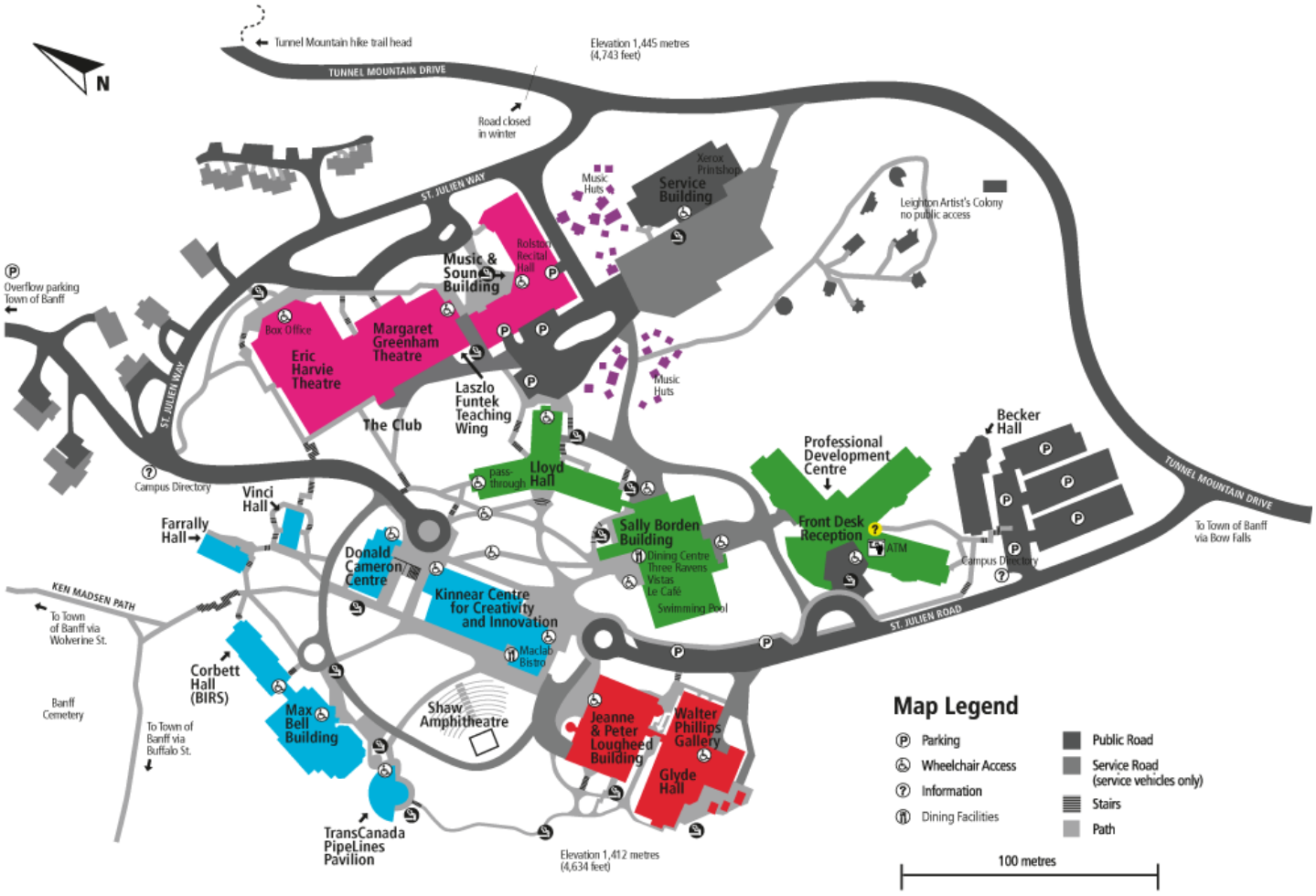
Most importantly though, we are grateful to the DOHaD Canada community for their interest. We hope that by attending the 4th DOHaD Canada meeting, you will find the Program engaging and profitable and that you will foster collaborations!

Meeting Organizers:

Jennifer Thompson, PhD
Assistant Professor
Department of Physiology and Pharmacology
Libin Cardiovascular Institute of Alberta
University of Calgary

Meghan Riddell, PhD
Assistant Professor
Departments of Obstetrics & Gynaecology and Physiology
University of Alberta

MAP OF BANFF CENTRE



DOHaD Canada Annual Scientific Meeting

CONFERENCE SCHEDULE

TUESDAY, FEBRUARY 11, 2020

2:00- 8:30 pm	**REGISTRATION**	Max Bell Central Foyer
4:45-5:45 pm	**DOHaD Canada Council Meeting** *Council Members only*	Max Bell Building, room 156
6:00-7:00 pm	Dinner	Sally Borden Building, Vistas Dining Room
7:00-7:20 pm	**WELCOME / OPENING REMARKS** Meghan Riddell, Jennifer Thompson, Co-Chairs Stephen Matthews, President, DOHaD Canada	Max Bell Auditorium
7:20- 8:20 pm	**KEYNOTE LECTURE** - Introduction by John Challis **JACOB E. (JED) FRIEDMAN, PhD** University of Oklahoma, USA *Microbes, macrophages and mitochondria: how early exposure to poor maternal diet programs adult metabolic disease* Trainee Moderator: Daniela Urrego	
8:20- 8:40 pm	**Trainee Flash Talks** (3 min each) • Brittany Gruber, University of Manitoba *Dysregulated glucose and fatty acid metabolism in pregnant adiponectin deficient mice contributes to the development of gestational diabetes mellitus* • Audrey St-Laurent, Laval University *Factors influencing physical activity levels in toddlers: results of the 3D FIT study* • Elizabeth Myles, Dalhousie University *Effects of Early Life Probiotic on Adult Anxiety, Weight, and Systemic Inflammation After Exposure to Western Diet* • Ousseynou Sarr, Western University *Western diet feeding during early life alters hepatic transcriptome and promotes lean Non-alcoholic fatty liver disease in young guinea* • Nicole Brunton, University of Manitoba *Data driven approaches to examine casual effects of maternal weight on offspring blood pressure at 18 years of age* • Sandra Lafortune, Université de Montréal *Stress During Pregnancy: Information Needs Assessment to Increase Awareness Among Pregnant Women*	
8:40-10:00 pm	**NETWORKING EVENT**	Kinnear Centre, room 105

WEDNESDAY, FEBRUARY 12, 2020

7:00 - 8:15 am	**REGISTRATION for Late Arrivals**	Max Bell Central Foyer
7:00 - 8:15 am	Breakfast	Sally Borden Building, Vistas Dining Room
8:15-8:20 am	**OPENING REMARKS** Meghan Riddell, Jennifer Thompson, Co-Chairs	Max Bell Auditorium
8:20-9:20 am	**KEYNOTE LECTURE** - Introduction by Kent Thornbrug **LUCILLA POSTON, PhD** King's College London, UK *DOHaD, maternal obesity and diabetes*	
SESSION 1	**ENVIRONMENTAL IMPACTS ON THE MICROBIOME** Moderator: Deb Sloboda -Trainee Moderator: Danilo Fernandes da Silva	Max Bell Auditorium
9:20-9:50 am	**Invited Speaker** Anita Kozyrskyj, PhD, University of Alberta *Re-wilding the infant gut microbiome*	
9:50-10:05 am	**Trainee Talk** Charles Dupras, McGill University *Human rights in the postgenomic era: Challenges and opportunities arising with epigenetics*	
10:05-10:25 am	Coffee Break	Max Bell Central Foyer
SESSION 2	**ENVIRONMENTAL INFLUENCES ON NEUROBIOLOGY** Moderator: Gerlinde Metz - Trainee Moderator: Delhaes Flavien	
10:25-10:55	**Invited Speaker** Deborah Kurrasch, PhD, University of Calgary *Sensitivity of the rodent developing hypothalamus to maternal stressors*	Max Bell Auditorium
10:55-11:05	**Trainee Talk** Preeti Kar, University of Calgary *Associations between breastfeeding during infancy and white matter microstructure in young children*	
11:05-11:35	**Invited Speaker** Ryan Van Lieshout, MD, PhD, McMaster University *If you're happy and you know it clap your hands: Emotion regulatory changes in the infants of women treated for postpartum depression*	
11:35-11:50	**Trainee Talk** Bahar Amani, McMaster University *Postpartum depression and neurobiological outcomes in infants: A systematic review*	

11:50- 12:00	**Trainee Flash Talks** (3 mins each) • Stephanie King, University of Lethbridge *Transgenerational and Multigenerational Prenatal Stress Induces Altered Epigenetic Marks and Gene Expression in the Placenta and Fetal Cortex* • Camille Bastien Tardif, Université de Montréal *The effect of an exercise intervention program on cardiorespiratory and skeletal muscle function in young adults born preterm – The HAPI Fit project*	
12:00 – 1:15	Lunch	Sally Borden Building, Vistas Dining Room
1:15 – 1:30	**2021 World Congress on DOHaD** Janice Bailey and John Challis	Max Bell Auditorium
SESSION 3	**ENVIRONMENTAL INFLUENCES ON THE CARDIOVASCULAR SYSTEM** Moderator: Sandra Davidge - Trainee Moderator: Tamara Gutierrez	Max Bell Auditorium
1:30-1:35	**Housekeeping** Meghan Riddell, Jennifer Thompson, Co-Chairs	
1:35-2:05	**Invited Speaker** Stephane Bourque, University of Alberta *Iron deficiency in pregnancy: a deceptively complex health issue in Canada and abroad*	
2:05-2:20	**Trainee Talk** Gregory Robinson, Western University *The effects of delta-9-tetrahydrocannabinol and cannabidiol on fetal heart development in mice*	
2:20-2:35	**Trainee Talk** Ronan Noble, University of Alberta *Maternal iron restriction in pregnancy causes cardiac dysfunction and morphological changes in neonates*	
2:35-3:05	**Invited Speaker** Phoebe Stapleton, Rutgers University, USA *Cardiovascular susceptibility in offspring after maternal engineered nanomaterial exposure*	
3:05-3:15	**Trainee Flash Talks** (3 mins each) • Efrah Yousuf, McMaster University *Persistence of bacteria in the preterm infant gut weeks after probiotic supplementation in the NICU* • Jia Hang Li, University of Alberta *Effect of Perinatal Iron Deficiency on Markers of Neonatal Cardiac Mitochondrial Biogenesis and Maturation*	

- Joshua Heynen, University of Lethbridge
  Cumulative Ancestral and Lifetime Adversities Alter Stress Vulnerability in Metabolic Pathways in a Two-Hit Stress Model

3:15-3:35 pm	Coffee Break	Max Bell Central Foyer

SESSION 4 **SOCIAL ENVIRONMENT AND DOHaD**

Moderator: Gerry Giesbrecht - Trainee Moderator: Roberta Bgeginski

3:35-4:05	**Invited Speaker** Maria Ospina, University of Alberta *Social determinants of health in DOHaD research*	Max Bell Auditorium
34:05-4:20	**Trainee talk** Camilla A Michalski, University of Toronto *Maternal cannabis use and adverse birth outcomes*	
4:20-4:30	**Trainee Flash Talks** (3 mins each) • Yulia Fahkr, University of Alberta *Tumour necrosis factor-A (TNF-A) and sphingosine 1-phosphate (S1P) independently impact syncytialization without synergistic effects* • Carmen Tessier, University of Alberta *The Impact of Maternal Prenatal Depression on Infant Gut Colonization of C. Difficile and Microbiota Composition at 3-4 Months of Age*	
4:30-5:30	**DOHaD Canada AGM Business Meeting**	Max Bell Auditorium
5:30-5:45	Closing remarks and awards Meghan Riddell, Jennifer Thompson	

SPEAKERS - FACULTY

Jacob E. (Jed) Friedman, PhD

Dr. Jacob E. (Jed) Friedman received his B.S. and Ph.D. in Physiology in 1990 and did post-doctoral training in Endocrinology and Molecular Nutrition at Case Western Reserve University in Cleveland, Ohio. Dr. Friedman was a member of the Biochemistry and Nutrition faculty from 1993-2000 where he worked on molecular mechanisms for insulin resistance and insulin signaling in human and mouse models of Diabetes. In 2000 Dr. Friedman was recruited to the University of Colorado in Pediatrics (Neonatology) and worked closely with clinicians and basic scientists to develop a program focused on Maternal Nutrition and Healthy Development. He was also director of the Colorado NIH-Nutrition and Obesity Research Center Molecular and Cellular Analytical core lab, with appointments in Pediatrics, Medicine, Biochemistry and Molecular Genetics.

Dr. Friedman uses novel approaches to studying molecular mechanisms for developmental programming in mouse, monkey, and man. He is a leader in the field of maternal nutrition, obesity, diabetes, and their impact on disease mechanisms across the lifespan, particularly the early origins of obesity and Pediatric Non-Alcoholic Fatty Liver Disease. He has authored >150 studies with multiple clinical investigators in the area of Gestational Diabetes, insulin action, metabolomics, liver disease, and more recently the human microbiome. He has received over $37 million in NIH grants and has mentored >57 MD and PhD post-doc fellows (9 Ks, 4 F32s, 5 RO1s), the majority of whom hold faculty positions (Instructor, or above) at biomedical research institutes across the US.

Over the last 10 years he has been part of 7 NIH or Gates Foundation omics-driven team science grants (as PI or co-I) in partnership with Biostatistics, Bioinformatics, and Epigenetics at Colorado Anschutz Medical Center, and Baylor College of Medicine. Dr. Friedman was the recipient of the 2013 American Diabetes Association Award Norbert Freinkel Award for outstanding contributions to the field of Diabetes and Pregnancy.

In January 2019 Dr. Friedman was named the new Director of The Harold Hamm Diabetes Center and Vice-Provost for Diabetes programs at The University of Oklahoma Health Sciences Center and Chickasaw Professor of Physiology at the OUHSC School of Medicine.

Lucilla Poston, PhD

Professor Lucilla Poston is the Tommy's Charity Professor of Maternal & Fetal Health and director of the Tommy's Maternal and Fetal Research Unit based at St Thomas' Hospital. She is the Research Lead for the Women's Health Clinical Academic Group (CAG) within King's Health Partners. She leads a large multidisciplinary research team which investigates disorders of pregnancy including premature birth, pre-eclampsia and the complications arising from maternal obesity. Her own research group focuses on maternal nutrition, obesity and gestational diabetes, with a focus on the early life origins of health and disease. Lucilla is an honorary Fellow of the Royal College of Obestricians and Gynaecologists (FRCOG) and was elected Fellow of the Academy of Medical Sciences in 2009. She was appointed as NIHR Senior Investigator, Emeritus status in 2017, having succeeded twice in open competition. In the same year, Lucilla was awarded a CBE for services to Women's Health.

Anita Kozyrskyj, PhD

Anita Kozyrskyj is Professor of Pediatrics at the University of Alberta, Canada. She is PI of the SyMBIOTA research program on environmental shaping of the infant gut microbiome, and development of child overweight and atopic disease in the CHILD Cohort Study. SyMBIOTA was funded by one of 7 team grants from the 2010 CIHR Microbiome Initiative and is now part of 2019 CIHR IMPACTT microbiome research network. Dr. Kozyrskyj's SyMBIOTA program has generated 40 papers and 2 book chapters. Her first infant gut microbiota paper on cesarean delivery received the 2014 CMAJ Bruce Squires Award for the most influential publication. Her findings on infant gut microbiota and food sensitization were presented to the US National Academies of Sciences, Engineering, and Medicine Committee on Food Allergy. She is associate editor of the J Dev Orig Health Dis editorial board and was co-editor of the 2016 special issue on "The Gut Microbiome and Immunity: How it is Shaped in Early Life."

Ryan Van Lieshout, MD, PhD

Dr. Van Lieshout is the Canada Research Chair in the Perinatal Programming of Mental Disorders and the Albert Einstein/Irving Zucker Chair in Neuroscience at McMaster University. He is an associate professor in the Department of Psychiatry and Behavioural Neurosciences and a psychiatrist interested in developing and testing interventions for maternal mental health problems during pregnancy and the postpartum period. He is also focused on disseminating these interventions and examining their impact on the intergenerational transmission of psychopathology from mothers to their infants.

Deborah Kurrasch, PhD

Deborah M Kurrasch is an Associate Professor in the Department of Medical Genetics at the University of Calgary and a Scientist at the Alberta Children's Hospital Research Institute. Dr Kurrasch's research is focused on characterizing the genetic programs that govern hypothalamic development using both mice and zebrafish as model organisms, and also seeks to understand how exposure to environmental chemicals in utero changes these developmental processes. Her work is funded by the Canadian Institutes of Health Research, Natural Sciences and Engineering Research Council of Canada, among other private foundations, and she currently is the Lead PI on a large, multi-center grant funded by Brain Canada.

Stephane Bourque, PhD

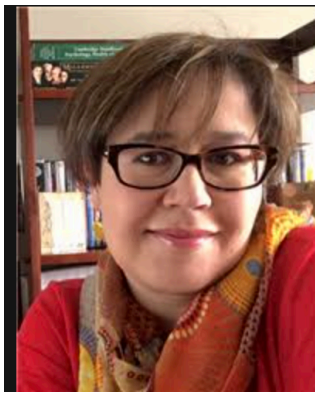
Stephane Bourque is an Assistant Professor in the Departments of Anesthesiology & Pain Medicine, Pharmacology and Pediatrics at the University of Alberta. He currently holds a Tier 2 Canada Research Chair in Developmental and Integrative Cardiovascular Pharmacology. He received his PhD from Queen's University in 2009, and then pursued a postdoctoral fellowship at the University of Alberta before joining its faculty in 2014.

His research program encompasses two broad areas of cardiovascular pharmacology. The first focuses on understanding how iron deficiency in pregnancy affects growth and development of the fetus, and in turn predisposes the offspring to cardiovascular disease in later life. Iron deficiency is the most common nutritional deficiency worldwide, and pregnant women are among the most susceptible. Diagnosis and treatment for iron deficiency in pregnancy is deceptively complex, which underscores the high prevalence despite widespread supplementation and food-fortification efforts. The goal of his work is to develop tools to diagnose iron deficiency and anemia earlier in pregnancy, and novel therapeutics to improve outcomes in these complicated pregnancies. The second focuses on understanding the mechanisms underlying the development of vasoplegia and cardiovascular collapse in the progression from sepsis to septic shock. More recently, his team has also begun studying the implications of neonatal sepsis and recovery on subsequent cardiovascular development and function in adulthood.

His research program is currently funded by the Canadian Institutes of Health Research, the Women and Children's Health Research Institute at the University of Alberta, the Canadian Foundation for Innovation, and the Royal Alexandra Hospital Foundation.

Phoebe Stapleton, PhD, ATC

Dr. Stapleton is an Assistant Professor in the Department of Pharmacology and Toxicology and resident scientist in EOHSI at Rutgers University. She is a microvascular physiologist by training who investigates perturbations associated with normal physiological challenges (e.g., toxicological exposure, pregnancy, disease, exercise). Recently, she has applied her expertise in a gestational model, focused on maternal environmental exposures to aerosolized particulates and the impact to the mother, developing fetus, and surviving young.



Maria Ospina, PhD

Maria Ospina is an assistant professor with the Department of Obstetrics & Gynecology, a perinatal epidemiologist and a WCHRI member. Her program of research involves the routine use of perinatal and administrative health data and other clinical data sources to examine the impact of early-life factors on long-term health and the role of social determinants on maternal, perinatal and childhood health trajectories. Her work is supported by the Canadian Institutes of Health Research, the Lung Association, and through the generous supporters of the Lois Hospital for Women through the Women and Children's Health Research Institute.

Brittany L Gruber, Laura K Cole, Bo Xiang, Grant M Hatch, Vernon W Dolinsky, Department of Pharmacology and Therapeutics, University of Manitoba

Dysregulated glucose and fatty acid metabolism in pregnant adiponectin deficient mice contributes to the development of gestational diabetes mellitus

Introduction: Gestational diabetes mellitus (GDM) is a common pregnancy-related condition with implications for both maternal and neonatal health. Adiponectin is a fat derived hormone that improves insulin sensitivity and in pregnant women, low levels of adiponectin are associated with elevated risk for GDM. We hypothesize that adiponectin deficiency causes fatty liver during pregnancy, contributing to the development of GDM.

Methods: We compared the glucose and pyruvate tolerance of pregnant (3rd trimester) adiponectin knockout (KO) (strain B6;129-Adipoqtm1Chan/J) and wild-type (WT) mice, and assessed the regulation of glucose and fatty acid metabolism in the liver. Impact of adiponectin supplementation at the end of the second trimester was measured by administering adenovirus expressing full-length adiponectin and comparing to control containing GFP.

Results: In the third trimester, fasting pregnant adiponectin KO mice are hyperglycemic (9.2mmol/L vs. 7.7mmol/L in controls, $p<0.05$) and glucose intolerant relative to WT controls. Adiponectin KO mice have elevated gluconeogenesis (determined by pyruvate tolerance test), which is accompanied by increases of hepatic gluconeogenic genes such as Pck (2-fold, $p<0.05$) and G6pc (3-fold, $p<0.05$), which are not responsive to insulin. Pregnant adiponectin KO mice develop hepatic steatosis and a 3-fold ($p<0.05$) elevation in hepatic triglycerides relative to wild-type. Hepatic fat deposition in adiponectin KO mice is accompanied by a corresponding ~4-fold increase ($p<0.05$) in Fasn gene expression which is important for fatty acid biosynthesis in the liver. Gestational weight gain and food consumption were similar in KO and wild-type mice. Adenoviral-mediated adiponectin supplementation to pregnant adiponectin KO mice improved glucose tolerance, prevented fasting hyperglycemia, and attenuated fatty liver development.

Conclusion: Adiponectin deficiency during pregnancy contributed to hepatic steatosis and dysregulation of gluconeogenesis and consequent hyperglycemia. Adiponectin supplementation in pregnancy rescues hepatic steatosis and improves glucose tolerance.

Audrey St-Laurent, Laval University

Factors influencing physical activity levels in toddlers: results of the 3D FIT study

Introduction. Since physical activity (PA) is a complex behavior formed at an early age, a better knowledge of its correlates could help target children at risk to be less active. We aimed to assess paternal, maternal and early childhood factors influencing toddlers' PA levels.

Methods. We included father-mother-child triads (n=216) from an ancillary study (3DFIT, N=302) of the 3D Birth Cohort (Québec, Canada). One-hundred prenatal and childhood characteristics from various domains (demography, anthropometry, pregnancy disorders, delivery, lifestyles, child's temperament and mental/psychomotor/language development) were collected from medical records or valid questionnaires. Children's PA levels at 2 years were assessed using an accelerometer (GT3X+, Actigraph). Linear or logistic regressions were performed to evaluate the influence of potential factors on four PA outcomes: total PA, moderate-to-vigorous PA, counts/15seconds and achievement of PA

recommendations (≥180 minutes/day at any intensity). Variables associated with ≥1 PA outcomes at $p < 0.15$ in bivariate analysis were entered in multivariate analysis and retained in final models at $p < 0.10$.

Results. Results: At 2.0±0.1 years, 3.5% of toddlers were overweight/obese and 38.4% did not meet PA recommendations (no significant difference between child's sex). However, girls aged of 2 engaged in less total PA than boys (difference of 18 minutes/day, $p < 0.05$). Factors positively associated with ≥1 PA outcomes were child's gross motor skills (Bayley-III), structured PA practice, number of produced words, temperament (surgency), eating too fast and fruits/vegetables intakes (≥4 times/day). Factors negatively associated with ≥1 PA outcomes were children's sex (being a girl), growth velocity (birth–3months), hours spent in bed per night, maternal education and having an history of hypertensive disorders of pregnancy [HDP]. Our final models explained (R2) 24% to 28% of PA levels variability at 2 years.

Conclusion. We identified temperament (surgency), eating and sleep behaviors, number of produced words and HDP as new correlates of toddlers' PA levels.

Elizabeth Myles, Dalhousie University

Effects of Early Life Probiotic on Adult Anxiety, Weight, and Systemic Inflammation After Exposure to Western Diet

Introduction. Microbes are abundant and have a profound impact on human biology and behaviour. In the gut, the presence or absence of specific bacterial species is directly related to environmental factors, such as diet and infection, which can induce disease or dysfunction in the host. We hypothesized that administration of the probiotic, Probio'Stick®, would have a protective effect on systemic inflammation, anxiety, and weight and food intake changes after exposure to a Western diet.

Methods. Probio'Stick® or its placebo was administered daily to breeder mother rats voluntarily via oral syringe at a dosage of 1 billion Colony Forming Units (CFUs) per mL at 11 am (± 1 hour). Administration continued throughout pregnancy (n = 8) and breastfeeding (n = 7 successful pregnancies). Upon weaning, a total of 62 male and female Long-Evans rats were given the same Probio'Stick® or its placebo along with a Western or control diet. Differences in inflammatory markers in plasma collected at sacrifice following acute predator odour stress, anxiety-like behaviours in the Open Field Test (OFT) and Light-Dark Box (LDB), and food intake and weight were analyzed via treatment by diet by sex factorial ANOVAs.

Results. Overall, it was found that probiotic treatment: 1) led to a greater inflammatory response following acute stress perhaps due to the lack of inhibition from enhanced stress hormone release; 2) led to fewer escape behaviours during anxiety testing; 3) resulted in decreased food intake and weight in males; and 4) prevented weight gain in response to significantly increased food intake in females.

Conclusion. Our findings partially support our hypothesis, although more work is needed to clarify some effects, particularly with the inflammatory response. The results show that Probio'Stick® has the potential for intervening in anxiety and metabolic disorders and highlight the importance of diet and sex differences on health outcomes.

Ousseynou Sarr, Western University

Western diet feeding during early life alters hepatic transcriptome and promotes lean Non-alcoholic fatty liver disease in young guinea

Introduction. Non-alcoholic fatty liver disease (NAFLD) is strongly associated with obesity but is occurring in increasing numbers in young non-obese patients and is known as "lean NAFLD", whose underlying

pathophysiology is not well understood. We aimed to advance mechanistic understanding of lean NAFLD using guinea pigs fed a western diet (WD) during postnatal growing phase.

Methods. Normally in utero grown guinea pig offspring were randomly assigned to receive ad libitum a control (CD) diet or WD (high fat/high sugar + 0.25% cholesterol) from weaning to postnatal day (PND) 150 (young adulthood). In vivo computed tomography (CT, ~ PDN 120), organ weight determinations and hepatic histology analyses (150 PDN) were undertaken. Hepatic differentially expressed genes (DEGs) were identified using the GeneChip™ Guinea Pig Gene 1.1 ST Array Plate and TAC software (-22, FRD p-value < 0.05). Functional analysis was carried out on DEGs using g:Profiler.

Results. CT and adipose tissue weights, revealed that male and female WD offspring were not obese. However, at PND 150, male and female WD offspring developed hepatomegaly, prominent hepatic steatosis, lobular liver inflammation and fibrosis, all indicative of NAFLD. Genes involved in cell cycle, lysosome, ECM-receptor interaction, p53 and AGE-RAGE signaling pathways, and genes that are targeted by miR-335-5p, were over-expressed in WD male and female livers ($p < 0.05$). Steroid biosynthesis pathway was however down-regulated in WD livers of both sexes. In WD male livers, PPAR signalling genes were up-regulated, while focal adhesion, amoebiasis and cytokine-cytokine receptor interaction pathways, and genes that are targeted by miR-133a-3p, miR-29b-3p and miR-199b-5p were up-regulated in WD female livers ($p < 0.05$).

Conclusion. These data highlight miR-335-5p, lysosomes, control of hepatic cell-division cycle, ECM, AGE-RAGE system and steroid biosynthesis as central to early life NAFLD development and could be used to define biomarkers and to develop tools to calculate a lean NAFLD risk score.

Nicole Brunton, University of Manitoba

Data driven approaches to examine casual effects of maternal weight on offspring blood pressure at 18 years of age

Introduction. It is unclear if maternal overnutrition during pregnancy increases risk of offspring heart disease. This study aimed to examine the relationship between maternal pre-pregnancy body mass index (BMI) and offspring systolic blood pressure (SBP) at 18 years old.

Methods. Multivariate regression and causal mediation analysis were performed within 3700 mother – offspring pairs from a prospective birth cohort. The main exposure was maternal pre-pregnancy BMI categorized as healthy weight, overweight, or obese for regression and treated as continuous for causal mediation analysis. The main outcome was offspring BP considered as elevated-normal BP (SBP 130/>80mmHg) at 18 years. Age-standardized BMI Z-scores and latent class growth analysis (LCGA) were used to quantify the mediating factor of offspring BMIZ trajectories between 7 and 18 years. Analyses were adjusted for social class, pre-eclampsia, sex, and maternal tobacco use during pregnancy.

Results. The odds of elevated BP (aOR: 1.6; 95% CI: 1.1-2.3) and hypertension (aOR: 2.1; 95% CI: 1.4-3.1) were higher in offspring from women that were obese prior to pregnancy compared to those that were healthy weight. LCGA identified five distinct offspring BMIZ trajectories. SBP (125 ± 12 vs 117 ± 10 mmHg, $p < 0.001$) and the odds of hypertension (aOR: 3.8; 95% CI: 2.8-5.1) at 18 years were significantly higher in offspring with sustained high BMIZ trajectory compared to sustained low normal. Casual mediation analysis revealed that maternal BMI directly (OR: 1.14; 95% CI: 1.03-1.25) and indirectly through offspring BMIZ trajectories (OR: 1.12; 95% CI: 1.08-1.15) increased offspring SBP at 18 years of age.

Conclusion**.** Maternal obesity prior to pregnancy is associated with increased risk of hypertension in offspring at 18 years of age, partly mediated by an elevated BMIZ score trajectory throughout childhood and adolescence.

Sandra Lafortune, Université de Montréal

Stress During Pregnancy: Information Needs Assessment to Increase Awareness Among Pregnant Women

Introduction. Prenatal maternal stress (PNMS) is associated with suboptimal child development; however, it is unknown how aware pregnant women are of these facts. We aimed to improve understanding about women's knowledge about, and interest in, the consequences of PNMS.

Methods. Our first cohort (n=100) was pregnant during the 2016 Fort McMurray wildfire in Alberta. The second cohort (n=241) included Montreal mothers who were not exposed to a natural disaster in pregnancy. Both cohorts completed our questionnaire to assess their agreement with statements based on the PNMS literature. Women were also asked whether, during their last pregnancy, they would have liked to have known more about the potential consequences of PNMS.

Results. Although the cohorts differed significantly on income, education, and language, there was no difference between the two groups with respect to their interest in receiving information about PNMS: 67.2% of the total sample would have liked to have known more about this topic during their last pregnancy. In the exposed cohort, higher disaster-related PNMS levels (Peritraumatic Dissociative Experience Questionnaire (PDEQ)) were associated with better PNMS knowledge ($r = 0.31$, $p < 0.01$), even in a multiple regression model controlling for sociodemographic variables and objective exposure to the natural disaster (p=0.012, 95%CI: [0.007; 0.054]). Women interested in receiving more information experienced higher PNMS levels (Peritraumatic Distress Inventory (PDI)) than those who were not interested (p=0.02, 95%CI: [1.18; 10.88]). Social support and age interacted with PNMS levels to predict their knowledge about PNMS ($p < 0.05$).

Conclusion**.** We found in women from diverse backgrounds a generalized interest to know more about the potential effects of PNMS on their children, supporting the need for an awareness campaign.

Charles Dupras, Yann Joly, Emmanuelle Rial-Sebbag, Centre of Genomics and Policy, McGill University

Human rights in the postgenomic era: Challenges and opportunities arising with epigenetics

Background: Over the past twenty-five years, international organizations have adopted human rights declarations in attempt to address emerging ethical, legal and social concerns associated with genetic research and technologies. While pointing to important challenges and potential issues in genetics, the focus of these declarations on genetics has been criticized by some authors for supporting the idea that there is something unique about our genes.

Methodology: In this paper, we add to this criticism by pointing out gaps and flaws in current gene-focused human rights declarations, in light of recent developments in the field of epigenetics.
Results: First, we show that these documents do not provide guidance for the responsible governance of epigenetic data (e.g., privacy protection) and ethical use of individual epigenetic information (e.g., nondiscrimination). This is particularly concerning given the interest recently demonstrated by insurance companies, forensic scientists and immigration agencies in using epigenetic clock technologies. Second, we argue that findings in epigenetics could contribute to the promotion of particular sets of human rights, namely, economic, social and cultural (second-generation) rights, and solidarity (third-generation) rights.

Discussion: We conclude with a call for greater attention by international bioethics and human rights organizations to epigenetics and other 'postgenomic' human biovariants, such as microbiomic, proteomic, metabolomic, neuromic and phenomic variants, in the coming years.

Preeti Kar, Jess E Reynolds, Melody N Grohs, Rhonda C Bell, Megan Jarman, Deborah Dewey, Catherine Lebel, University of Calgary

Associations between breastfeeding during infancy and white matter microstructure in young children

Introduction: The World Health Organization recommends exclusive breastfeeding for 6 months followed by continued breastfeeding; however, associations between breastfeeding and brain development in the context of perinatal/sociodemographic variables remain unclear. This study aims to investigate whether breastfeeding exclusivity for 6 months and total duration of any breastfeeding is associated with white matter development in young children.

Methods: This study included a sample of 84 mothers and their 86 healthy children (43 males). Breastfeeding data was collected at 3, 6, and 12 months postpartum as well as at the child's magnetic resonance imaging scan. Children underwent diffusion tensor imaging between 2.34-6.97 years of age; some children returned multiple times providing 333 datasets in total. Linear regression tested for associations between breastfeeding exclusivity/duration and fractional anisotropy (FA; measure sensitive to myelination/axonal packing/fibre coherence) for the whole brain and 10 individual white matter tracts controlling for confounders.

Results: Exclusively breastfed females had higher FA in white matter of the whole brain and individual tracts compared to not exclusively breastfed females.

Bahar Amani, Ryan Van Lieshout, Department of Psychiatry & Behavioural Neurosciences, McMaster University

Postpartum depression and neurobiological outcomes in infants: A systematic review

Background: The emergence of postpartum depression (PPD) at a critical point in offspring neurodevelopment make it a time-sensitive illness. PPD affects the emergence and consolidation of neurobiological pathways responsible for stress responses, emotion regulation, and cognitive functioning. These pathways are linked with negative mental health outcomes in offspring across the lifespan and are important targets for preventive intervention. To date, there are no systematic reviews examining associations between maternal postpartum depression and the neurobiological function in offspring. The purpose of the present study was to locate and synthesize the results of studies that examine the neurobiological consequences of PPD on infant offspring.

Methodology: We performed searches of the peer-reviewed literature published between 1990 and November 2019 using the following electronic databases: MEDLINE, EMBASE, PsycINFO, and Web of Science. The search strategy included terms related to postpartum depression, infant, and measures of biological pathways and neural systems including neuroimaging, brain activity, vagal tone, and cortisol reactivity.

Results: A total of 32 studies (out of 835 references retrieved from bibliographic databases) met inclusion criteria and were included in this systematic review. Studies included both observational and intervention studies.

Discussion: A small, but growing body of literature suggests that PPD can disrupt the development of important neurobiological pathways in offspring. For this reason, timely detection and treatment is imperative to promoting optimal neurodevelopment and health trajectories in the offspring of women

with PPD. Research utilizing larger samples and stronger study designs (e.g., randomized controlled trials) are required to provide the insights needed to prevent the intergenerational transmission of risk from mother to infant and before its myriad negative consequences manifest.

Stephanie King, University of Lethbridge

Transgenerational and Multigenerational Prenatal Stress Induces Altered Epigenetic Marks and Gene Expression in the Placenta and Fetal Cortex

Introduction. Prenatal stress has been shown to increase the susceptibility to adverse neonatal outcomes as well as psychopathology including anxiety and depression and the effects of exposure to prenatal stress can generate transgenerationally inheritable epigenetic and transcriptomic signatures linked to impaired mental and physical health. The objective of this study is to investigate the mechanistic effects of transgenerational and multigenerational exposure to prenatal stress on the developing fetal brain and placenta.

Methods. Four generations of Long-Evans rats were bred for this study. The parental (F0) generation gestating rats were exposed to stress during gestational days 12-18. The transgenerational lineage was bred to the F3 generation without any further stress exposure. The F3 generation multigenerational lineage experienced three successive generations of the stress paradigm. Control, transgenerational, and multigenerational lineage fetuses and placentas were collected at G21. Both the fetal cortex and placenta of the F1-F3 generations were used for DNA methylation, miRNA, and mRNA analyses in order to assess epigenomic and transcriptomic changes.

Results. Results demonstrated that ancestral transgenerational and multigenerational exposure to prenatal stress did not appear to have a strong effect on the F1 generation but caused significant changes in DNA methylation, mRNA, and miRNA expression in the placenta and embryonic cortex of the F2 and F3 generations. Transgenerational changes included alteration of gene pathways associated with neurological diseases and placental dysfunction. Interestingly, there was an overlap in epigenomic and transcriptomic changes between the placenta and fetal cortex, suggesting that the placenta may be used for a potential biomarker to predict molecular changes in the brain correlated with pathologies in adulthood.

Conclusion. The discovery of early predictive and prognostic biomarkers of neurological disease associated with ancestral exposure to prenatal stress is critical for early life therapeutic interventions that prevent and mitigate psychological and neurological diseases as well as improving public health outcomes.

Camille Bastien Tardif, Université de Montréal

The effect of an exercise intervention program on cardiorespiratory and skeletal muscle function in young adults born preterm – The HAPI Fit project

Introduction. Some studies suggest individuals born preterm have reduced exercise capacity. The pathophysiology of exercise limitation following preterm birth remains unclear and may be a consequence of impairment of systems responsible for oxygen delivery and consumption; cardiovascular, pulmonary and muscular systems. We aimed to evaluate and compare changes in cardiorespiratory and muscular fitness pre/post a 14-week supervised exercise intervention in adults born preterm (PT) vs. term (T).

Methods. The proposed sample consists of 21 PT (< 29 weeks of gestation) and 36 T. They underwent a cardiovascular and resistance training program three times/week. Pre- and post-intervention

assessments included cardiopulmonary (VO2max) and muscular testing (endurance, strength and flexibility). Descriptive statistics were calculated as mean ± standard deviation. Repeated-measure ANOVA were used for time and group comparison with p≤0.05 considered for significance.

Results. Prior to intervention, strength [grip strength: PT: 55.8±19.8 vs T: 69.2±22.9kg (p=0.037); vertical jump: PT: 27.3±11.4 vs T: 48.1±22cm (p=0.001)], flexibility [PT: 22.2±11.7 vs T: 32.3±9.7cm (p=0.002)] and FEV1/CVF ratio [PT: 77.4±6.7 vs T: 82.8±6.8% (p=0.011)] of PT and T were different. Both PT and T improved their muscle endurance [push-ups: PT: 13.3±9.7 à 19.1±11.5 repetitions (p=0.008) and T: 12.2±7.1 to 16.7±8.8 repetitions (p=0.001); sit-ups PT: 16.9±18.6 to 25.4±20.7 repetitions (p=0.041) and T: 24.2±16.9 to 29.2±17.3 repetitions (p=0,191)], their strength of the lower body [vertical jump; PT: 27,3±11,4 to 30,8±15,5cm (p=0,079) and T: 48,1±22 to 5.7±21cm (p=0.005)] and their VO2max [P: 27.6±7.4 to 33.1±6.9ml\min*kg (p=0.001) and T: 29.2±7.3 to 33±7ml\min*kg, (p=0.000)], without differences between groups. Differences in muscle function were no longer observed between PT and T following the intervention.

Conclusion. Terms have a better skeletal muscle profile initially. An intervention through physical activity allows cardiorespiratory and muscular improvement in PT and represents a non-pharmacological measure to be promoted in this at-risk population in order to avoid long-term morbidity.

Ronan Noble, Jason Li, Andrew Woodman, Richard Mah, Ferrante Gragasin, Luke Eckersley, Stephane Bourque, Department of Pediatrics, University of Alberta

Maternal iron restriction in pregnancy causes cardiac dysfunction and morphological changes in neonates

Introduction: Iron deficiency (ID) is the most common nutritional deficiency worldwide, and affects an estimated 39% of pregnant women globally. ID causes organ-specific patterns of hypoxia, mitochondrial dysfunction and oxidative stress in the fetus, however the effects on the offspring's developing heart have not been studied. By virtue of iron's role in ensuring oxygen delivery to the body, we sought to determine how the reduced oxygen carrying capacity associated with anemia during pregnancy and shortly after birth would affect cardiac morphology and function.

Methods: Sprague Dawley rats were fed an iron-restricted or iron-replete diet (control) prior to and throughout pregnancy. After birth, all dams were fed an iron-replete diet. On postnatal day (PD) 4, 14, and 28, hearts of male and female offspring were examined by echocardiography.

Results: Maternal iron restriction throughout pregnancy reduced maternal hemoglobin (-31%; P<0.001) and offspring hemoglobin from birth through PD14 (-48%, P<0.001; -25%, P=0.013). ID offspring exhibited growth restriction (-19%; P<0.001), which persisted through PD28 (-30%; P<0.001). When normalized to bodyweight, ID pups had increased heart weights at PD4 (+60%; P<0.001) and PD14 (+72%; P<0.001) and diastolic chamber volumes (+31%, P=0.005; +28%, P=0.056; respectively), and these values returned to control levels by PD28. After adjusting for body weight, ID offspring had reduced ejection fraction at PD4 (-15%; P=0.024) and PD14 (-19%; P=0.004), which normalized by PD28. These changes corresponded to a reduction in oxygen delivery on PD4 (-41%; P<0.001) and PD14 (-31%; P=0.05), which recovered completely by PD28.

Conclusion: Perinatal ID causes morphological and functional changes in the neonatal heart. With no corresponding increase in cardiac output, these results suggest a systolic dysfunction, which may reflect inadequate or maladaptive compensation in the wake of perinatal anemia. These findings may have important implications for the short and long-term cardiac health of anemic babies.

Efrah Yousuf, McMaster University

Persistence of bacteria in the preterm infant gut weeks after probiotic supplementation in the NICU

Introduction. Probiotics may reduce the prevalence of necrotizing enterocolitis in early preterm infants and are increasingly used in Neonatal Intensive Care Units (NICU). The long-term impact of probiotics on the preterm gut remains unclear. We hypothesized that a probiotic containing four Bifidobacterium strains would colonize the hospitalized preterm infant gut.

Methods. Stool was collected every other day from hospitalized preterm infants enrolled in the Baby & Pre-Mi study, as well as at term, 6 weeks, 12 weeks, and 5 months corrected age (CA). A policy change introduced probiotics to the study NICU, resulting in probiotic exposure for 8 infants (PT-P). 14 infants without exposure to this probiotic (PT-C) and a cohort of healthy, unexposed full-term infants from the Baby & Mi study (FT-C), were used as comparator groups. Microbial community profiling was completed through amplification of the v3 region of the 16S rRNA gene and subsequent DNA sequencing with the Illumina platform. Amplicon sequence variants (ASVs) were inferred from trimmed data using the DADA2 pipeline.

Results. Four Bifidobacterium ASVs were found to be highly abundant in PT-P infants compared to PT-C infants following probiotic supplementation. The relative abundance of these suspected probiotic ASVs was significantly higher at term in PT-P infants and remained elevated to 5 months CA. No significant differences in the abundance of these ASVs were detected between groups at 5 months. At term, the gut microbiome of PT-P infants more closely resembled the gut microbiome of 10-day old FT-C infants than PT-C infants at term. The gut microbiota of both preterm groups converged with the term-born gut microbiomes by 6 weeks CA.

Conclusion. Suspected probiotic strains of bacteria may persist up to 5 months post-supplementation and potentially colonize the preterm infant gut. Further research is needed to understand their impact on the gut microbiome and infant health.

Jia Hang Li, University of Alberta

Effect of Perinatal Iron Deficiency on Markers of Neonatal Cardiac Mitochondrial Biogenesis and Maturation

Introduction. Iron deficiency (ID) is the most common nutritional disorder in the world, and pregnant women are the most vulnerable group. ID during pregnancy can alter developmental trajectories and predispose offspring to cardiovascular diseases. Recently, we found evidence of cardiac dysfunction, increased mitochondrial content, and impaired mitochondrial respiration in the hearts of neonatal ID rats. Given that the perinatal heart is highly metabolically active and undergoing rapid changes, we hypothesized that perinatal ID would stimulate mitochondrial biogenesis and disrupt cardiomyocyte maturation postnatally.

Methods. Female Sprague Dawley rats were fed either an iron-restricted or an iron-replete diet before and during pregnancy. On postnatal days (PD)1, 14, and 28, ventricles were collected from male and female pups. Protein levels of mitochondrial biogenesis effectors (PGC-1α, AMPK : pAMPK ratio, Sirt1, Sirt3) and markers of cardiomyocyte maturation (α-MHC : β-MHC ratio) and damage (cTnI/T) were assessed by Western Blot. All data were analyzed by 2-way ANOVA.

Results. Male and female ID pups had reduced hemoglobin at PD1 and 14 ($P < 0.0001$, both) but recovered by PD28. ID pups were also growth restricted at all time points ($P < 0.001$, both) and had increased relative heart weights at PD1 and PD14. PGC-1α levels increased with age in both sexes ($P=0.004$, both) but there

was no overall effect of perinatal ID. cTnT levels were decreased in ID pups of both sexes at PD28 (P=0.02), but not at other time points. No differences in cTnI were observed. The α-MHC : β-MHC ratio was decreased in female ID pups (P=0.007 overall), but not in males.

Conclusion. Our preliminary results indicate no upregulation of PGC-1α due to ID. Neonatal ID hearts show signs of increased cardiomyocyte damage and impaired maturation. Results for the remaining markers will provide insights into the mechanisms by which perinatal ID affects cardiac development and long-term cardiovascular health.

Joshua Heynen, University of Lethbridge

Cumulative Ancestral and Lifetime Adversities Alter Stress Vulnerability in Metabolic Pathways in a Two-Hit Stress Model

Introduction. Chronic prenatal maternal stress (PNMS) usually has an adverse impact on the developing fetus and lifetime health. Preexisting ancestral stress may also raise vulnerability to recurrent stress and failure to cope as adversity accumulates. This study was designed to test the hypothesis that ancestral PNMS can increase the vulnerability to acute or chronic stress with respect to cellular metabolic functions.

Methods. Forty-eight male rats from the third filial generation (F3) were derived from three different lineages: (1) a transgenerational PNMS lineage where only the F0 mother was exposed to stress; (2) a multigenerational PNMS lineage where the mother from each generation was exposed to stress; and (3) a control lineage with no experimental stress exposure. Each of these groups were exposed to both an acute and chronic stressor in adulthood. Blood was then collected, processed, and the metabolomic profiles (spectra) were acquired on a 700 MHz NMR spectrometer. A data reduction step (binning) was employed, and univariate and multivariate statistical testing was applied to the metabolite concentrations. Metabolite identification and pathway analysis were performed in order to interpret the biological relevance of the data

Results. Identification of the significant bins display separation of the metabolomes among groups at varying levels. The metabolomic variations revealed that each experimental group responded differently to the same stressors. The metabolic pathways of glycine, serine, and threonine, as well as the aminoacyl-tRNA biosynthesis pathway were significantly altered between each pairing of the chronically stressed groups.

Conclusion. The findings from this study suggest that being exposed to multiple hits of stress exacerbates stress sensitivity and vulnerability. A dysfunctional aminoacyl-tRNA synthesis pathway proposes a mechanism for stress-induced protein mistranslation and misfolding with potential pathogenic consequences. The results support the hypothesis that ancestral and lifetime stress cumulatively and differentially affect the metabolic response to stress.

Camilla A Michalski, Rayjean Hung, Ryan Seeto, Kellie Murphy, Stephen Matthews, Cindy-Lee Dennis, Jennifer Brooks, Joanna Henderson, Stephen Lye, Robert Levitan, Julia A Knight

Maternal cannabis use and adverse birth outcomes

Introduction: Canada has one of the highest cannabis consumption rates in the world, and given that cannabinoids readily cross the placental barrier, there exists a critical need to understand the effects of cannabis on fetal development. This study had two objectives: to determine 1) the factors associated with prenatal cannabis use, and 2) whether self-reported cannabis use is associated with the following outcomes: low birth weight, preterm birth, or small size for gestational age (GA) infants.

Methods: Maternal lifestyle questionnaire data and infant clinical data was gathered from 2229 participants in the Ontario Birth Study between 2013-2019. Women were asked about their cannabis use within three months of finding out they were pregnant, as well as during pregnancy. Multivariable linear and logistic regression was used to estimate factors associated with maternal cannabis use and to determine the association between use and selected birth outcomes.

Results: Cannabis use has increased among OBS participants since 2013. Women who use cannabis prior to finding out they were pregnant (N=216) were younger, of lower socioeconomic status, and more likely to use alcohol, tobacco, and prescription pain medication. The infants of these women were, on average, 86.8 grams lighter (95%CI: -155.3, -18.2), and had 2 times the odds of being small for GA (95%CI: 1.2, 3.3).

Conclusion: The homogeneity of the study population combined with detailed covariate measures allowed for better isolation of the effects of cannabis use (in the weeks leading up to pregnancy) on birth outcomes. Even so, an association was found, suggesting early pregnancy may be a crucial window of fetal cannabis exposure. Seeing as the birth outcomes measured in this study are intermediate outcomes that implicate adverse health outcomes later in life, prenatal care guidelines should emphasize the potential for adverse birth outcomes.

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Tumour necrosis factor-A (TNF-A) and sphingosine 1-phosphate (S1P) independently impact syncytialization without synergistic effects

Background: Preeclampsia (PE) is a pregnancy disorder with lifetime consequences for the child. In PE, trophoblast (TB) syncytialization is disrupted. One factor hindering syncytialization and increasing TB apoptosis is TNF-α. In endothelial cells, TNF-α mediates apoptosis through a bioactive sphingolipid, sphingosine 1-phosphate (S1P). Like TNF-α, S1P induces TB apoptosis and inhibits syncytialization. However, it is unknown if S1P mediates TNF-α effects in TBs. We propose that sphingosine kinase 1 (SK1), a S1P synthesizing enzyme, is a feasible target downstream of TNF-α to improve syncytialization.

Hypothesis: SK1 expression increases in term placental chorionic explants and primary human trophoblast cultures treated with TNF-α. TNF-α decreases syncytialization by activating SK1. Methods: After 3-4 days of culture to allow original syncytium sloughing, explants were treated with TNF-α (0-10 ng/mL) and/or PF-543 (SK1 antagonist, 1 μM) up to 48 hrs. Re-syncytialization was assessed using E-cadherin immunofluorescence staining (n=3). SK1 mRNA expression in explants (qRT-PCR, n=4) was quantified after 0-48hrs. Primary term TBs were cultured with TNF-α (0-20 ng/mL) for 24 hrs. Syncytialization (hCG ELISA; n=3), cell viability (LDH release assay; n=3), and SK1 expression (immunofluorescence, n=5; qRT-PCR, n=5) were measured. Analysis was by one-way ANOVA.

Results: The greatest reduction in explant re-syncytialization by TNF-α treatment occurred at 10ng/mL after 48 hrs. 1ng/mL TNF-α, the physiological level in PE, decreased re-syncytialization by 40.9±5.2% ($p=0.05$). Inhibiting SK1 decreased syncytialization by 24.69±1.29%. Blocking SK1 in the presence of TNF-α did not rescue re-syncytialization. No change in SK1 expression occurred. In primary TBs, TNF-α (1-20ng/mL) decreased hCG levels ($p<0.01$) without affecting LDH levels. SK1 expression did not change in TNF-α treated primary TBs.

Discussion: TNF-α decreases syncytialization independently of SK1 activity without affecting viability or SK1 mRNA expression. However, endogenous SK1 activity is important. Thus, TNF-α and S1P independently impact syncytialization without synergistic effects. Funding: CIHR, FOMD, FGSR, MatCH.

Carmen Tessier, University of Alberta

The Impact of Maternal Prenatal Depression on Infant Gut Colonization of C. Difficile and Microbiota Composition at 3-4 Months of Age

Introduction. Approximately 30% of healthy infants are asymptomatically colonized with Clostridioides difficile (C. difficile). Infants colonized with this pathogen have an increased risk for allergic sensitization and atopy. This study aimed to examine the impact of maternal prenatal depression on the colonization of C. difficile in infants at 3-4 months of age.

Methods. This was a substudy of 1,500 term infants from the CHILD Cohort Study. Maternal reports were used to measure prenatal depression and feeding method. Birth mode was retrieved from hospital records. Fecal samples were collected at 3 months after home assessment. Analysis of C. difficile was performed using quantitative polymerase chain reaction (qPCR) with appropriate primers. Logistic regression was used to determine the association between maternal prenatal depression and C. difficile colonization at 3-4 months of age.

Results. In our sample, one-third (31%) of the infants were colonized with C. difficile at three months of age. During their third trimester of pregnancy, 24% of mothers reported clinically significant depressive symptoms. Prenatal depression significantly increased the odds of C. difficile colonization in the infant (Odds Ratio [OR]=1.44, 95% Confidence Interval [CI], 1.11-1.85; p=0.006), adjusted for birth mode and breastfeeding status. The odds of C. difficile colonization was significantly higher for both formula ($p < 0.001$) and mixed feeding methods ($p < 0.001$), as well as in infants born by caesarean section (p=0.002). The presence of C. difficile in the infant gut at age 3-4 months altered microbiota composition by enriching abundance of Rumminococcaceae and Lachnospiricaea, and depleting Bifidobacteriaceae.

Conclusion. At 3-4 months of age, infants of mothers who experienced prenatal depression had significantly increased risk of C. difficile colonization in their gut. Our findings further suggest that maternal mood may contribute to alterations in early infant microbiome, in addition to known infant gut microbiota determinants, such as feeding method and birth mode.

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