# *James A. Low Research Day*
# *Department of Obstetrics & Gynaecology*

## *Friday, April 21st, 2023*

Queen's UNIVERSITY

*Cover Photo: Agnes Benidickson Field*
*Courtesy of: Queen's University/Bob Weisnagel*

# James A. Low Research Day

*Donald Gordon Centre*
*Friday, April 21st, 2023*

*"Research is to see what everybody else has seen, and to think what nobody else has thought."*

*– Albert Szent-Györgyi*

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|---|---|
| 7:30 – 8:05 | **Coffee and Continental Breakfast** *(Poster and Oral Presentation Set-up)* |
| 8:05 – 8:10 | Opening Remarks (Dr. Maria Velez, Resident Research Director) |
| **8:10–9:50** | **Morning Session** \| *Chair: Dr. Maria Velez* |
| 8:10 | (O1) **Aisha Nathoo**<br>Pregnancy outcomes in survivors of adolescent and young adult breast cancer: a population-based cohort study. |
| 8:30 | (O2) **Priya Premranjith**<br>Metals and Time to Pregnancy: The Maternal-Infant Research on Environmental Chemicals (MIREC) Study |
| 8:50 | (O3) **Wafa Khoja**<br>The Effect of the COVID-19 Pandemic on Monthly Trends in Adolescent Conception in Kingston, ON |
| 9:10 | (O4) **Taylor Nelles-McGee**<br>Intravenous Ketamine for Pain Control in First Trimester Surgical Abortion: Interim Analysis of a Randomized Controlled Trial |
| 9:30 | (O5) **Anisha Dubey**<br>Retrospective review on different hysterectomy approaches for endometrial cancer |
| **9:50-10:50** | **Health Break & Poster Viewing**<br>***(Presenters available P1-P9)*** |
| 10:50 | **Keynote Speaker:** Dr. Deshayne Fell<br>Safety and effectiveness of immunization during pregnancy for mothers and infants: Where have we been and what does the future hold? |
| 11:50 | **Group Photo** (Everyone meet outside on front steps) *View 2019 as example* |
| **12:00–13:00** | **Lunch** |

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| **13:00–14:20** | **Afternoon Session 1 |** *Chair: Dr. Chandrakant Tayade* |
| 13:00 | (O6) **Samantha Levang**<br>Characterizing Sexual Minority Individuals with Endometriosis in Relation to Sexual Majority Individuals with Endometriosis |
| 13:20 | (O7) **Stanimira Aleksieva**<br>Examining the role of thymic stromal lymphopoietin in the endometriotic lesion microenvironment |
| 13:40 | (O8) **Alison McCallion**<br>Th9 Cells and Estrogen Signaling in Endometriosis Pathophysiology |
| 14:00 | (O9) **Katie Zutautas**<br>Presence of Tertiary Lymphoid Structures in Endometriosis |
| **14:20-14:35** | **Health Break** |
| **14:35–16:15** | **Afternoon Session 2 |** *Chair: David Natale* |
| 14:35 | (O10) **Lauren Brown**<br>Investigating the impact of valproic acid on placental development in CD-1 mice |
| 14:55 | (O11) **Logan Germain**<br>Exposure to the environmental endocrine disrupting chemical, triphenyl phosphate, alters the epigenome of embryonic cells in an aquatic in vitro model |
| 15:15 | (O12) **Avery McGinnis**<br>Investigating the Differentiation Potential of EomesPOS Mouse Trophoblast Cells |
| 15:35 | (O13) **Juliette Wilson-Sanchez**<br>Characterization of circulating immune cells in female patients with hypothyroidism |
| 15:55 | **Summation & Program Close** |
| **16:00–17:30** | **Wine & Cheese Reception, Atrium**<br>*(Awards Presentation) View 2022 Recipients* |

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| Poster Presentations | |
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| P1 | **Ali Tafazoli**<br>Aspirin and Endometrial Cancer: Re-visiting the Antithrombotic/Anti-Cancer Properties |
| P2 | **Shreya Anil Kumar**<br>Examining the Effect of Chemotherapy on Platelet Count and Function in Women with Breast and Gynecological Cancer |
| P3 | **Marina Ivanova**<br>Impacts of nutrition on uterine fibroids in premenopausal patients: a systematic review and meta-analysis |
| P4 | **Nakeisha Lodge-Tulloch**<br>Innate immune reprogramming in mothers and their offspring following an inflammatory pregnancy in a murine and human model |
| P5 | **Karina Fainchtein**<br>The Utility of Thromboelastography in Monitoring Coagulation Profile in Women with Cancers Under Chemotherapy |
| P6 | **Megan Cull**<br>Mechanisms of in utero-initiated benzene toxicity in the placenta |
| P7 | **Gabrielle Fava & Alexa Toews**<br>The role of inflammation-induced pregnancy complications in subsequent risk of maternal cardiovascular and metabolic disease |
| P8 | **Ainsley Johnstone**<br>Should women who screen GDM-negative and give birth to a macrosomic baby complete an HbA1C test before discharge from the hospital? |

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# Abstracts

Oral Presentations

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## (O1) Pregnancy outcomes in survivors of adolescent and young adult breast cancer: a population-based cohort study.

Aisha Nathoo[a] (MSc Candidate), Susan Brogly[ab], Maria P. Velez[ac]

*Department of Public Health Sciences, Queen's University. Kingston, ON, Canada[a]; Department of Surgery, Queen's University. Kingston, ON, Canada[b]; Department of Obstetrics and Gynaecology, Queen's University. Kingston, ON, Canada[c]*

**Objectives:** Breast cancer (BC) accounts for over 30% of cancer among adolescent and young adult (AYA) women aged 15-39 years. Little is known about pregnancy outcomes in this population. The objectives of this study were (1) to describe demographic differences between AYA BC survivors in Ontario and females with no cancer history and (2) to determine whether AYA BC survivors have an increased risk of adverse pregnancy outcomes.

**Study methods:** A retrospective cohort was created using administrative health data, including all live singleton and multiple births >22 weeks' gestation to women in Ontario aged 15-50 between April 2006 to March 2018. Exposed women were AYA BC survivors (N=474) and unexposed included deliveries to women with no cancer history (N=1,189,506). Standardized differences were used to assess differences in baseline characteristics by exposure. Modified Poisson regression was used to estimate the relative risk between AYA BC and adverse pregnancy outcomes including preeclampsia, preterm birth, small for gestational age birth, and Caesarean section (planned or unplanned). Models were adjusted for maternal age, parity, income quintile, immigration status, rurality, chronic hypertension, obesity, alcohol exposure, and smoking during pregnancy.

**Results:** Mean time from BC diagnosis to index pregnancy was 4.94 (SD 3.18) years. AYA BC survivors were older at delivery, more likely to have a higher income quintile, live in urban areas, have chronic hypertension, and have alcohol exposure during pregnancy, but were less likely to smoke during pregnancy than unexposed women. In adjusted models, BC was associated only with an increased risk of planned (aRR 1.27; 95% CI 1.08-1.49) and unplanned (aRR 1.41; 95% CI 1.20-1.66) Caesarean section.

**Conclusions:** AYA BC diagnosis is associated with an increased risk of Caesarean section, both planned and unplanned. Future studies need to investigate factors involved in the casual pathway of this association.

**Funding source:** CIHR, CGS-M, Franklin Bracken Fellowship

**Table 1.** Risk of adverse pregnancy outcomes in Ontario by adolescent and young adult BC exposure, 2006-2018.

| Outcome | Crude RR (95% CI) | Adjusted RR (95% CI) |
|---|---|---|
| Preeclampsia | 0.89 (0.58-1.36) | 0.75 (0.49-1.15) |
| Preterm Birth | 1.03 (0.72-1.46) | 0.91 (0.64-1.29) |
| Small for Gestational Age | 1.05 (0.78-1.40) | 1.03 (0.78-1.36) |
| Planned Caesarean Section | 1.67 (1.42-1.95) | 1.27 (1.08-1.49) |
| Unplanned Caesarean Section | 1.79 (1.51-2.12) | 1.41 (1.20-1.66) |

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## (O2) Metals and Time to Pregnancy: The Maternal-Infant Research on Environmental Chemicals (MIREC) Study

Priya Premranjith (MSc), Will King, Maria P. Velez.

*Department of Public Health Sciences and Department of Obstetrics and Gynecology.*

**Objective:** The aim of this study is to evaluate the relationship between toxic metals (i.e., arsenic, cadmium, lead, manganese, and mercury) and time to pregnancy (TTP) in a Canadian population among females.

**Methods:** A total of 1562 participants were eligible. TTP in months was ascertained retrospectively, via self-report, during the first trimester of pregnancy. The five metals were measured in first-trimester blood samples. Descriptive statistics (percentage detected and medians) were computed. Cox proportional hazard models for discrete-time data generated Fecundity Odds Ratios adjusted (aFOR) for maternal age, obesity, and income. FORs estimate the odds of becoming pregnant each cycle, given specific exposure. FORs < 1 denote a longer TTP, and FORs > 1 denote a shorter TTP.

**Results:** Detection rates of serum levels of all five metals were high among participants. Median concentrations were: 0.83 µg/L arsenic, 0.20 µg/L cadmium, 0.63 µg/dL lead, 8.79 µg/L manganese, and 0.72 µg/L mercury. Crude FORs in serum metal concentrations were not associated with TTP. After adjustment, we observed a slightly shorter TTP for the highest compared to the lowest quartile of exposure for lead (>0.85 µg/dL aFOR 1.38, CI 95% 1.02 - 1.50).

**Conclusion:** We observed a relationship with lead exposure in the opposite direction of the study hypothesis, that is, Pb exposure was associated with a shorter TTP. A limitation of the study is that only one measurement of exposure was available for each individual after conception. Further research is necessary to test these findings.

**Funding:** CIHR, OGS, Franklin Bracken Fellowships

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# (O3) The Effect of the COVID-19 Pandemic on Monthly Trends in Adolescent Conception in Kingston, ON

Wafa Khoja (Meds 2024), Jessica Pudwell, Ashley Waddington,

*Department of Obstetrics and Gynecology and Queen's University*

**Objective:** Knowledge of trends in adolescent conception rates can aid in delivery of targeted contraceptive and prenatal resources. Conception rates during the COVID-19 pandemic years (2020-2021) are compared to pre-pandemic years (2016-2019) in Kingston, ON.

**Study methods:** Patients aged ≤19 years old at estimated date of conception between 2016-2021 who were seen for a pregnancy related visit at Kingston Health Sciences Centre were included. Pregnancies that ended <20 weeks gestational age (GA) were captured using ICD-10 procedure codes for pregnancy loss or termination. Data for births that occurred ≥20 weeks GA were obtained from the BORN database. Month and year of conception were calculated using chart review based on diagnostic imaging reports or provider estimates of GA.

**Results:** 897 adolescent conceptions were captured between January 1st, 2016, and December 31st, 2021, with 54.6% of these pregnancies ending <20 weeks GA. Results were separated between age groups <18 years old and 18-19 years old at the time of conception. Overall, there has been a decline in adolescent conception rates between January 2016- December 2021 (test for trend $p<0.001$). Contrary to published trends of peak adolescent conceptions in March 2004-2008, mean conceptions were highest in January in the <18 group; and in January and February in the 18-19 group during 2016-2019. These trends did not continue through the pandemic years. There was no significant decline in the number of conceptions during periods of lockdown.

**Conclusions:** Conception rates in Kingston's adolescent population have been decreasing since 2016. Conception rates differ between age groups <18 years old and 18-19 years old for monthly trends, with January and February having higher rates of conception than most other months in 18–19-year-olds. Pandemic years showed no significant seasonal trends in conception rates compared to pre-pandemic years Further, pre-pandemic monthly conception rates differ from previously established trends and provide opportunity to deliver targeted contraceptive and prenatal resources to the youth of Kingston, ON.

**Funding Source:** None

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# (O4) Intravenous Ketamine for Pain Control in First Trimester Surgical Abortion: Interim Analysis of a Randomized Controlled Trial

Taylor Nelles-McGee (Meds 2025); Ashley Waddingtona; Jessica Pudwell[a]; Irene Zouros[b]; M. E. Sophie Gibson[a]

*[a]Department of Obstetrics and Gynecology and Queen's University bDepartment of Family Medicine and Queen's University*

**Background:** Surgical abortion is common, with most completed in the first trimester. Gold standard pain control is intravenous (IV) Fentanyl and Midazolam, requiring continuous cardio-respiratory monitoring. This can be challenging in settings where this monitoring is unavailable. Ketamine is a sedative and analgesic without the cardio-respiratory depression risk associated with IV opioids and represents a potential alternative. Investigating non-opiate pain control methods where appropriate is also imperative in the context of the opioid crisis.

**Objective:** This is an interim analysis of (N=45) participants from a randomized controlled trial (RCT) comparing IV Ketamine, oral (PO) Morphine, and IV Fentanyl for pain control in first trimester surgical abortion (FTSA) with the hypothesis that Ketamine will provide better pain control than Morphine.

**Methods:** The trial is a double-blind, single-center superiority trial of three parallel groups. Potential participants were ≥18 years old with confirmed intrauterine pregnancy of gestational age <12 weeks. Pain was assessed using the Visual Analogue Scale (VAS) and the Wong-Baker Faces Pain Rating Scale.

**Results:** Two participants were excluded post-randomization for a total of (N=43) treated. Findings indicate that Ketamine (N=14) provides better intra-operative pain control than Morphine (N=15) and Fentanyl (N=14, $p<0.001$). The Ketamine group evidenced more satisfaction with anesthetic method than the Morphine group ($p=0.017$). No serious adverse events were observed in any group.

**Conclusions:** Findings support continuation of the RCT and may lead to increased access to more optimal pain control in settings where continuous cardio-respiratory monitoring is unavailable without increasing adverse events. Results highlight Ketamine as a compelling non-opiate pain control option in FTSA.

**Keywords:** procedural sedation, ketamine, fentanyl, morphine, therapeutic abortion

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## (O5) Retrospective review on different hysterectomy approaches for endometrial cancer (Work in Progress)

Anisha Dubey (R3), Maria Fernanda Huicochea Munoz, Melody Wyslobicky, Mahshid Hosseini, Jessica Pudwell, Anita Agrawal

*Department of Obstetrics and Gynecology Queen's University*
*Division of Gynecologic Oncology*

**Objectives:** Endometrial cancer is the most common gynecologic malignancy in Canada, with over 8000 new diagnoses in 2022. Surgical management is the mainstay of treatment and with the advances in minimally invasive surgery (MIS), there has been a shift towards use of MIS for patients with endometrial cancer. Our study aims to compare the surgical and oncologic outcomes of hysterectomy approaches for endometrial cancer, including recurrence and survival rates for those undergoing MIS or open surgery.

**Methods:** Retrospective chart review for all endometrial cancer cases from Kingston Health Sciences Centre between January 2017 to April 2020. Variables were collected and categorized. Statistical analysis was completed for all surgical outcomes and Kaplan-Meier analysis was used to compare survival and recurrence rates.

**Results:** A total of 119 cases were included in this review thus far. 41 (34.4%) of these cases were total laparoscopic hysterectomies and laparoscopic-assisted vaginal hysterectomies and 78 (65.6%) were total abdominal hysterectomies. The early complication rates ($p<0.001$) and length of stay ($p<0.001$) were lower in the laparoscopic group compared to the abdominal group. Despite the abdominal group including more cases with stage 3 and 4 disease, there were no differences in survival outcomes and recurrence rates between the groups ($p<0.74$).

**Conclusion:** Overall laparoscopic approaches for treatment of endometrial cancer result in better surgical outcomes, while oncologic outcomes remain the same between both laparoscopic and abdominal groups.

**Funding Source:** None

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## (O6) Characterizing Sexual Minority Individuals with Endometriosis in Relation to Sexual Majority Individuals with Endometriosis

Samantha Levang (PhD Student), Caroline Pukall.

*Department of Psychology at Queen's University*

**Objective(s):** Endometriosis is a painful, chronic inflammatory condition that can significantly disrupt sexual function and is associated with negative outcomes in mental health, relationship satisfaction, and quality of life (Friggi Sebe Petrelluzi et al., 2012; Smorgick et al., 2013). Although up to 10% of women are affected by endometriosis (As-Sanie et al., 2019), most studies examining this condition have enlisted heterosexual cisgender participants and have focused on sexual and pain outcomes through a heteronormative lens (e.g., examining pain and sexual distress resulting from penile-vaginal intercourse). As a result, there is little research on the experience and outcomes of endometriosis in individuals who identify as sexual minorities (e.g., lesbian, bisexual). By including individuals who identify as a sexual minority, and thus taking a broader view of lived experiences of those with endometriosis, we may gain insight into the pain characteristics, sexual outcomes, and endometriosis history of individuals who are often excluded from this field of research.

**Methods:** The current study was conducted online and recruited individuals with a self-reported clinician-identified diagnosis, or a self-reported suspected diagnosis, of endometriosis. Inclusion criteria for the current study included (1) identifying as 18 years of age or older, (2) being fluent in reading and writing English, and (3) currently in an intimate and/or romantic relationship with a partner or partners. All eligible participants completed questions about sociodemographics and endometriosis history in addition to empirically validated measures on pain characteristics and sexuality. Differences between pain and sexuality-related outcomes as well as endometriosis history among individuals who identified as a sexual minority or sexual majority were examined via chi-square analyses and independent samples t-tests.

**Results:** Participants were 523 individuals who identified as a sexual minority (27.2%) or sexual majority (72.8%) with a confirmed (92.2%) or suspected (7.8%) diagnosis of endometriosis. Chi-square analyses revealed significant differences among perceived disability status, $\chi 2$ (2, N = 523) = 22.46, p <.001, endometriosis stage, $\chi 2$ (5, N = 523) = 13.50, p = .019, pain pattern, $\chi 2$ (3, N = 523) = 13.03, p = .005, pain onset, $\chi 2$ (2, N = 523) = 7.47 p = .024, and whether the participant experienced chronic pain (pain experienced for 3 months or more), $\chi 2$ (1, N = 523) = 4.67, p = .031. Independent samples t-tests revealed significant differences among current pain intensity (p = .045) and sexual flexibility (p < .001). No significant between-groups differences were found in pain catastrophizing, pain anxiety, sexual pleasure, sexual satisfaction, sexual distress, and sexual self-consciousness.

**Conclusion:** As one of the first investigations of the pain characteristics, sexual outcomes, and endometriosis history of individuals who identify as a sexual minority with endometriosis, the current study offers a critical first step towards advocating for inclusion of underrepresented participants with endometriosis. In addition, it generates evidence to better inform scholars, researchers, and healthcare practitioners about how to improve patient care and improve the of quality of life for all individuals with endometriosis.

**Funding Source(s):** Canadian Institutes of Health Research (CIHR) Project Grant (178118) and the International Society for the Study of Women's Sexual Health (ISSWSH) Scholars in Women's Sexual Health Research Grant Program

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## (O7) Examining the role of thymic stromal lymphopoietin in the endometriotic lesion microenvironment

Stanimira Aleksieva (M.Sc. Candidate), Harsha Lingegowda, Alison McCallion, Katie Zutautas, Danielle Sisnett, Chandra Tayade,

*Queen's University, Kingston, ON, Canada.*

**Objectives**: Endometriosis is a chronic disease where lesions comprised of stromal cells, glandular epithelial cells, and immune cells grow outside the uterus. Endometriosis is postulated to develop due to improper clearance of menstrual debris that has entered the peritoneum via retrograde menstruation. However, the immune factors that are altered in patients to prevent ectopic tissue removal remain elusive. Thymic stromal lymphopoietin (TSLP) is an alarmin shown to be present within ectopic endometriotic lesions, induce endometriotic stromal cell proliferation, and modulate immune cell activation. For instance, TSLP could promote alternative macrophage polarization, a population associated with reduced tissue clearance and increased endometriotic lesion size. This leads to the hypothesis that TSLP and TSLP receptor (TSLPR) are expressed in endometriotic lesions and modulate lesion-associated proliferation, inflammation, and vascularization. This project will (1) characterize TSLP expression in patient samples (i.e., lesions, peritoneal fluid, serum), (2) determine how recombinant TSLP treatment modulates the function of endometriosis-representative and immune cell lines, and (3) evaluate the impact of recombinant TSLP treatment on endometriotic lesion growth and inflammation in a mouse model of endometriosis.

**Methods:** To evaluate TSLP expression in patients and controls, immunohistochemistry was conducted on a tissue microarray constructed with matched patient eutopic and ectopic endometrial tissue (n = 19) and control endometrial tissue (n = 15). To understand the impact of TSLP on endometriosis-representative cell lines, human endometriotic epithelial cells, human endometrial stromal cells, and mouse bone marrow-derived macrophages (BMDMs) were treated with recombinant TSLP. Resultant cell proliferation and apoptosis was evaluated with fluorometric assays, and BMDM polarization was examined using flow cytometry.

**Results:** TSLP expression was significantly elevated in the stromal cells of patient endometriotic lesions compared to control endometrium and significantly reduced in the epithelial cells of patient endometriotic lesions compared to patient eutopic endometrium. TSLP treatment did not impact the proliferation and apoptosis of the aforementioned cell lines. TSLP treatment was shown to significantly reduce TSLPR expression and promote alternative BMDM polarization.

**Conclusion:** Altered TSLP expression in patient ectopic lesions compared to control endometrium indicates that the alarmin could be dysregulated and implicated in endometriosis development. To further assess differences in TSLP expression, future research will measure TSLP mRNA levels in patient lesions and control endometrium. Recombinant TSLP treatment did not impact the proliferation and apoptosis of endometriosis-representative cell lines. This indicates that the alarmin allows cells to persist in its presence. Future experiments will evaluate the impact of TSLP treatment on additional cell lines, such as endometriotic stromal cells, and perform co-cultures to observe cellular interactions in response to treatment. Reduced TSLPR expression and alternative polarization in BMDMs indicates that cells are responsive to TSLP, and that the alarmin could contribute to reduced tissue clearance. Future research will involve the induction of endometriosis in C57BL/6 mice and subsequent treatment with recombinant TSLP to examine the effects of the alarmin on lesion growth and immune cell infiltration into the peritoneal microenvironment.

**Funding:** CIHR, Queen's University.

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## (O8) Th9 Cells and Estrogen Signalling in Endometriosis Pathophysiology

Alison McCallion (PhD Candidate), Danielle Sisnett (PhD Candidate), Katherine Zutautas (PhD Candidate), Chandrakant Tayade.

*Department of Biomedical and Molecular Sciences (Reproductive and Developmental Sciences), Queen's University.*

**Introduction:** The interface of endocrine and immune dysregulation affecting endometriosis (EM) lesion growth is an evolving concept. Interleukin-9 (IL-9) is a cytokine with roles in inflammation and fibrosis. IL-9 is a vital growth factor for mast cells, which have been implicated in EM pathophysiology. T helper 9 (Th9) cells are IL-9-producing T cells involved in inflammatory diseases like cystic fibrosis and endometrial carcinoma. Within endometrial carcinoma, IL-9 production by Th9 has been found to be regulated by estrogen. The relationships between Th9, mast cells and E2 have not been defined in EM pathophysiology.

**Aims:** Understand involvement of IL-9 and Th9 cells in EM pathophysiology, both independently and with respect to mast cell activity. Define the role of Th9 cells within a mouse model of EM and discern effects of E2 on IL-9-producing immune cell populations.

**Methods:** Using our EM mouse model, groups of C57Bl/6 mice were treated with or without E2 and received adoptive transfer of Th9-like lymphocytes or saline control. Peritoneal fluid (PF), blood plasma and EM lesions were collected; flow cytometry was used to classify immune cell populations in PF and spleen. Using primary human peripheral blood mononuclear cells (PBMC), CD4+ T cells were driven in culture towards Th9 phenotype. Then, in vitro experiments were conducted with hormonal treatments of estrogen and progesterone to capture cytokinic signalling responses within human Th9 cell populations. Human mast cell line HMC-1 cells were "co-cultured" with conditioned media from Th9-PBMC culture supernatants to capture cytokinic signalling relationships.

**Results:** E2-treated mice showed a significant reduction in splenic populations of IL-9-producing immune cells (Th, mast cells) and IL-9R-expressing cells (neutrophils, CD8a+ dendritic cells). E2 increased PF concentration of IL-9-modulating cytokines (IL-6, CXCL-10). Plasma concentrations of IL-9 significantly decreased in E2-treated mice but not untreated mice. In vitro, E2 treatments significantly increased IL-9 production from human Th9-driven PBMC, along with several other chemotactic and inflammatory cytokines. Co-culture experiments with HMC-1 cells revealed rich cell crosstalk influenced by hormonal conditions, where cytokinic secretory responses were significantly magnified downstream upon mast cell exposure to Th9-driven PBMC media.

**Significance:** These results demonstrate an impact of E2 on IL-9-producing T cells and Th9/mast cell signalling within EM. Continuing to decode the complex immunopathophysiology of EM will lead to new opportunities in therapeutic development.

**Funding Source:** CIHR, Queen's University.

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## (O9) Presence of Tertiary Lymphoid Structures in Endometriosis

Katherine B. Zutautas[1] (PhD Candidate), Minqi Xu[2], Timothy Childs[2], Madhuri Koti[1] Chandrakant Tayade[1]

[1]*Department of Biomedical and Molecular Sciences, Queen's University*
[2]*Kingston General Hospital, Kingston Health Sciences Centre*

**Introduction:** Tertiary lymphoid structures (TLS) are organized immune cell aggregates present in non-lymphoid tissues. Found in conditions with chronic inflammation, TLS serve as a reservoir for immune cell replenishment and activation, with the potential for beneficial or deleterious consequences. In reproductive cancers (endometrial and ovarian), the presence of TLS is associated with improved patient prognosis, however in autoimmune disease, TLS perpetuate autoreactivity. Recently, TLS have been identified within peritoneal lesions of endometriosis patients. As endometriosis is a chronic inflammatory gynaecological disease with hallmarks of immune dysfunction that parallel both cancer and autoimmunity, further characterization is needed to determine if TLS are consistent features of endometriosis.

**Objective:** To investigate whether TLS are present within the endometriosis lesion microenvironment across disease phenotypes.

**Methods:** Study cohort consists of n=121 matched lesion (ectopic) and endometrium (eutopic) from endometriosis patients and n=120 control endometrium samples. A subset of samples indicating TLS presence (n=18; n=6 ectopic/eutopic/control) were sectioned and stained using a multiplex immunohistochemistry panel identifying classic TLS cell types: $CD3^+$ and $CD8^+$ T cells, $PNAd^+$ high endothelial venules, $CD208^+$ dendritic cells, $CD21^+$ follicular dendritic cells, and $CD79a^+$ B cells.

**Results:** Preliminary results show presence of markers associated with classic TLS organization in ectopic and eutopic tissues. Analysis is in progress to determine if TLS can be associated with endometriosis pathophysiology and lesion phenotype.

**Impact:** These findings provide insight into the dynamic role of the endometriosis lesion microenvironment in sustaining immune cell function and inspire research into the prognostic implications for patients.

**Funding Source:** CIHR

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## (O10) Investigating the impact of valproic acid on placental development in CD-1 mice (Research Proposal)

Lauren Brown (MSc. Candidate), Lihua Xue, and Louise Winn.

*Department of Biomedical and Molecular Sciences, Queen's University.*

**Objective:** Valproic acid (VPA) is a potent teratogen that causes numerous adverse pregnancy outcomes. In particular, VPA causes fetal growth restriction (FGR) which is most commonly associated with placental insufficiency, characterized as inadequate transplacental nutrient transport to the fetus. Gestational exposure to teratogens, such as VPA, can disrupt placental structural or functional development, resulting in placental insufficiency and, consequently, FGR. Although VPA-induced teratogenicity is well-studied, there is a significant gap in knowledge regarding the effect of VPA on the placenta. As such, the objective of this study is to assess the impact of VPA on placental development by measuring the relative size of each placental layer.

**Methods:** A CD-1 mouse pregnancy model will be used to investigate the effect of in utero VPA exposure on the placenta. On gestational day (GD) 9, pregnant dams will be subcutaneously injected with either 400 mg/kg VPA or saline as a vehicle control. On GD18, the dams will be sacrificed, and the fetal and placental tissues will be excised. Fetus, fetus head, and placenta weights will be measured. Weight measurements will be analyzed to determine whether VPA-exposed fetuses are growth restricted. Placentas will be subsequently fixed, paraffin-embedded, and sectioned onto slides for histological analysis. The mouse placenta comprises three major zones: the maternal decidua, the junctional zone, and the labyrinth zone. To determine the effect of VPA on placental development, alkaline phosphatase (AP) staining counterstained with nuclear fast red will be used to visualize the placental layers. This staining technique will clearly define the borders of the labyrinth and junctional zone, allowing for the measurement of their area relative to the whole placenta.

**Results:** It is hypothesized that VPA-exposed fetuses and placentas will be significantly smaller compared to the saline controls. Additionally, I expect that VPA-exposed placentas will exhibit a significantly enlarged labyrinth zone. The placental labyrinth zone mediates nutrient and oxygen delivery to the fetus, which is essential for normal fetal growth and development. An enlarged labyrinth zone may indicate that VPA impacts placental structural development by altering placental vascularization.

**Conclusion:** Despite the significant teratogenic risk, VPA is still widely prescribed to women of childbearing potential as a mood stabilizer for bipolar disorder or anti-epileptic. Discontinuing long-term VPA treatment during pregnancy is ill-advised, as this can potentially induce manic or epileptic episodes, harming the health of the mother and fetus. Additionally, FGR is associated with several short- and long-term consequences that severely impact the quality of life. As such, it is essential to study VPA-induced toxicity such that a future preventative therapy may be developed, thereby increasing the number of successful, healthy pregnancies from VPA-treated women.

**Funding Source:** CIHR, Queen's University

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## (O11) Exposure to the environmental endocrine disrupting chemical, triphenyl phosphate, alters the epigenome of embryonic cells in an aquatic in vitro model

Logan Germain (MSc. Candidate), Alexa Muir, Veronica Duffy, Lihua Xue, Louise Winn.

*Department of Biomedical and Molecular Sciences, Department of Environmental Sciences.*

**Objective(s):** The objective of this study was to determine whether exposure to the flame retardant and ubiquitous environmental pollutant called triphenyl phosphate (TPP) alters the epigenome. It is known that TPP is an endocrine disrupting chemical and that exposure to TPP can alter gene expression in metabolic and estrogenic signaling pathways in exposed generations. Endocrine disrupting chemical exposure is increasingly being associated with changes to the epigenome and gene expression. As such, I hypothesize that exposure to TPP causes changes to the epigenome, in a cell-type specific manner – with greater changes seen in germline cells compared to somatic cells.

**Study Methods:** This study used two immortalized cell lines derived from trout: STE-137 is derived from embryonic tissue and RTGill-W1 is derived from epithelial tissue. Both cell lines were exposed to either 0 (control), 40 or 80 $\mu$M of TPP for 24 hours. This exposure regimen was chosen based on being below the determined No Observed Effect Concentration for cell viability and cell proliferation that was previously established by the Winn Lab. Following exposure, the cells were harvested, and their histones were acid extracted. Histone were separated using SDS-PAGE and detection of post-translation histone modifications were detected via immunoblotting. Fluorescent signal for the histone modifications of interest were normalized to their respective loading control signal and expressed relative to control signal (0 $\mu$M of TPP). One-way ANOVA's were performed to between the fluorescence values of each concentration point and Tukey's multiple comparison test was performed post-hoc (n = 3).

**Results:** Results show that post-translational modifications on histone H3 are altered in the embryonic cells following TPP exposure, but not in the somatic epithelial cells. Statistical analysis shows that levels of histone H3 acetylation is significantly reduced in the embryonic cells, at both 40 and 80 $\mu$M of TPP. No difference was seen in histone H3 acetylation in the epithelial cells at any concentration point. Levels of histone H3 mono-methylation was significantly reduced in the embryonic cells, at 80 $\mu$M of TPP, while no difference was seen in the epithelial cells at any concentration point.

**Conclusion(s):** These results show that TPP exposure alters the epigenome of germline cells. Histone H3 acetylation is a well-established marker for transcriptional activation, while histone H3 mono-methylation on lysine 9 is a well-established maker for transcriptional repression. The alterations of these histone modifications in the embryonic cells, but not in the somatic cells, suggests that exposure to TPP during fetal development may alter gene expression in the developing embryo, and may have detrimental effects on human and ecosystem health.

**Funding Source:** NSERC, CGS-M NSERC Award, Queen's University

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## (O12) Investigating the Differentiation Potential of EomesPOS Mouse Trophoblast Cells

Avery McGinnis (MSc Candidate)1, Megan Cull (PhD Candidate)1, Nichole Peterson (Senior Laboratory Technician)2, Dr. David Natale (Principal Investigator)1,2

*Departments of 1Biomedical and Molecular Sciences, 1Obstetrics and Gynaecology, Queen's University, Kingston, ON, Canada*

**Objective:** Mouse trophoblast stem (TS) cells can be derived from polar trophoblast of the blastocyst or from trophoblast cells of the extraembryonic ectoderm (ExE) of the developing placenta, until embryonic day (E) 6.5. Eomesodermin (Eomes) is a transcription factor required for and used to identify TS cells. During early development, Eomes is restricted to the ExE and by E7.5, to the chorion after which its expression declines and is detectable in a small number of cells in the labyrinth layer. The junctional zone and labyrinth layers of the placenta are thought to develop independently from layer-specific progenitor cells of the ectoplacental cone and chorion, respectively. Eomes-expressing TS cells in vitro, differentiate to all trophoblast sub-types of the placenta; however, our objective was to assess their developmental potential in vivo.

**Methodology:** Genetic lineage tracing was used to evaluate the in vivo differentiation potential of EomesPOS trophoblast, using a tamoxifen-inducible, Eomes-Cre mouse crossed with a conditionally expressed Ai6 reporter mouse. Cre was activated at E7.5-9.5, permanently marking all placental EomesPOS trophoblast and daughter cells with green fluorescence. This was combined with immunofluorescent antibody staining to assess differentiation in placentas collected at E17.5.

**Results:** Daughters of EomesPOS trophoblast contributed to both placental layers. Antibody staining revealed that EomesPOS cells gave rise to sinusoidal trophoblast giant cells and layer II syncytiotrophoblast within the labyrinth, as well as glycogen trophoblast and spongiotrophoblast within the junctional zone. However, EomesPOS cells did not appear to give rise to EpcamPOS labyrinth progenitors within the chorionic plate and lower labyrinth.

**Conclusions:** EomesPOS trophoblast have the capacity to differentiate and contribute to both layers of the placenta in vivo after E6.5. Future studies will use this approach to lineage trace EomesPOS trophoblast in the later-stage placenta and assess their role in placental pathology.

**Funding Source:** This work is supported by a CIHR MSc Graduate Scholarship (CGS-M; AM) and NIH/NICHD Operating Grant (DRCN)

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## (O13) Characterization of circulating immune cells in female patients with hypothyroidism.

Juliette Wilson-Sanchez[1,2] (Masters Student), Priyanka Yolmo[1,2], Jessica Pudwell[3], Maria Velez[3], Madhuri Koti[1,2,3].

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*2. Division of Cancer Biology and Genetics, Queen's Cancer Research Institute, Kingston, Canada.*
*3. Department of Obstetrics and Gynecology, Queen's University, Kingston, Canada.*

**Objective:** Thyroid disease is 5-20 times more likely in women than men, and the incidence of the disease increases with age. Previous reports have demonstrated increased inflammatory scores in patients with hypothyroidism. Many studies have associated history of hypothyroidism to increased mortality in several female cancers, although the mechanism behind why hypothyroidism results in poor clinical outcomes is unclear. In this study, we aimed to investigate if female patients with hypothyroidism exhibited different peripheral immune cell profiles as a result of increased inflammation associated with hypothyroidism.

**Study Methods:** Participants were recruited from an outpatient reproductive endocrinology clinic in the Kingston General Hospital. Female patients with a history of hypothyroidism (n=15) were eligible to join the study regardless of current levothyroxine use. Healthy controls (n=25) were identified based on thyroid stimulating hormone (TSH) values within the normal range and no previous history of hypothyroidism or any other autoimmunity. Each participant donated 9-12mL of venous blood for isolation of their peripheral blood mononuclear cells (PBMCs). Each PBMC sample was processed for multiparametric flow cytometric analysis of both adaptive and innate immune cell populations. Analysis of flow cytometry data was carried out using FlowJo after appropriate sample quality control and compensation. Using GraphPad Prism, student t-tests were performed to determine statistical differences between the hypothyroid group and healthy controls for each immune cell population of interest.

**Results:** Significant increases in myeloid cell populations were observed in patients with hypothyroidism compared to healthy controls. Classical dendritic cells, intermediate monocytes, and classical monocytes were all increased in these patients. In addition, several helper T cell populations and B cells were slightly increased in hypothyroid patients, although these differences were not statistically significant.

**Conclusion:** Our findings indicate distinct differences between the immune cell profiles of female patients with hypothyroidism and their healthy counterparts. As we observed these differences patients treated with levothyroxine, these differences are likely downstream consequences from the continuous cell death at the level of the thyroid and the respective response to such inflammation. This concept is further confirmed as patients with elevated TSH did not exhibit significant differences from other hypothyroid patients. These findings highlight a potential chronic inflammatory state in female patients with hypothyroidism. Differences in key innate immune responders may be disadvantageous in the context of other diseases such as cancer, given that these cells are some of the first responders to malignant transformation. As such, it is essential to continue further research to understand the consequences of hypothyroidism as a long-term chronic comorbidity.

**Funding source:** Ontario Graduate Scholarship, Canadian Foundation for Innovation, Early Researcher Award; Ontario Ministry of Research Innovation and Science

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# Abstracts

## Poster Presentations

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# (P1) Aspirin and Endometrial Cancer: Re-visiting the Antithrombotic/Anti-Cancer Properties

Ali Tafazoli (PharmD PhD)[1], Maha Othman (MD PhD)[1,2,3]

[1] *Department of Biomedical and Molecular Sciences, School of Medicine, Queen's University, Kingston, Ontario, Canada*
[2] *School of Baccalaureate Nursing, St Lawrence College, Kingston, Ontario, Canada*
[3] *Clinical Pathology Department, Faculty of Medicine, Mansoura University, Mansoura, Egypt*

**Objectives:** Endometrial cancer (EC) is among the 4 top cancers diagnosed in women and is highly thrombogenic. Venous thromboembolism is estimated as high as 8% in patients with this malady. Cancer modifies platelet activity and platelets are also known to affect tumor growth, survival, angiogenesis, and apoptosis. Aspirin is a common anti-platelet drug used in prevention and treatment of cardiovascular disease but its preventive and therapeutic value in cancer has only been described in a few cancer types. Considering the availability, affordability, and safety of aspirin as an effective medication, assessment of its potential benefits in endometrial cancer will be valuable. In this study, we aim to explore the literature to assess the use of aspirin in preventive and therapeutic regimens of endometrial cancer.

**Study method:** Due to sparsity of data in this field we applied a narrative review style for the study. We searched the PubMed database using MeSH terms “Endometrial Neoplasms” and “Aspirin" without any limitation or filters. Studies focusing on non-steroidal anti-inflammatory drugs instead of aspirin and those with focus on all or different cancer types other than EC were excluded. Checking the references within the references also showed acceptable precision in the selected articles for this narrative exploration.

**Results:** Nineteen articles resulted from this search, and were divided into 4 categories including in vitro, preventive, therapeutic and review articles. Overall, the findings for use of aspirin for prevention and adjuvant use were more abundant compared to the observations negating its use. However, three factors prevented making a clear recommendation about aspirin use in EC. First, lack of studies exclusively evaluating the effect of aspirin in EC without incorporating cardiovascular indications. Secondly, a considerable number of studies were not able to find a positive effect for aspirin. However, generally the safety of aspirin uses were reported or at least no specific negative effect was evaluated or reported. Thirdly, at least in one study, increased mortality was reported for aspirin use during the disease related care. The evidence to support aspirin use as an antithrombotic in EC is very low.

**Conclusion:** The current evidence for the value of aspirin use in EC is limited. Therefore, carefully designed randomized controlled trials will be required before making a firm recommendation about its use.

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# (P2) Examining the Effect of Chemotherapy on Platelet Count and Function in Women with Breast and Gynecological Cancer

Shreya Anil Kumar (BScH)[1], Yousra Tera[1,2], Mazen Assar[1,3], Yoon Jin Suh[1,3], Maria Karizhenskaia[3], Karina Fainchtein[1], Anita Agrawal[4], Mihaela Mates[5], Maha Othman[1,2,3]

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*[5] Department of Oncology, Queen's University, Kingston, Ontario, Canada*

**Objectives:** Examine changes in platelet count, mean platelet volume and platelet aggregation with chemotherapy cycles over time. Determine the association of the above changes with cancer progression, bleeding tendency, or thrombotic events.

**Study Methods:** A single centre, prospective, longitudinal cohort study of newly diagnosed adult cancer patients. Patients planned to receive the recommended anticancer chemotherapy for gynecological and breast cancers were recruited. Blood samples were taken prior to chemotherapy and then again pre cycles 2 and 3. ADP-induced platelet aggregation was performed using Chrono-Log #592. Platelet count and Mean Platelet Volume were assessed at the same frequent time points. Baseline demographics, menopausal status, BMI, Khorana score, VTE risk factors were recorded. Paired t-test and repeated measure ANOVA were used to assess the effect of each chemo cycle compared to the basal level.

**Results:** A total of 32 newly diagnosed patients aged 35-85 (17 breast, 10 endometrial, 5 ovarian), prescribed chemotherapy (27% neo-adjuvant, 67% adjuvant, 6% both) were evaluated to date. 53% of patients were under platinum-based chemotherapy, 22% of patients had comorbidities, and 21% had metastatic disease. Platelet count, size and aggregation are all within normal range, however all values are seen to be decreasing after each chemotherapy cycle. Paired t-test indicated significant reduction in platelet count ($p=0.0001$), size ($p=0.0001$) and aggregation ($p=0.0001$) after the first dose of chemotherapy. Repeated measures ANOVA indicated significant difference in platelet count ($p=0.0001$), size ($p=0.0001$), and aggregation ($p=0.0001$) with chemotherapy overtime. No thrombotic events were recorded.

**Conclusion(s):** Data from this pilot study indicates platelets undergo quantitative and functional changes following chemotherapy and/or in association with cancer progression. Platelets show diverse changes after chemotherapy and unlike expected, aggregation is inhibited in this patient cohort. The effect of cancer chemotherapy on coagulation is complex and requires attention. Future work will focus on assessing these effects in each specific cancer type.

**Funding Source:** St. Lawrence College Ignite Fund and Department of Biomedical and Molecular Sciences 499 Student Fund.

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## (P3) Impacts of nutrition on uterine fibroids in premenopausal patients: a systematic review and meta-analysis.

Marina Ivanova (Meds 2025), Ally Soule (Meds 2024), Jessica Pudwell (MSc, MPH), Olga Bougie (MD, FRCSC, MPH).

*Department of Obstetrics and Gynecology and Queen's University.*

**Objective:** Uterine fibroids are the most common gynecological tumours and may be associated with significant disease burden. Modifiable lifestyle factors, particularly nutrition, have been noted to play a protective role. This review synthesized the findings from existing literature examining the association between nutrition and fibroid incidence and severity.

**Study methods:** Published studies were identified through searching MEDLINE, Embase, CINAHL, Web of Science and grey literature. Randomized controlled trials and observational studies investigating associations between diet, nutritional status and fibroids in premenopausal subjects were included. Methodological quality was assessed using the Newcastle-Ottawa Scale and the Risk of Bias-2 tools. Data was pooled using random effects modelling. An I2 statistic was used to evaluate heterogeneity. Evidence quality was evaluated using Grading of Recommendations Assessment, Development and Evaluation.

**Results:** From 9931 studies identified, 40 full texts were included. Patients with fibroids had lower mean serum Vitamin D levels (MD -5.50 ng/mL, CI -6.99, -4.01, $p<0.001$) and were more likely to be Vitamin D deficient (OR 2.61, CI 1.64, 4.16, $p<0.001$), compared to those without fibroids. Additionally, patients receiving Vitamin D supplementation had a significant decrease in fibroid size (SMD -5.69%, CI -10.63, -0.76, $p=0.02$), compared to controls. Included studies also endorsed protective effects of a plant-based diet and green tea extract.

**Conclusions:** This review underscores the role of dietary nutrition, in particularly vitamin D, in fibroid development and progression. Vitamin D supplementation and dietary intervention may reduce the prevalence and/or fibroid disease burden, however further research is needed to support this recommendation.

**Funding source:** Project was supported by the Department of Obstetrics and Gynecology at Queen's University.

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## (P4) Long-term innate immune reprogramming in mothers and their offspring following an inflammatory pregnancy in a murine and human model.

Nakeisha Lodge-Tulloch (Ph.D. Candidate), Jean-François Paré, Tiziana Cotechini, Charles Graham.

*Department of Biomedical and Molecular Sciences and Queen's University.*

**Objective:** Pregnancy complications such as pre-eclampsia (PE) and fetal growth restriction (FGR) are known to be associated with aberrant maternal inflammation and placental stress. The latter can lead to the release of damage associated molecular patterns (DAMPS) from the placenta which can bind and activate pattern recognition receptors (PRRs) found on innate immune cells. Innate immune reprogramming is a phenomenon in which cells of myeloid lineage acquire memory through epigenetic reprogramming following exposure to an inflammatory stimulus. This subsequently results in an altered response (i.e., enhanced or dampened) after re-exposure to a similar or heterologous stimulus. We examined whether inflammation induced FGR in a murine model is associated with reprogramming of innate immune cells in dams and their offspring, which could be linked to an increased risk of disease in later life, such as risk of subsequent complications of pregnancy. We also examined reprogramming of innate immune cells in peripheral blood collected from women who had normal pregnancies and women who had complicated pregnancies (PE and FGR).

**Study methods:** To examine whether inflammation induced FGR leads to innate immune reprogramming, pregnant C57BL/6 mice aged 49-56 days were administered saline (N=4) or 20 µg/kg lipopolysaccharide (LPS) (N = 2) on gestational day (GD) 10.5. To assess for innate immune reprogramming, bone marrow monocytes were isolated from mononuclear cells collected from dams three weeks after delivery and from their offspring (F1) at reproductive age (four weeks after delivery). Isolated bone marrow monocytes were exposed to the pathogen associated molecular patterns (PAMPs) LPS and Pam3Cys in vitro for 24h. Concentrations of various pro- and anti-inflammatory cytokines were measured in the resulting cell-free supernatants using a multiplex platform (Eve Technologies, Calgary AB). In parallel, we also assessed innate immune reprogramming in humans experiencing a complicated pregnancy. Third-trimester pre-labor peripheral blood was collected from women who had pregnancy complications (N= 13) or not (N=5). Monocytes were purified and exposed to a secondary challenge with LPS in vitro. Reprogramming of innate immune cells was assessed as previously described.

**Results:** Preliminary results of cytokine levels in murine monocyte cultures from dams and their offspring revealed a decrease in IL-10 and TNF-a concentrations respectively after secondary challenge with PAMPs. This is indicative of innate immune reprogramming following LPS-induced FGR in pregnancy. Similarly, human monocytes isolated from peripheral blood (PE and FGR) exhibit innate immune reprogramming in pregnancy complications, as shown by an increase in IL-10 levels after secondary challenge with LPS.

**Conclusion(s):** These results provide a rationale to further investigate whether long-term innate immune reprogramming is mechanistically linked to an increased risk of disease, including increased risk of subsequent pregnancy complications. Linking innate immune reprogramming to an increased risk of subsequent pregnancy complications could lead to the development of better therapeutic interventions or preventive measures.

**Funding source:** Supported by the Canadian Institutes of Health Research (CIHR).

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# (P5) The Utility of Thromboelastography in Monitoring Coagulation Profile in Women with Cancers Under Chemotherapy

Karina Fainchtein (BScH)[1], Yousra Tera[1,2], Mazen Assar[1,3], Yoon Jin Suh[1,3], Maria Karizhenskaia[3], Shreya Anil Kumar[1], Anita Agrawal[4], Mihaela Mates[5], Maha Othman[1,2,3]

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*[5] Department of Oncology, Queen's University, Kingston, Ontario, Canada*

**Objectives:** To assess TEG's diagnostic value of a hypercoagulable state in breast and gynecological oncology patients undergoing chemotherapy. To determine if hypercoagulability detected by TEG can improve Khorana score application in these patients.

**Study Methods:** A single centre, prospective, longitudinal cohort study of newly-diagnosed adult breast and gynecological cancer patients. Patients planning to receive the recommended anticancer chemotherapy treatments were recruited. Blood samples were collected prior to chemotherapy and prior to chemotherapy cycles 2 and 3. Thromboelastography was performed on the blood samples using a TEG® 5000 Hemostasis System and the following major parameters were evaluated: R time, alpha (α) angle, maximum amplitude (MA) and clotting index (CI), time to clot formation (R), speed of clot propagation (α), rate of clot formation (K), strength/stability of clot (MA), Clot lysis after 30 min. of MA (LY30) and clotting index (CI; a value that is based on the four parameters above). Baseline demographics, cancer data, BMI, Khorana score and VTE risk factors were recorded. Repeated measure ANOVA and one-way ANOVA were used to assess the effect of chemotherapy on the TEG parameters.

**Results:** A total of 30 newly-diagnosed patients aged 35-85 (15 breast, 10 endometrial, 5 ovarian cancer), prescribed chemotherapy (27% neo-adjuvant, 67% adjuvant, 6% both) were evaluated to date. Of patients, 53% received platinum-based chemotherapy, 30% had comorbidities, 23% had metastatic disease. TEG detected hypercoagulability in samples 2, 3 based on a significant reduction in R ($p=0.0105$), K ($p=0.0001$), and a significant increase in α angle ($p=0.0004$), MA ($p<0.0001$), CI ($p<0.0001$). 21-68% of patients had hypercoagulable TEG traces based on various TEG parameters. Khorana score was assessed in 27 patients (6 low risk, 18 intermediate, 2 high risk). MA and CI significantly increased with intermediate and high-risk Khorana scores compared to low-risk ($p=0.03$ and $P=0.03$ respectively). No thrombotic events were recorded.

**Conclusion(s):** TEG can detect hypercoagulability in breast and gynecological cancer patients undergoing chemotherapy. TEG MA and CI can potentially be used alongside the Khorana score to improve thrombosis risk assessment of patients. The effect of cancer chemotherapy on coagulation is complex and requires attention. Future work will focus on assessing these effects in each specific cancer type.

**Funding Source:** St. Lawrence College Ignite Fund.

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## (P6) Mechanisms of in utero-initiated benzene toxicity in the placenta (Study Proposal)

Megan Cull (Ph.D. Candidate), Lihua Xue, Louise Winn.

*Dept. of Biomedical and Molecular Sciences, Queen's University.*

**Objective(s):** When pregnant mothers are exposed to drugs and environmental chemicals, their unborn child has an increased risk for developmental toxicity. Benzene is an abundant environmental chemical and a known human carcinogen, making exposure during pregnancy an important concern. Benzene can cross the placenta, which is the organ critical for fetal growth and development, as it establishes the maternal-fetal vascular interface. Benzene metabolism leads to oxidative stress and increased reactive oxygen species (ROS) production, in utero hematopoietic damage, and a higher risk of childhood leukemia development. ROS can affect the regulation of gene expression, cell growth, and cell death, and they can directly damage DNA. However, the interaction between these factors in the placenta and their relevance to the in utero carcinogenicity of benzene is unknown. I hypothesize that in utero benzene exposure results in fetal growth restriction (FGR) and increases ROS, leading to increased placental DNA damage. My objectives include: 1) To determine the impact of in utero benzene exposure on the structure and function of the placenta and 2) To investigate the mechanisms of placental dysregulation and DNA damage. I intend to assess sex differences in all objectives.

**Study Methods**: I am using an in vivo mouse model to study in utero-initiated benzene toxicity that was previously established by the Winn Lab. Pregnant CD-1 dams will be exposed to 200 mg/kg benzene dissolved in corn oil, or corn oil only (control) by intraperitoneal (i.p.) injection on gestational days (GDs) 8, 10, 12, and 14. Dams will be sacrificed 2, 6, and 24 hours following the final benzene dose. Sex determination will be done by PCR. Fetus and placenta weights will be measured to assess whether benzene exposure alters their growth. Placentae will be used for immunohistochemical (IHC) analysis. IHC of isolectin-B4 and alkaline phosphatase (AP) will be used to identify the fetal and maternal blood spaces, respectively, to assess how benzene alters placenta vasculature structure. I will investigate the levels of ROS in the placentae by flow cytometry, markers of ROS damage by measuring oxidized DNA and proteins, and global DNA damage using TUNEL staining. Evidence suggests that benzene must first be metabolized to exert toxicity and that human, as well as mouse placentae, have detectable myeloperoxidase (MPO) levels. Therefore, I intend to study the enzymatic activity of MPO using a commercially available MPO ELISA kit.

**Results:** I expect that in utero benzene exposure will have a sex-dependent impact on placental morphology and FGR. I predict that benzene will increase placental levels of ROS, ROS damage and DNA damage, and anticipate that greater toxicity will be evident in placentae with higher MPO enzymatic activity. I anticipate that females will have a more severe response to in utero-initiated benzene toxicities as compared to males.

**Conclusions:** This work aims to develop a fundamental understanding of the mechanisms of in utero benzene exposure and its toxicities on the placenta. The outcomes of this proposed research will have important implications for the development of policy around the use of, and exposure to, benzene, specifically in the vulnerable population of pregnant females and their unborn children.

**Funding Source:** CIHR, Queen's University

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## (P7) The role of inflammation-induced pregnancy complications in subsequent risk of maternal cardiovascular and metabolic disease

Gabrielle Fava (M.Sc. Candidate)[1], Alexa Toews (M.Sc. Candidate)[1], Nakeisha Lodge-Tulloch (Ph.D. Candidate), Dr. Charles Graham.

*Department of Biomedical and Molecular Sciences, Queen's University.*
*[1]These authors are both presenters.*

**Objectives:** Complications of pregnancy are associated with aberrant inflammation during gestation. Additionally, women that have miscarried are at an increased risk of cardiovascular and metabolic disease. Murine studies have revealed increased risk factors for cardiometabolic diseases following pregnancy complications, but not overt disease. Therefore, we believe that a second inflammatory 'hit', such as a high fat diet, is necessary to produce disease. We aim to determine the effects of inflammatory complications of pregnancy followed by a high fat diet on the maternal cardiovascular and metabolic systems by assessing: 1) cardiovascular structure and function; 2) cardiac and pancreatic histopathology; 3) biomarkers of cardiovascular disease (CVD) and type 2 diabetes mellitus (DM2); 4) glucose metabolism and insulin levels; 5) serum lipid profiles.

**Study Methods:** C57BL/6 mice are injected intraperitoneally with lipopolysaccharide (LPS, 50 µg/kg) to induce fetal loss, or saline (controls) on gestational day 10.5. Fourteen days after injection, mothers are transitioned to a high fat diet (60% kcal from fat) for 10 weeks to induce chronic low-grade inflammation. Control groups consist of pregnant mice fed a regular fat diet, non-pregnant mice fed a high fat diet, and non-pregnant mice fed a regular fat diet. Echocardiography is used to assess cardiac structure and alterations in systolic and diastolic cardiovascular function. Cardiac hypertrophy is measured using the ratio of the weights of each heart chamber to tibial length. Weight gain is tracked every 2-3 days beginning at gestational day 19.5. Alterations in glucose metabolism and insulin release are assessed with an intraperitoneal glucose tolerance test (IPGTT). Blood glucose and insulin levels are measured at 0-, 15-, 60-, and 120-minutes post-glucose bolus. The ratios of the weights of the pancreas and liver to body weight are measured to assess hypertrophy. At euthanasia, cardiac blood is collected to analyse levels of CVD biomarkers such as thrombomodulin, as well as hemoglobin A1c levels to assess DM2 development. Hearts, pancreases, and livers are collected to assess histology and morphology. Echocardiography and weight gain data are analyzed using one-way ANOVAs with the Holm-Sidak test to control for multiple comparisons. IPGTT results were assessed with two-way ANOVAs using the Tukey's multiple comparisons test. Significance was defined as $P < 0.05$.

**Results:** Only mice on a regular fat diet have completed the study. Analysis of mitral valve flow revealed significantly reduced no flow times in pregnant mice treated with LPS ($P = 0.0424$) and PBS ($P = 0.0350$) compared to non-pregnant LPS-treated mice. There was also a significant increase of glucose concentration at the 60-minute time point of LPS-treated pregnant mice compared with non-pregnant mice treated with LPS ($P = 0.0138$).

**Conclusion:** These results support the hypothesis that pregnancy complications can lead to the development of risk factors for cardiometabolic diseases. Further study is needed to determine if an additional source of inflammation, such as a high fat diet, is necessary to produce overt disease. These results may help to create care guidelines for women following complicated pregnancies to mitigate their risk of future heart and metabolic diseases.

**Funding Source:** CIHR

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## (P8) Should women who screen GDM-negative and give birth to a macrosomic baby complete an HbA1C test before discharge from the hospital?

Ainsley Johnstone (BHSc 2023), Jessica Pudwell, Graeme Smith.

*Department of Obstetrics and Gynecology and Queen's University*

**Background**: Macrosomia, which is defined by birth weight above 4000g, has been reported to be a predominant outcome of gestational diabetes mellitus (GDM). The current screening strategy for GDM involves a 50g glucose challenge test (GCT) during pregnancy, for which a variety of sensitivity values have been reported, making the potential for false negative results a concern due to the long-term implications of GDM.

**Objective(s):** This study aimed to determine the utility of HbA1c testing for women who screened GDM-negative during pregnancy and delivered a macrosomic infant. The study also aimed to determine if any predictive factors for a positive HbA1c test result can be identified.

**Study methods:** A retrospective review was conducted of patients who delivered a macrosomic infant (>4000g) from July 2022 to January 2023 at Kingston Health Sciences Centre, who were not diagnosed with GDM during pregnancy and did not have pre-existing diabetes (n=116). Patients who received HbA1c testing were categorized according to HbA1c result into Normal (<5.7%) and Abnormal (≥5.7%) groups. Kruskal-Wallis, chi-square tests, and analysis of variance were used to compare groups, with post hoc tests corrected using the Bonferroni method. Analysis was completed with IBM SPSS Statistics, version 27.

**Results:** From the study sample, 38 patients received an HbA1c test after delivery and 78 patients did not receive an HbA1c test after delivery. Offspring of patients who received HbA1c testing had significantly higher birth weights with a median of 4345.0 (IQR, 4067.5–4487.5) compared to a median of 4140.0 (IQR, 4070.0–4260.0) for patients who did not receive testing ($p<0.01$). Out of 38 patients who received the HbA1c test, 10 patients (26.3%) obtained abnormal results, indicating false negatives on the 50g GCT. Based on test results within the sample, the NPV of the 50g GCT was calculated to be 0.74. Patients who had abnormal HbA1c results had significantly lower gestational weight gain with a median of 9.5 kg (IQR, 5.3–14.3) compared to a median of 19.5 kg (IQR, 12.2–21.8) for patients who had normal results ($p<0.05$).

**Conclusion(s):** Findings from this study indicate that early postpartum HbA1c testing may be a useful way to identify women who were false negatives on the 50g GCT. Given that women who receive false negative results are vulnerable to the long-term implications of GDM due to receiving limited follow-up testing and treatment, further research on the utility of postpartum HbA1c screening is critical.

**Funding Source:** None

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**Keynote Speaker**

## Dr. Deshayne Fell

**Title:** Safety and effectiveness of immunization during pregnancy for mothers and infants: Where have we been and what does the future hold?

**Summary:** Globally, immunization during pregnancy is increasingly recognized as an important strategy for protecting pregnant individuals and their newborns from infectious diseases. Influenza, pertussis and COVID-19 vaccines are now routinely recommended for pregnant individuals in many countries, including Canada. In Ontario, our unique data sets have provided an opportunity to evaluate vaccine safety and effectiveness in this priority population using routinely-collected electronic health care data such as the BORN birth registry, health administrative databases, and laboratory data. The objectives of this presentation are to: provide an overview of the history and rationale for immunization during pregnancy, highlight findings from a program of research on maternal immunization in Ontario, and review the status of new vaccines under development for future implementation in the obstetrical population.

**Bio:** Dr. Deshayne Fell is an Associate Professor in the School of Epidemiology and Public Health at the University of Ottawa, a Scientist in the Children's Hospital of Eastern Ontario Research Institute, and an Adjunct Scientist at ICES. Dr. Fell is a perinatal researcher who works extensively with the provincial birth registry (BORN Ontario) and with linked health administrative data at ICES. Since the 2009 H1N1 influenza pandemic, her primary research focus has been on infection and immunization during pregnancy. She has been a member of two WHO working groups related to immunization during pregnancy and for the past two years, led a province-wide project to evaluate COVID-19 vaccination during pregnancy, supported by the COVID-19 Immunity Task Force.

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*We are pleased to announce the 2022 Oral and Poster Presentation Winners:*

| **BEST ORAL PRESENTATION** | |
|---|---|
| **Session 1**<br><br>**Katie Zutautas**<br>Dysregulation of Leukemia Inhibitory Factor; Implications for Endometriosis Pathophysiology | **Session 2**<br><br>**Sarenna Lalani**<br>Population and diagnostic characteristics of patients diagnosed with gestational diabetes mellitus before and during the COVID-19 pandemic<br><br>&<br><br>**Victoria Sa**<br>Availability, Quality, and Implementability of Canadian Clinical Practice Guidelines for Female Sexual Dysfunction |
| **BEST POSTER PRESENTATION** | |
| **Room 1**<br><br>**Allison McCallion**<br>Mast cells in the pathophysiology of Endometriosis<br><br>&<br><br>**Jennifer Armstrong**<br>A peripartum vascular assessment of women with preeclampsia | **Room 2**<br><br>**Alexa Fine**<br>Attention Deficit Hyperactivity Disorder in Children Born to Mothers with Infertility: A Population Based Cohort Study |

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