Obstetrics & Gynaecology
UNIVERSITY OF TORONTO

29th ANNUAL RESEARCH DAY
& Henderson Lecture

FRIDAY, MAY 4, 2012

JRR Macleod Auditorium & Stone Lobby
Medical Sciences Building, University of Toronto,
1 King's College Circle, M5S 1A8
8:00 a.m. to 6:30 p.m.
Abstracts due early March 2012

Lecturer: Patrick Catalano MD

Professor, Reproductive Biology,
MetroHealth Medical Center/Case Western Reserve

Topic: Maternal Obesity and Pregnancy: Much Ado about Something

http://www.obgyn.utoronto.ca/Research/ResearchDay.htm

For additional information or assistance, please contact Helen Robson at
helen.robson@utoronto.ca

29th Annual Research Day & Henderson Lecture

The Department of Obstetrics & Gynaecology 29th Annual Research Day took place on Friday, May 4, 2012. Trainees from the Department gave 14 oral and 62 poster presentations that were excellent and included both basic and clinical work. There was also an informative and thought-provoking Henderson Lecture, delivered by **Patrick Catalano MD**, Professor, Reproductive Biology in the MetroHealth Medical Center/CaseWestern Reserve University. His engaging topic was "*Maternal Obesity and Pregnancy: Much Ado about Something."*

I would like to thank everyone who participated, the staff who helped put it together, and also extend special thanks to all those faculty members who acted as Chairs and Judges and to the Research Committee, particularly Stephen Lye as Chair.

The **2012 JW Knox Ritchie Research Awards** for best abstract/presentation by trainee category were awarded during the celebratory wine and cheese reception at the end of the day. I am pleased to announce the following winners:

Clinical Fellow: Kimberley Garbedian (Supervisor: Kimberley Liu).**The Impact of Vitamin D Status on Implantation and Clinical Pregnancy Rates Following In Vitro Fertilization.** Kimberley Garbedian, Miranda Boggild, Joel Moody, Kimberley Liu.

Post-Doctoral Fellow: Sascha Drewlo (Supervisor: John Kingdom) The PPAR- agonist Rosiglitazone Reverses sFLT1 Hyper-secretion from First Trimester Placental Villi in a GCM1-Dependent Manner. Sascha Drewlo, Fergus McCarthy, Khrystyna Levytska, Louise Kenny, John Kingdom.

Resident: Stéphanie Backman (Supervisor: Theodore J Brown) **Interleukin-1β (IL-1β)-Stimulated Inflammatory Gene Expression in Fallopian Tube Epithelial Cells is reversed by Glucocorticoids.** Stéphanie Backman, Alexandra Kollara, Carl Virtanen, Theodore J Brown.

Graduate Student: Theresa Chow (Supervisor: Ian Rogers) **Improved Survival of Umbilical Cord Derived Donor Cells in Bone Marrow Transplantation due to Trogocytosis.** Theresa Chow, Jennifer Whiteley, Ian Rogers.

Student: Sarah Cao (Supervisor: Andrea Jurisicova) **Role of Bim in Oocyte Survival.**Sarah Cao, Shakib Omari, Andrea Jurisicova.

The **Frederick R Papsin Award** for postgraduate resident in final year of training, based on teaching ability, mentorship activities and leadership, as chosen by peers, was awarded to **Karthika Devarajan.**

Please join me in congratulating the winners. I would also like to commend all the participants, both oral and poster presenters, for their valuable contribution to the continued success of Research Day.

Sincerely,
Alan Bocking
Alan D. Bocking, MD
Gordon C. Leitch Chair
Department of Obstetrics and Gynaecology

PROGRAM-AT-A-GLANCE

RESEARCH DAY 2012
Medical Sciences Building, University of Toronto

Friday, May 4, 2012
MORNING

7:30 am on	**Poster Set-up for Presenters** (Stone Lobby)
8:00 am	**Registration & Continental Breakfast** (JJR Macleod Auditorium Lobby)
8:25 – 8:30 am	**Welcome: Dr. Alan Bocking, Chair** (JJR Macleod Auditorium)
8:30 – 9:45 am	**Oral Session I (O1-O5)** (JJR Macleod Auditorium) **Chair/Judge:** Dr Heather Shapiro **Judges:** Drs S Lee Adamson and Stephen Matthews
9:45 – 10:05 am	**Coffee Break & Poster Session I Walkabout** (JJR Macleod Auditorium Lobby and Stone Lobby)
10:05 – 11:05 am	**Poster Session I Tour** (Stone Lobby) **Groups A-F**

	Chairs/Judges	Judges
A	Drs Michelle Letarte and Stephen Lye	Dr Jason Dodge
B	Drs Carl Laskin and Theodore J Brown	Dr Robert Casper
C	Drs Howard Berger and Isabella Caniggia	Dr Ori Nevo
D	Drs Rose Kung and Lisa Allen	Dr Adrian Brown
E	Drs Anne Claessens and Yaakov Bentov	Dr Marjorie Dixon
F	Drs Elliott Lyons and Guylaine Lefebvre	Dr Joan Murphy

11:10 am– 12:10 pm	**Oral Session II (O6-O9)** (JJR Macleod Auditorium) **Chair/Judge:** Dr Allan Covens **Judges:** Drs John Kingdom and Rachel Spitzer

PROGRAM-AT-A-GLANCE

RESEARCH DAY 2012
Medical Sciences Building, University of Toronto

Friday, May 4, 2012
AFTERNOON

12:15 – 1:15 pm **Lunch** (Donnelly Atrium and Lounge)

1:20 – 2:35 pm **Oral Session III (O10-O14)** (JJR Macleod Auditorium)
Chair/Judge: Dr Richard Pittini
Judges: Drs Clifford Librach and Ellen Greenblatt

2:35 – 3:05 pm **Coffee Break & Poster Session II Walkabout**
(JJR Macleod Auditorium Lobby and Stone Lobby)

3:05 – 4:05 pm **Poster Session II** (Stone Lobby)
Groups G-K

	Chairs/Judges	Judges
G	Drs Wendy Wolfman and S Lee Adamson	Dr Christine Derzko
H	Drs Ian Rogers and Prati Sharma	Dr Rebecca Arthur
I	Drs Robert Casper and Andrea Jurisicova	Dr Sony Sierra
J	Drs John Kingdom and Danny Lovatsis	Dr Sari Kives
K	Drs Denise Belsham and Marcus Bernardini	Dr Navid Esfandiari

4:05 – 4:20 pm **Poster Takedown** (Stone Lobby)

4:30 – 5:30 pm **Henderson Lecture** (JJR Macleod Auditorium)
Dr. Patrick Catalano MD
Professor, Reproductive Biology
MetroHealth Medical Center/CaseWestern Reserve University

Topic: ***Maternal Obesity and Pregnancy: Much Ado about Something***

Closing Remarks: Dr. Alan Bocking (JJR Macleod Auditorium)

5:30 – 6:30 pm **Wine and Cheese Reception and Frederick R Papsin and JW Knox Ritchie Research Awards Presentations** (JJR Macleod Auditorium Lobby)

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Patrick Catalano MD
Maternal Obesity and Pregnancy: Much Ado about Something

WINE & CHEESE RECEPTION: 5:30 – 6:30 P.M.

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Obstetrics & Gynaecology
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29th ANNUAL RESEARCH DAY
Friday, May 4, 2012

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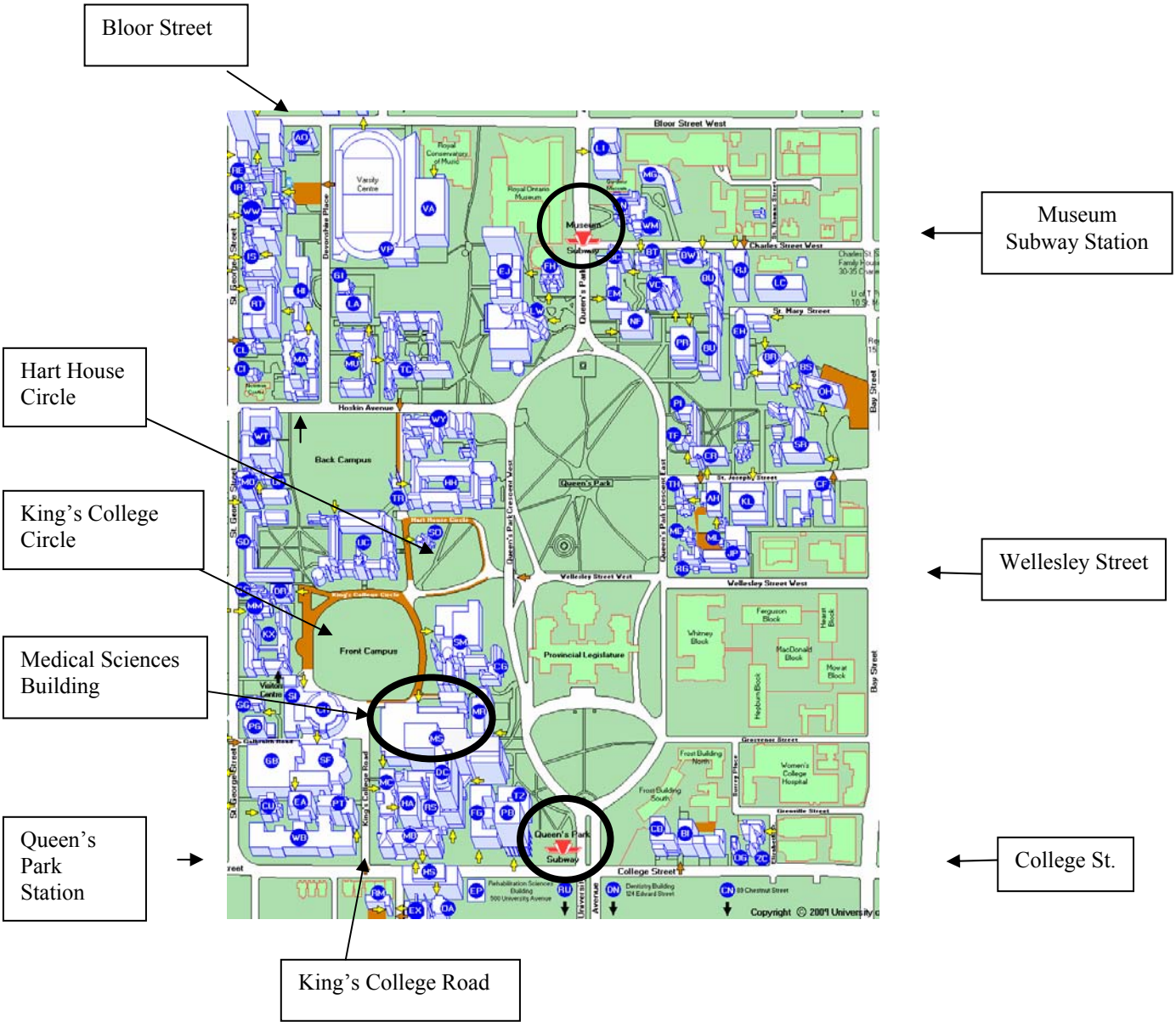
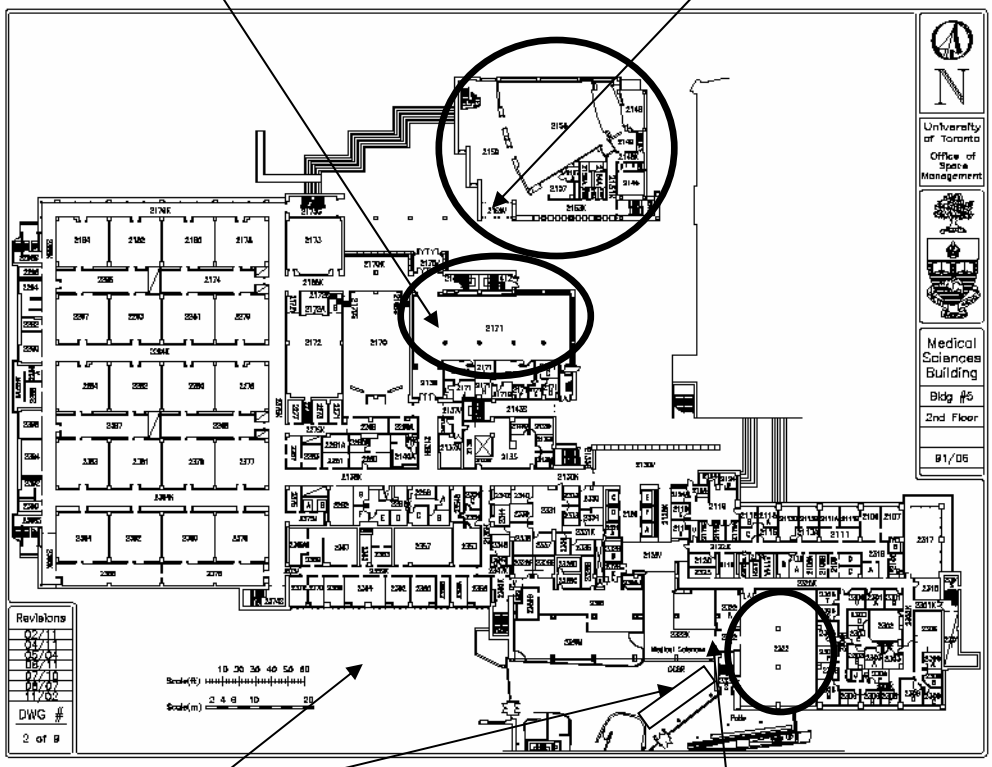


Medical Sciences Building
1 King's College Circle M5S 1A8

Stone Lobby Entrance
(Poster Presentations)

JJR Macleod Auditorium Entrance
(Oral Presentations)



Lunch Buffet Line

Donnelly Atrium

Lounge Entrance for Lunch Seating

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8:25 – 8:30 a.m. **Welcome: Dr. Alan Bocking, Chair** (JJR Macleod Auditorium)

8:30 – 9:45 a.m. **ORAL SESSION I** (JJR Macleod Auditorium)

(O1-O5) (5 presentations @15 minutes: 10 minute presentation + 5 minutes for questions)
Chair/Judge: Dr Heather Shapiro
Judges: Drs S Lee Adamson and Dr. Stephen Matthews

8:30-8:45 **O1 The Effect of High AMH and High Antral Follicle Count on IVF Success and Pregnancy Rate in Young Egg Donors**
Shir Dar [F](1,2), Stephanie A Grover (1), Clifford L Librach (1, 2, 3).
(1) CReATe Fertility Centre, (2) Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynaecology, Sunnybrook Health Sciences Centre and Women's College Hospital, (3) Department of Obstetrics & Gynaecology, University of Toronto.

8:45-9:00 **O2 Radiologic Imaging Patterns of Gynecologic Patients: Does Physician Specialty Matter?**
Gennady Miroshnichenko [F](1), Rachel Kupets(2), Lawrence Paszat(3).
(1)Division of GynAecologic Oncology, Department of Obstetrics and GynAecology, University of Toronto; (2)Division of Gynaecologic Oncology, Sunnybrook Health Sciences Centre, University of Toronto; (3)Institute for Clinical Evaluative Sciences, Sunnybrook Health Sciences Centre, University of Toronto.

9:00-9:15 **O3 Radical Vaginal Trachelectomy- Fertility Outcomes and Significance of the Lower Uterine Segment Presence in the Superior Margin of the Pathologic Specimen.**

Gennady Miroshnichenko [F](1), Allan Covens(2), **John Snelgrove [R]**(3), Nadia Ismil(4), Sharon Nofech-Mozes(4), Valerie Dube(4), Mahmoud Khalifa(4), Ghorab Zeina(4)
(1)Division of Gynaecologic Oncology, Department of Obstetrics and Gynaecology, University of Toronto; (2)Division of Gynaecologic Oncology, Sunnybrook Health Sciences Centre, University of Toronto; (3)Department of Obstetrics and Gynaecology, University of Toronto; (4)Department of Anatomical Pathology, Sunnybrook Health Sciences Centre, University of Toronto.

9:15-9:30 **O4 Prenatal Diagnosis and Clinical Outcomes in Pregnancies Complicated by Breus' Mole**

Abdulmohsen Alanjari [F](1), Sarah Keating S (2), Greg Ryan (1),JCP Kingdom (1).
(1)Maternal-Fetal Medicine Division, Department of Obstetrics & Gynaecology, Mount Sinai Hospital, (2)Department of Patthology, Mount Sinai Hospital

9:30-9:45 **O5 LOX, TIMP, MMP and ADAMTS2 Enzymes Expression in Vaginal Tissue of Premenopausal Women with and without Pelvic Organ Prolapse**

Hala Kufaishi [G](1,4), Oksana Shynlova (1), Harold Drutz(2,4), Stephen Lye(1,2,3), May Alarab(1,4)(1)Samuel Lunenfeld Research Institute, Mount Sinai Hospital, (2)Obstetrics & Gynaecology; (3)Physiology and (4)Urogynaecology, Mount Sinai Hospital, University of Toronto.

9:45-11:05 am **POSTER SESSION I**

9:45-10:05 am **Coffee Break & Poster Session I Walkabout** (JJR Macleod Auditorium Lobby and Stone Lobby)

10:05 – 11:05 am **Poster Session I Tour, Groups A-F** (Stone Lobby)
(3-5 minute presentation + 5 minutes for questions)

GROUP A:

Chairs/Judges: Drs Michelle Letarte and Stephen Lye
Judge: Dr Jason Dodge

P-A1 **VEPH1 Inhibits Canonical TGF-β Signalling in Ovarian Cancer Cells by Impeding Nuclear Accumulation of SMAD2.**
Premalatha Shathasivam [G](1,2,3), A. Kollara(1,3), C. Virtanen(5), J. Wrana(1,4), and T. J. Brown(1,2,3).
(1)Samuel Lunenfeld Research Institute, Mount Sinai Hospital; and Departments of (2)Physiology, (3)Obstetrics and Gynaecology, and (4)Molecular Genetics,University of Toronto;(5)OCI Genomics Centre, Toronto, Ontario.

P-A2 **Pathways Associated with Differential Accumulation of Ascites in High Grade Serous Ovarian Cancer: A Search for Targeted Therapy to Control Ascites**.
Tomer Feigenberg [F], Carl Virtanen, Michelle Letarte, Marcus Bernardini, Blaise Clarke, Theodore J Brown, Barry Rosen, and K Joan Murphy. Department of Obstetrics and Gynaecology, University Health Network (UHN) and Mount Sinai Hospital; Hospital for Sick Children and Department of Immunology, University of Toronto; Department of Pathology, UHN, and the Ontario Cancer Institute Genomics Centre (OCIG), Toronto, Ontario.

P-A3 **Modulation of Androgen Receptor (AR) signaling by Ventricular Zone-expressed PH Domain-Containing Protein Homolog 1 (Veph1) in Ovarian Cancer Cells.**
Alexandra Kollara [O](1,2), Premalatha Shathasivam (1,2,3), Theodore J Brown (1,2,3).
(1) Samuel Lunenfeld Research Institute, Mount Sinai Hospital (2) Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Toronto, (3) Department of Physiology, Faculty of Medicine, University of Toronto

P-A4 **Impact of BRCA1/2 Mutation Status on Inflammatory Signalling by Fallopian Tube Epithelial Cells in Culture in Response to Follicular Fluid Exposure – Work-in-Progress.**

Angela Lau [G](1-3), Terry Colgan (2), Lisa Allen (2), Michèle Farrugia (2), Elyse Levinsky (2), Jodi Shapiro (2), Ellen M. Greenblatt (1,2), K. Joan Murphy (2, 4), Barry Rosen (2,4), Theodore J. Brown (1-3).
(1) Samuel Lunenfeld Institute, Mount Sinai Hospital, (2) Department of Obstetrics and Gynaecology, Mount Sinai Hospital (3) Department of Physiology, University of Toronto (4) Department of Gynaecologic Oncology, Princess Margaret Hospital

P-A5 **Sentinel Lymph Node Biopsy in Vulvar Cancer: A Health Technology Assessment for the Canadian Health Care Context**

Clare Reade [F](1), Waldo Jimenez (2), Daria O'Reilly (3), Al Covens (4).
(1) University of Toronto Gynaecologic Oncology Fellowship Program, McMaster University Health Research Methodology Program, (2) Gynecologic Oncology, Juravinski Cancer Centre, (3) PATH Research Institute, Department of Clinical Epidemiology & Biostatistics, McMaster University, (4) Gynecologic Oncology, Odette Cancer Centre

P-A6 **Effects of Veph1 on FoxO-regulated SOD2 in Epithelial Ovarian Cancer Cells in Response to Oxidative Stress**

Thomasina Spybey [G](1,2,3), Premalatha Shathasivam (1,2,3), Alexandra Kollara (1,2), Theodore Brown (1,2,3).
(1) Samuel Lunenfeld Research Institute, Mount Sinai Hospital (2) Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Toronto, (3) Department of Physiology, Faculty of Medicine, University of Toronto

GROUP B:

Chairs/Judges: Drs Carl Laskin and Theodore J Brown
Judge: Dr Robert Casper

P-B1 **Transforming Growth Factor-B1 Regulates Multidrug Resistance at the Developing Blood-Brain Barrier**

Stephanie Baello [G](1), M Iqbal(1), W Gibb (2), SG Matthews(1).
(1)Physiology, Obstetrics & Gynaecology, and Medicine, University of Toronto, and (2)Obstetrics & Gynecology, and Cellular & Molecular Medicine, University of Ottawa.

P-B2 **Capillary Rarefaction, a Phenomenon that Antedates Essential Hypertension Is Not Present in Low Birth Infants at Birth**

Rohan D'Souza [F](1),Rajendra Raghuraman(2), Preetha Nathan(3), Isaac Manyonda(3), Tarek Antonios(2)
(1) Maternal-Fetal Medicine Division, Department of Obstetrics &Gynaecology, Mount Sinai Hospital, Toronto, (2) Clinical and Developmental Sciences, St. George's University of London, UK (3) Department of Cardiac and Vascular Sciences, St. George's University of London, UK

P-B3 **Decidual Neutrophils: A Novel Angiogenic Population in the 2nd Trimester.**

Caroline E Dunk [O](1), H Amsalem(2), M Kwan(3), RL Jones(5), SJ Lye(1,2,4)
(1)Research Centre for Women's and Infants Health, Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto. (2)Department of Obstetrics and Gynecology, Hadassah-Hebrew University Medical Centers, Mount Scopus, Jerusalem, Israel, (3)Departments of Physiology and (4)Obstetrics and Gynaecology, Faculty of Medicine, University of Toronto, (5)Maternal and Fetal Health Research Centre, St Mary's Hospital, The University of Manchester, Manchester, UK

P-B4 **Activation of PPAR-g and HO-1 via Rosiglitazone in BeWo cells Recapitulates the *in vivo* Molecular Pathway**

Khrystyna Levytska [G](1,2), Sascha Drewlo(1,4), Dora Baczyk(1), John Kingdom(1,3,4)
(1) Program in Development and Fetal Health, Samuel Lunenfeld Research Institute, Mount Sinai Hospital; (2) Department of Laboratory Medicine and Pathobiology, University of Toronto; (3) Maternal-Fetal Medicine Division, Department of Obstetrics and Gynaecology, Mount Sinai Hospital; (4) Department of Obstetrics and Gynaecology, University of Toronto.

P-B5 **GSK3β reduces Mcl-1 Phosphorylation in Preeclamptic Placentae**
Jayonta Bhattacharjee [PD](1), Isabella Caniggia (1, 2, 3). (1) Samuel Lunenfeld Research Institute, Mount Sinai Hospital, (2) Departments of Obstetrics and Gynaecology, (3) Department of Physiology, University of Toronto.

P-B6 **Soluble VEGFR-1 (sFlt-1) and Hypoxia Decrease VEGFR-2 Expression in the Human Placenta**
Dennis K Lee [O](1), Isabella Caniggia(2) and Ori Nevo(1).
(1) OB/GYN, Sunnybrook Health Sciences Centre and (2) OB/GYN Mount Sinai Hospital, University of Toronto.

GROUP C:

Chairs/Judges: Drs Howard Berger and Isabella Caniggia
Judge: Dr Ori Nevo

P-C1 **Dual Specificity Phosphatase 9 (DUSP9) Regulation in Severe Early Onset Pre-eclampsia and in a Placental Villous Explant Model**
Marie J Czikk [F](1), Sascha Drewlo(2), Dora Baczyk (2), S. Lee Adamson (1,2), John CP Kingdom (1,2).
(1) Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Toronto,
(2) Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, Canada.

P-C2 **Developing an *in vitro* Model of Kidney Differentiation as a Tool To Help Us Understand Kidney Developmental Defects**
Manpreet Sambi [G](1,2), Theresa Chow (1,2), Jennifer Whiteley (1), Ian Rogers (1,2,3)
(1)Samuel Lunenfeld Research Institute, Mount Sinai Hospital, (2)Department of Physiology, University of Toronto, (3)Department of Obstetrics and Gynaecology, University of Toronto

P-C3 **Pro-Inflammatory Cytokines and Chemokines Induced by Mechanical Stretch of Myometrial Cells Promote Neutrophil Infiltration by Enhanced Adhesion and Transendothelial Migration**
Yu-Hui Lee [G](1,3), Oksana Shynlova (3), Stephen J. Lye (1,2,3)
(1) Departments of Physiology and (2) Ob/Gyn, University of Toronto, (3) Samuel Lunenfeld Research Institute, Mount Sinai Hospital.

P-C4 Characterization of *In Vitro* P-gp Transport in Human Placental Tissue Culture

Mohsen Javam [G](1), Melanie Audette(1), William Gibb(4),Stephen G. Matthews(1,2,3).
(1)Department of Physiology, (2)Obstetrics and Gynaecology and (3)Medicine, Faculty of Medicine, University of Toronto, (4) Obstetrics & Gynecology, and Cellular & Molecular Medicine, University of Ottawa.

P-C5 First Trimester Uterine Natural Killer Cells Migrate in Response to Secreted Cytokines in Trophoblast-Conditioned Media

Melissa Kwan [G](1,2), Caroline Dunk(2), Rebecca Jones(3), Sarah Keating(4), Stephen Lye (1,2,5).
(1) Department of Physiology, University of Toronto, (2) Research Centre for Women's and Infants' Health, Samuel Lunenfeld Research Institute, Mount Sinai Hospital, (3) Maternal & Fetal Health Research Centre, University of Manchester, United Kingdom, (4) Department of Pathology, Mount Sinai Hospital, (5) Department of Ob/Gyn, University of Toronto

P-C6 Glucose Sensing in mHypoA-GnRH/GFP Immortalized Hypothalamic Neurons

Sean A McFadden [G](1), Jennifer A Chalmers(1), Janet J Jang(1) Maria-Luisa Centeno(1), Denise D Belsham(1,2)
Departments of (1)Physiology,(2)OB/Gyn and Medicine, Faculty of Medicine, University of Toronto, and University Health Network.

GROUP D:

Chairs/Judges: Drs Rose Kung and Lisa Allen
Judge: Dr Adrian Brown

P-D1 **The Prevalence of Reproductive Tract Infections (RTI) in Adolescents at Presentation to Colposcopy**

Helena Frecker[R](1), Sari Kives(2), Mark Yudin(2)
(1) Department of Obstetrics and Gynaecology, University of Toronto, (2) Department of Obstetrics and Gynaecology, St. Michael's Hospital

P-D2 **Effect of EMR Implementation on Patient and Staff Satisfaction, and Chart Completeness in a Resource-Limited Ante-Natal Clinic in Kenya**

Alice Gray [M](1), Christe Henshaw(1), Julie Wright(1), Jessica Leah(1), Rachel F. Spitzer(1), Elkanah Omenge(2), Benjamin Chemwolo(2). (1)University of Toronto Department of Obstetrics and Gynaecology (2) Moi Teaching and Referral Hospital and Moi University School of Medicine Department of Reproductive Health, Eldoret, Kenya.

P-D3 **Maternal Experiences with Breastfeeding: A Comparison Between Women Who are Exclusively Breastfeeding and those Who are Formula-Feeding at Six Weeks**

Kristin Harris [M](1), Leanne DeSouza (2), Mark Yudin (2).
(1) Department of Medicine, University of Toronto, (2) Department of Obstetrics & Gynaecology, St. Michael's Hospital

P-D4 **A Survey of Postgraduate Training in Indigenous Women's Health in Obstetrics and Gynaecology**

Naana Afua Jumah [R](1), Rajiv Shah(1), Don Wilson(2).
(1) Department of Obstetrics and Gynaecology, University of Toronto, (2) Department of Obstetrics and Gynecology, University of British Columbia, Vancouver, BC.

P-D5 **Canadian Women's Attitudes toward Noninvasive Prenatal Testing of Fetal DNA in Maternal Plasma**

Lara Hasan (2), **Leanne R De Souza [G]**(2) Gerald Lebovic(2), Howard Berger(2)
(1) Case Western Reserve University; (2) Women's Health, St. Michael's Hospital, University of Toronto

GROUP E:

Chairs/Judges: Drs Anne Claessens andYaakov Bentov
Judge: Dr Marjorie Dixon

P-E1 Evaluation of Sperm Aneuploidy in Patients with Severe Oligozoospermia

Siamak Bashar [O](1); Naazish Alladin(1); Hanna Balakier(1); Clifford L. Librach(1,2,3); Sergey I. Moskovtsev(1, 3)
(1)CReATe Fertility Centre; (2) Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynaecology, Sunnybrook Health Sciences Centre and Women's College Hospital; (3) Department of Obstetrics & Gynaecology, University of Toronto.

P-E2 Correlation of Telomere Length and DNA Damage in Human Spermatozoa

Pamela L. Chan [G](1); Sergey I. Moskovtsev(1, 2); Shlomit Kenigsberg(1); Naazish Alladin(1); Clifford L. Librach(1, 2, 3)
(1) CReATe Fertility Center; (2) Department of Obstetrics & Gynaecology, University of Toronto; (3) Division of Reproductive Endocrinology and Infertility, Department of Obstetrics & Gynaecology, Sunnybrook Health Sciences Centre and Women's College Hospital.

P-E3 Neural Potential of First Trimester Human Umbilical Cord Perivascular Stem Cells

Anouk-Martine Teichert [O](1), Shlomit Kenigsberg(1), Leila Magdhen(1), Ashley Ramelloo(1), Schreiber Pereira(1), Clifford L. Librach(1)(2).
(1) CReATe Fertility Centre (2) Department of Obstetrics & Gynaecology, Sunnybrook Health Sciences Centre, Women's College Hospital, and the University of Toronto.

P-E4 The Impact of Vitamin D Status on Implantation and Clinical Pregnancy Rates Following *In Vitro* Fertilization

Kimberley Garbedian [F](1,2), Miranda Boggild(2), Joel Moody(3), Kimberley Liu(1,2)
(1)Reproductive Endorcrinology and Infertility Division, Department of Obstetrics & Gynaecology, Mount Sinai Hospital, (2)University of Toronto (3)Prosserman Centre for Health Research, Samuel Lunenfeld Research Institute, Mount Sinai Hospital

P-E5 **Improved Survival of Umbilical Cord Derived Donor Cells in Bone Marrow Transplantation due to Trogocytosis**

Theresa Chow [G](1,2), Jennifer Whiteley(1), Ian Rogers(1,2,3)
(1)Samuel Lunenfeld Research Institute, Mount Sinai Hospital, (2)Department of Physiology, University of Toronto, (3)Department of Obstetrics and Gynaecology, University of Toronto

P-E6 **3D Image Analysis of Chromatin Structure of Motile and Immotile Sperm Populations**

Naazish Alladin [O](1,2); Ayub Lulat(1); Sergey I. Moskovtsev(1,3); Clifford L. Librach(1,3,4).
(1) CReATe Fertility Center; (2) Department of Biomedical Sciences, Eastern Virginia Medical School; (3) Department of Obstetrics & Gynaecology, University of Toronto; (4) Division of Reproductive Endocrinology and Infertility, Department of Obstetrics & Gynaecology, Sunnybrook Health Sciences Centre and Women's College Hospital.

GROUP F:

Chairs/Judges: Drs Elliott Lyons and Guylaine Lefebvre
Judge: Dr Joan Murphy

P-F1 **Outcome of Laparoscopic Two-Team Sling, Tension Free Transvaginal Tape (TVT) and Transobturator Tape (TOT) for Women with Recurrent Stress Urinary Incontinence : A Retrospective Cohort Study.**

Seham Hassonah [F], Sebastian Medel, May Alarab, Harold Drutz
Urogynaecology Division, Department of Obstetrics and Gynaecology, Mount Sinai Hospital, University of Toronto.

P-F2 **Same-Day Discharge versus Overnight Stay after Laparoscopic Hysterectomy: A Prospective Assessment of Patient Safety and Patient Satisfaction [Research-in-Progress]**

Alice Pham [F], Rose C Kung, Herb Wong, Grace Y Liu, Jamie Kroft, Janet Bodley, Patricia E Lee
Department of Obstetrics & Gynaecology, Sunnybrook Health Sciences Centre

P-F3 **Maternal and Fetal Outcomes in Canadian Women after Bariatric Surgery (Work-in-Progress)**

Leslie Po [R](1), Kellie Murphy (1), Cynthia Maxwell (1)
(1) Maternal Fetal Medicine Division, Department of Obstetrics & Gynaecology, Mount Sinai Hospital, University of Toronto

P-F4 **Female Genital Tract Graft-vs-Host Disease: A Current Retrospective Patient Review.**

Adrienne LK Li [R](1), Wendy Wolfman(1)
(1) Department of Obstetrics & Gynaecology, Mount Sinai Hospital

P-F5 **Identification of Factors that Influence Full Disclosure during a Gynaecology Appointment**

Stuart L Douglas [M](1), Leanne R De Souza(2), Mark HYudin(2)
(1)Faculty of Medicine, University of Toronto, (2) Women's Health, St. Michael's Hospital, University of Toronto

ORAL SESSION II

11:10 am -12:10 pm **Oral Session II** (4 presentations @15 minutes: 10 minute presentation + 5 minutes for questions) **(O6-O9)** (JJR Macleod Auditorium)

Chair: Dr Allan Covens
Judges: Drs John Kingdom and Rachel Spitzer

11:10-11:25 **O6 Reduced Coq10 Gene Expression in Cumulus Cells with Aging**

Assaf Ben-Meir [F](1,2), Yaakov Bentov(1,2), Navid Esfandiari(2), Andrea Jurisicova(1,3), Robert F Casper(1,2,3)
(1)Research, Samuel Lunenfeld Research institute (SLRI); (2)Reproductive Endocrinology, Toronto Centre for Advanced Reproductive Techniques (TCART), (3)Obstetrics & Gynaecology, University of Toronto.

11:25-11:40 **O7 Risk of Preeclampsia in HIV-Positive Pregnant Women Receiving HAART: A Matched Cohort Study**

Talar Boyajian [M](1), Kellie Murphy(2)
(1)Faculty of Medicine, University of Toronto, (2) Mount Sinai Hospital, University of Toronto.

11:40-11:55 **O8 Brief Family History Questionnaire for Identification of Lynch Syndrome in Women with Newly Diagnosed Endometrial Cancer**

Lua Eiriksson [G](1), Melyssa Aronson(2), Blaise Clarke(3), Golnessa Mojtahedi(4), Aaron Pollett(5), Steve Gallinger(6), Amit Oza(7), Christine Massey(8), Marcus Bernardini(4), Helen MacKay(7), Sarah E. Ferguson(4)
(1)University of Toronto, Obstetrics & Gynaecology, Division of Gynecologic Oncology, (2)Mount Sinai Hospital, University of Toronto, Zane Cohen Centre for Digestive Diseases, (3)Toronto General Hospital, Department of Pathology, (4)Princess Margaret Hospital, Division of Gynaecologic Oncology, (5)Mount Sinai Hospital, University of Toronto, Pathology, (6)Toronto General Hospital, University of Toronto, Surgical Oncology, (7)Princess Margaret Hospital, Medical Oncology, (8)Princess Margaret Hospital, Biostatistics

11:55-12:10 **O9 Effect of *Lactobacillus rhamnosus* GR-1 (GR-1) on Cytokines and Chemokines in Maternal Plasma, Amniotic Fluid and Intra-uterine Tissues of Pregnant CD-1 Mice.**

Siwen Yang [G](1), Wei Li(1), John RG Challis(1), Sung O Kim(2), Gregor Reid(2), Alan D Bocking(1)
(1) Departments of Obstetrics and Gynaecology and Physiology, University of Toronto. (2) Department of Microbiology and Immunology, University of Western Ontario.

12:15 – 1:15 p.m. **LUNCH** (Donnelly Atrium and Lounge)

ORAL SESSION III

1:20 – 2:35 p.m. **Oral Session III (O10-O14)** (5 presentations @15 minutes – 10 minute presentation + 5 minutes for questions) (JJR Macleod Auditorium)

Chair/Judge: Dr Richard Pittini
Judges: Drs Ellen Greenblatt and Clifford Librach

1:20-1:35 **O10 Multidrug Resistance in the Developing Blood-Brain-Barrier (BBB): Interactions between Cytokines and Glucocorticoids (GCs)**
Majid Iqbal [G](1), Hay Lam Ho(1), Melanie C Audette(1), Sophie Petropoulos(1), William Gibb(2), Stephen G Matthews(1).
(1)Physiology, Obstetrics & Gynaecology, and Medicine, University of Toronto, and (2)Obstetrics & Gynecology, and Cellular & Molecular Medicine, University of Ottawa.

1:35-1:50 **O11 Trends in Menstrual Concerns and Suppression in Adolescents with Cognitive and Physical Challenges**
Yolanda Kirkham [F], Lisa Allen, Sari Kives, Nicolette Caccia, Rachel Spitzer, Anjali Aggarwal, Melanie Ornstein.
Section of Pediatric and Adolescent Gynaecology, Hospital for Sick Children, University of Toronto

1:50-2:05 **O12 Interleukin-1β (IL-1β)-Stimulated Inflammatory Gene Expression in Fallopian Tube Epithelial Cells is Reversed by Glucocorticoids**
Stéphanie Backman [R](1), Alexandra Kollara(1), Carl Virtanen(2), and Theodore J Brown(1). (1)Department of Obstetrics and Gynaecology, University of Toronto, (2)OCI Microarray Centre, Toronto.

2:05-2:20 **O13 Effect of VEGF Overexpression by Concepti on Maternal VEGF in Mice**
Abhijeet Minhas [G](1), Shannon Bainbridge(2), Dawei Qu(1), Hoon-Ki Sung(1), Andras Nagy(1,3), S Lee Adamson(1,2,4)
(1)Samuel Lunenfeld Research Institute, Mount Sinai Hospital; (2)Interdisciplinary School of Health Sciences, University of Ottawa; (30Department of Molecular Genetics, University of Toronto and (4)Department of Obstetrics & Gynaecology, University of Toronto.

2:20-2:35 **O14 The Safety of Methimazole and Propylthiouracil Use in Pregnancy**

Rinat Hackmon [F](1,2), Monica Blichowski[G](3), Dan Farine(1), Gideon Koren(2)(1) Maternal-Fetal-Medicine Division, Department of Obstetrics & Gynaecology, Mount Sinai Hospital, (2)Clinical Pharmacology and Toxicology Division, Hospital for Sick Children; (3)University of Toronto.

2:35– 4:05 p.m. **POSTER SESSION II**

2:35 – 3:05 p.m. **Coffee Break & Poster Session II Walkabout** (JJR Macleod Auditorium Lobby and Stone Lobby)

3:05 – 4:05 p.m. **Poster Session II Tour** (Stone Lobby)
(3-5 minute presentation + 5 minutes for questions)
Groups G-K

GROUP G:

Chairs/Judges: Drs Wendy Wolfman and S Lee Adamson
Judges: Dr Christine Derzko

P-G1 Vitrification of Human Spermatozoa without Permeable Cryoprotectants

Valeriy Kuznyetsov[O](1); Sergey I. Moskovtsev (1, 2); Ayub Lulat (1); Sergey Spiridonov (1); Michael Crowe (1); Clifford L Librach (1, 2, 3)
(1) CReATe Fertility Centre; (2) Department of Obstetrics & Gynaecology, University of Toronto; (3) Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynaecology, Sunnybrook Health Sciences Centre and Women's College Hospital.

P-G2 WITHDRAWN

P-G3 Can Fewer Eggs Make More Babies? Conversion of High-Response Gonadotropin Intrauterine Insemination Cycles as a Model for Mild Stimulation in Vitro Fertilization.

Kaajal Abrol [F], Heather Shapiro
(1) Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynaecology, Centre for Fertility and Reproductive Health, Mount Sinai Hospital

P-G4 **First Trimester Human Umbilical Cord Perivascular Cells (Fthuc-Pvcs) Can Differentiate towards the Hepatic Lineage Using a Two-Step Induction and Maturation Approach**

Leila Maghen(1), **Seok-Ho Hong [O]**(1), Ashley Rammeloo(1), Andrée Gauthier-Fisher (1), Clifford L. Librach(1,2,3)
(1) CReATe Fertility Center, (2) Department of Obstetrics and Gynaecology, University of Toronto, (3) Division of Reproductive Endocrinology and Infertility, Departments of Obstetrics and Gynaecology, Sunnybrook Health Sciences Centre and Women's College Hospital.

P-G5 **Pilot Study: A Comparison of Ovarian Reserve in BRCA Positive Women Versus Age-Matched BRCA Negative Controls**

Ariadne Daniel [F](1), Christine Elser(2), Ellen Greenblatt(1)
(1) Division of Reproductive Endocrinology and Infertility, Department of Obstetrics & Gynaecology, Center for Fertility and Reproductive Health, Mount Sinai Hospital
(2) Department of Oncology, University Health Network

P-G6 **Assessment of Global Methylation of Human Sperm**

Anouk-Martine Teichert(1), **Shlomit Kenigsberg [O]**(1), Anna Kop(2), Apurva Shirodkar(2), Naazish Alladin(1), Sergey Moskovtsev(1)(3), Philip A. Marsden(2), Clifford L. Librach(1)(3).
(1) CReATe Fertility Centre (2) Departments of Medicine, University of Toronto and Medical Research St. Michael's Hospital (3) Department of Obstetrics & Gynaecology, Sunnybrook Health Sciences Centre, Women's College Hospital, and the University of Toronto.

GROUP H:

Chairs/Judges: Drs Ian Rogers and Prati Sharma
Judge: Dr. Rebecca Arthur

P-H1 SSEA-4 Expression Marks a Highly Proliferative and Multipotent Subpopulation of First Trimester Human Umbilical Cord-Derived Perivascular Stem Cells

Leila Maghen [O](1), Seok-Ho Hong(1), Noah Schwartz(1), Clifford L. Librach(1,2,3)
(1) CReATe Fertility Center, (2) Department of Obstetrics and Gynaecology, University of Toronto, (3) Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynaecology, Sunnybrook Health Sciences Centre and the Women's College Hospital

P-H2 NLRP5 Regulates Autophagy in Preimplantation Embryos. (Work-in-Progress)

Taline Naranian[G](1,2), AlaPerumalsamy(1), Russanthy Velummailum(1), Tong ZhiBin(3), Igor Jurisica(4), Lawrence Nelson(3) and Andrea Jurisicova(1,2).
(1)Samuel Lunenfeld Research Institute, Obstetrics and Gynaecology, Mount Sinai Hospital (2)Department of Physiology, Mount Sinai Hospital, University of Toronto, (3)Developmental Endocrinology Branch, National Institutes of Child Health and Human Development, National Institutes of Health, (4) Ontario Cancer Institute, Princess Margaret Hospital.

P-H3 Real-Time PCR Array-Based Gene Expression Profiling of Human Umbilical Cord-Derived Perivascular Cells.

Ashley Rammeloo[O](1), Shlomit Kenigsberg(1), Seok-Ho Hong(1), Leila Maghen(1), Anouk-Martine Teichert(1), Andree Gauthier-Fisher(1), and Clifford L. Librach(1,2,3)
(1) CReATe Fertility Center,(2) Department of Obstetrics and Gynaecology, University of Toronto (3)Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynaecology, Sunnybrook Health Sciences Centre and Women's College Hospital.

P-H4 Role of Bim in Oocyte Survival

Sarah Cao [UG](1), Shakib Omari (1,3), Andrea Jurisicova (1,2,3). (1) Department of Physiology Maternal-Fetal Medicine Division,(2) Department of Obstetrics & Gynaecology, Mount Sinai Hospital, University of Toronto, (3) SLRI Mount Sinai Hospital.

P-H5 **Central Mechanisms for the Direct Inhibitory Effects of Gonadotropin-Inhibitory Hormone (GnIH) on Gonadotropin-Releasing Hormone (GnRH) using Novel Hypothalamic Cell Models**

Nicole Gojska[G](1) and Denise D. Belsham(1, 2).
(1)Departments of Physiology, University of Toronto, (2) Obstetrics and Gynaecology, and Medicine, University of Toronto; Division of Cellular and Molecular Biology, Toronto General Hospital Research Institute, University Health Network

P-H6 **Utilizing Two Different Extraction Methodologies to Determine a Correlation Between Sperm DNA Damage and Sperm Protein Profile.**

Jonathan Zicherman[O](1); Shlomit Kenigsberg(1); Nina Replete(1); Naazish Alladin(1); Ashley Rammeloo(1); Sergey I. Moskovtsev(1,2); Clifford L. Librach(1,2,3).
(1) CReATe Fertility Center; (2) Department of Obstetrics & Gynaecology, University of Toronto; (3) Division of Reproductive Endocrinology and Infertility, Department of Obstetrics &

GROUP I:

Chairs/Judges: Drs Robert Casper and Andrea Jurisicova
Judge: Dr Sony Sierra

P-I1 **Effects of Prenatal Synthetic Glucocorticoid Exposure on Hypothalamo-Pituitary-Adrenal (HPA) Function in Juvenile Offspring**

Paul Blakeley [G](1), Vasilis Moisiadis(1), Stephen Matthews(1-3)
(1)Department of Physiology, Faculty of Medicine, University of Toronto, (2)Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Toronto, (3)Department of Medicine, Faculty of Medicine, University of Toronto

P-I2 **Umbilical Cord Diameter Percentile Curves and their Correlation to Birth Weight and Placental Pathology**

Leslie K Proctor [M](1,2), Brendan Fitzgerald(1), Wendy L Whittle(2), Navid Mokhtari(1), Ellen Lee(1), Geoffrey Machin(1,3), John CP Kingdom(2,3), Sarah J Keating(1,3).
Departments of (1) Pathology and Laboratory Medicine and (2) Obstetrics and Gynaecology (Division of Maternal-Fetal Medicine), Mount Sinai Hospital, (3) University of Toronto

P-I3 **Number and Activation Status of Uterine Natural Killer Cells Suggest a Novel Role in the Second Trimester of Pregnancy**

Jianhong Zhang [PD](1), Caroline E Dunk(1), Stephen J Lye(1,2,3)
(1)Samuel Lunenfeld Research Institute, Mount Sinai Hospital, (2) Department of Physiology, University of Toronto, (3)Department of Obstetrics and Gynaecology, University of Toronto.

P-I4 **Antenatal Dexamethasone Exposure in Mice Does Not Affect Levels of SNAT Proteins in the Placental Microvillous Membrane**

Melanie C Audette [G](1), Majid Iqbal (1), John RG Challis (1-4), Rebecca L Jones (4), Colin P Sibley (4), Stephen G Matthews (1-3).
Departments of (1)Physiology, (2)Obs/Gyn and (3)Medicine, University of Toronto, (4)Maternal and Fetal Heath Research Centre, School of Biomedicine, University of Manchester, UK.

P-I5 **Transabdominal Amnioinfusion in Premature Preterm Rupture of Membranes: A Systematic Review and a Meta-Analysis**

Shay Porat [F](1),Hagai Amsalem(1), Kellie E. Murphy(1), Prakesh S Shah(2)
(1)Department of Obstetrics & Gynaecology and (2)Department of Neonatology, Mount Sinai Hospital, University of Toronto.

P-I6 **Anti-Mullerian Hormone as a Marker of Fertility in IVF and IUI Therapy: A Pilot Study.**

Marjorie Dixon [F](1), **Timothy Evangelista [O]**(2).
(1)Division of Reproductive Endocrinology & Infertility, Department of Obstetrics and Gynaecology, University of Toronto, (2) University of Guelph-Humber

GROUP J:

Chairs/Judges: Drs John Kingdom and Danny Lovatsis
Judge: Dr Sari Kives

P-J1 **A Review of Laparoscopic Sacrocolpopexy: Surgical Outcomes, Complications and Failures**

Katherine Lo [F], Patricia Lee
Urogynaecology Division, Department of Obstetrics and Gynaecology, Sunnybrook Health Sciences Centre

P-J2 **Attitudes and Expectations of Canadian Women in Labour towards Point of Care HIV Testing on The Labour and Delivery Unit**

Salikah Iqbal [R](1), Leanne De Souza(2), Mark Yudin(2)
(1)University of Toronto, (2) St Michael's Hospital, Obstetrics, Gynaecology and Reproductive Infectious Disease

P-J3 **Cervico-Vaginal Inflammatory Changes in IUCD Users: A Pilot Study**

Priya Sharma [R](1), Rupert Kaul (2), Mark Yudin(3)
(1)Department of Obstetrics & Gynaecology, University of Toronto (2) Departments of Medicine and Immunology, University of Toronto (3) Department of Obstetrics and Gynaecology, St. Michael's Hospital

P-J4 **Prevalence of Unidentified/Subclinical Hypothyroidism in Two Urban Prenatal Populations: Can Predisposing Maternal Risk Factors be Identified?**

Kathy Truong [O](1), Megan McDonnell[O](2), Heather Edwards (3), Christine Derzko (4).
(1) University of Calgary, Faculty of Medicine, (2) The Commonwealth Medical College, Scranton, Pennsylvania, (3) Department of Obstetrics & Gynaecology, University of Calgary, (4) Department of Obstetrics & Gynaecology, St. Michael's Hospital, University of Toronto

P-J5 **Outcomes from a Radical Hysterectomy Training Program in a Low Resource Setting in Africa.**

Samantha Young[M](1), Peter Itsura(2), Hellen Muliro(2), Brendan Charles(3), Astrid Christoffersen-Deb(1), Rachel Spitzer(4), Barry Rosen(3), Elkanah Omenge Orango(2).
(1)University of Toronto (2)Department of Reproductive Health, Moi Teaching and Referral Hospital, Moi University (3)Gynaecology-Oncology, Princess Margaret Hospital (4)Department of Obstetrics and Gynaecology, Mount Sinai Hospital, University of Toronto

P-J6 **Power, Passenger, Passage…and Physician?: Changing Obstetrical Practice as a Determinant of the C-Section Rate at a Toronto Community Hospital**

Gregory Handrigan[M](1), Brenda Woods (2), Leke Badmos (2), Kellie Murphy(3), Melissa Tai (2)
(1) Undergraduate Medical Education, Faculty of Medicine, University of Toronto, (2) Family Birthing Centre, Toronto East General Hospital, (3) Maternal Fetal Medicine, Mount Sinai Hospital.

GROUP K:

Chairs/Judges: Drs Denise Belsham and Marcus Bernardini
Judge: Dr Navid Esfandiari

P-K1 **Effects Of Placental VEGFA Deficiency on Pregnancy in Mice**

Han Li [G](1), Dawei Qu (1), Hoon-Ki Sung (1), Andras Nagy(1,4), S Lee Adamson(1,2,3)**.** (1) Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Depts of (2) Physiology, (3)Obstetrics & Gynaecology, and (4)Molecular Genetics, University of Toronto.

P-K2 **The Impact of the International Association of Diabetes and Pregnancy Study Groups (IADPSG) Diagnostic Thresholds for Gestational Diabetes Mellitus (GDM) on the Incidence of GDM in a Canadian Inner-City Multi-Ethnic Population.**

Karli Mayo [R](1), H Vandenberghe (2), R Kedar(3), H Berger(3).
(1) Department of Obstetrics & Gynaecology, University of Toronto (2) Department of Laboratory Medicine & Biochemistry, St. Michael's Hospital (3) Maternal Fetal Medicine, Department of Obstetrics & Gynaecology, St. Michael's Hospital

P-K3 **Altered Mechanisms of Acid Sphingomyelinase Regulation and Processing in Preeclampsia**

Megan Melland-Smith [G](1,2,3), Martin Post(4), Isabella Caniggia(1,2,3)
(1)Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Departments of (2)Obstetrics and Gynaecology and (3)Physiology, (4)Hospital for Sick Children, University of Toronto.

P-K4 **Transgenerational Effects of Antenatal Synthetic Glucocorticoid Treatment on Learning and Memory**
Vasilis Moisiadis [G](1), Alisa Kostaki(1), Jeff Emack(1), Stephen G. Matthews(1,2,3). (1)Departments of Physiology, (2)Obstetrics and Gynaecology and (3)Medicine, Faculty of Medicine, University of Toronto.

P-K5 **Kick-Starting Action: Canadian Women's Understanding of Fetal Movement Guidelines**
Susan Pakenham [R](1), Andrea Copeland(2) and Dan Farine(3). (1)Department of Obstetrics and Gynaecology, University of Toronto; (2)Faculty of Science, Queen's University; (3)Department of Obstetrics and Gynaecology, Mount Sinai Hospital, University of Toronto

P-K6 **The PPAR-γ agonist Rosiglitazone Reverses sFLT1 Hyper-secretion from First Trimester Placental Villi in a GCM1-Dependent Manner**
Sascha Drewlo [PD](1), Fergus McCarthy(2), Khrystyna Levytska(1), Louise Kenny, PhD(2), John Kingdom(1). (1)Samuel Lunenfeld Research Institute, Mount Sinai Hospital, (2) University College Cork, Anu Research Centre, Ireland.

4:05 – 4:20 p.m. **Poster Takedown** (Stone Lobby)

4:30 – 5:30 p.m. **Henderson Lecture** (JJR Macleod Auditorium)
Dr. Patrick Catalano
Professor, Reproductive Biology
MetroHealth Medical Center/CaseWestern Reserve University
Topic: ***Maternal Obesity and Pregnancy: Much Ado about Something***

Closing Remarks: Dr. Alan Bocking (JJR Macleod Auditorium)

5:30 – 6:30 p.m. **Wine and Cheese Reception** and **Frederick R Papsin** and **JW Knox Ritchie Research Awards Presentations**
(JJR Macleod Auditorium Lobby)

THE HENDERSON LECTURE

The D. Nelson Henderson Lectureship in Obstetrics and Gynaecology was established in 1965, through the generosity of the Henderson family, in honour of Dr. Donald Nelson Henderson, a highly respected clinician-scientist and eminent member of the Department of Obstetrics and Gynaecology at the Toronto General Hospital.

Dr Patrick Catalano

We are very pleased to welcome the Henderson Lecturer this year, **Patrick Catalano MD**, Professor, Reproductive Biology, MetroHealth Medical Center/Case Western Reserve University, whose interests include obesity and diabetes and their effects on mother and fetus in pregnancy. His topic for the Henderson Lecture is: *Maternal Obesity and Pregnancy: Much Ado about Something*. Dr Catalano has over 140 peer-reviewed publications and has received continuous National Institute of Health funding since 1987. Among Dr. Catalano's most recent honours is the March of Dimes 2011 Agnes Higgins Award for outstanding achievement in the field of maternal-fetal nutrition.

Previous Henderson lecturers and topics:

2011 **Dr Philip Castle,** American Society of Clinical Pathology (ASCP) Institute, USA
Separating the Wheat from the Chaff: The Paradigm of Human Papillomavirus (HPV) and Cervical Cancer

2010 **Dr. Jane Norman,** University of Edinburgh, UK, Edinburgh Tommy's Centre for Maternal and Fetal Health Research
Being Born Too Soon – Do Obstetricians Have Anything to Offer?

2009 **Dr. David L Keefe,** University of South Florida, Tampa, Florida, USA
Burning The Candle at Both Ends – A Telomere Theory of Reproductive Aging

2008 **Dr. Andrew Berchuck**, Duke University Medical Center, Durham, North Carolina, USA
Individualized Ovarian Cancer Treatment and Prevention in the Genomic Era

2007 **Dr. David Phillips,** University of Southampton, UK
Small Babies, Stress and the Metabolic Syndrome

2006 **Dr. Robert L Reid,** Queen's University, Kingston, Ontario.
Bringing Scientific Discovery into the Public Domain: Rigour and Responsibility

2005 **Dr. Chris Redman,** University of Oxford, UK
A New View of Pre-Eclampsia

2004 **Dr. JB Trimbos,** Leiden University, The Netherlands
Nerve Sparing in Radical Surgery: Technique and Proof of Principle

2002 **Dr. David A Grimes,** Family Health International, North Carolina, USA
Potholes on the Road to Evidence-Based Practice

2001 **Dr. DT Baird,** University of Edinburgh, UK
Hormonal Control of Folliculo-Genesis: The Key to Successful Reproduction

2000 **Dr. Les Myatt,** University of Cincinnati, USA
Prediction of Preeclampsia – Is it Possible?

AWARDS

Frederick R Papsin Award

The Dr. Frederick R. Papsin Postgraduate Award was inaugurated in 2003 in memory of Dr. Frederick R Papsin, Chief of the Department of Obstetrics and Gynaecology at Mount Sinai Hospital from 1971 to 1988. The award is presented to a postgraduate resident in the final year of training, and is based on teaching ability, mentorship activities and leadership, as chosen by the winner's peers. There have been seven recipients, Dr. Andrea Lausman (2005), Dr. Kerry Myckan (2006), Dr. Matthew Morton (2007), Dr. Shereen Chirayilkalam (2008), Dr. Lynne Zolis (2009), Dr. Rebecca Cash (2010), and Dr Eliane Shore (2011).

JW Knox Ritchie Research Awards

Dr. JW Knox Ritchie

The JW Knox Ritchie Research Awards were endowed by a grateful. medical staff at the Department of Obstetrics and Gynaecology, Mount Sinai Hospital and the University of Toronto, on the occasion of Dr. Ritchie's retirement from the position of Chief for Mount Sinai and Chair for the University of Toronto Departments of Obstetrics and Gynaecology in 2003.

The JW Knox Ritchie Research Awards are awarded for best abstract/presentation by trainee category (Graduate Student, Resident, Clinical Fellow, Post-Doctoral Fellow, Medical Student).

Previous recipients of the JW Knox Ritchie Research Awards:

2011
Post-Doctoral Fellow: **Fergus McCarthy** (Supervisor: J. Kingdom)
Clinical Fellow: **Tania Dumont** (Supervisor: L. Allen) AND **Kimberley Garbedian** (Supervisor: B. Cruickshank)
Resident: **Daniela Caprara** (Supervisor: M. Yudin)
Graduate Student: **Crystal Chan** (Supervisors: E. Greenblatt and T. J. Brown)
Medical Student: **Ingrid Lai** (Supervisor: E. Greenblatt)

2010
Post-Doctoral Fellow: **Alicia Tone** (Supervisor: T.J. Brown)
Clinical Fellow: **Dini Hui** (Supervisor: N. Okun)
Resident: **Mara Sobel** (Supervisor: J. Kingdom)
Graduate Student: **Jocelyn Ray** (Supervisor: I. Caniggia)
Medical Student: **Marie Wegener** (Supervisor: S. Ferguson)

2009
Post-Doctoral Fellow: **Sascha Drewlo** (Supervisor: J. Kingdom)
Clinical Fellow: **Clarissa Bambao** (Supervisor: M. Shier)
Resident: **Kelly Chu** (Supervisor: K. Murphy)
Graduate Student: **Shadab Rahman** (Supervisor: R. Casper)
Medical Student: **Erika Frasca** (Supervisor: O. Nevo)

2008 Post-Doctoral Fellow: **Christine Wong** (Supervisor: R. Casper)
Clinical Fellow: **Marcus Bernardini** (Supervisor: A. Covens)
Resident: **Taymaa May** (Supervisor: T.J. Brown)
Graduate Student: **Maryam Yeganegi** (Supervisor: A. Bocking)
Medical Student: **Sue Jin Kim** (Supervisor: W. Whittle)

2007 Post-Doctoral Fellow: **Sascha Drewlo** (Supervisor: J. Kingdom)
Clinical Fellow: **Kimberly Liu** (Supervisor: E. Greenblatt)
Resident: **Taymaa May** (Supervisor: T. Brown)
Graduate Student: **Ingrid Lai** (Supervisor: A. Jurisicova)
Medical Student: **K. Ashley Hawrylyshyn** (Supervisor: J. Murphy)

2006 Post-Doctoral Fellow: **Jing Xu** (Supervisor: I. Caniggia)
Clinical Fellow: **Valérie Dubé** (Supervisor: T. Colgan)
Resident: **Amanda Selk** (Supervisors: E. Greenblatt & H. Shapiro)
Graduate Student: **Alicia A Tone** (Supervisors: P. Shaw & T. Brown)

ORAL ABSTRACTS

ABSTRACT #O1

The Effect of High AMH and High Antral Follicle Count on IVF Success and Pregnancy Rate in Young Egg Donors

Shir Dar [F](1,2), Stephanie A. Grover (1), Clifford L. Librach (1, 2, 3).
(1) CReATe Fertility Centre, (2) Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynaecology, Sunnybrook Health Sciences Centre and Women's College Hospital, (3) Department of Obstetrics & Gynaecology, University of Toronto.

Background: Many young women have high antral follicle count and high ovarian volume that match the ovarian part of the Rotterdam criteria. These young women could be either a normal variant or part of the PCOS patient group. There is a debate in the literature regarding the success rate of IVF cycles in PCOS patients. Higher number of eggs were reported without change in the pregnancy rate in PCOS patients in one study, whereas, a higher miscarriage rate and no difference in immature oocytes were reported in PCOS patients in a different study.
Objective: To analyze if there is a difference in the number of eggs retrieved, the number of embryos produced, the fertilization rate, OHSS rate and the pregnancy rate in the egg donor population based on differences in their AMH levels and antral follicle count.
Methods: This is a retrospective observational study in which data from 190 egg donor cycles was collected. The egg donors were 19-38 years of age. The cycles were stratified by (1) AMH levels (low ≤15 pmol/L, medium 16-28 pmol/L, high 29-48 pmol/L, very high ≥49 pmol/L) and (2) AMH levels and antral follicle count (AFC) (low ≤11, medium 12-23, high 24-78). The outcomes analyzed were number of eggs retrieved, number of viable embryos and pregnancy rate. All the donors had a long protocol starting on the second day of their period with birth control pills (desogestrel 0.15mg ethinyl estradiol 0.03mg marvelone^{R}), GnRH agonist starting on the 8th day in a dosage of 0.1 (Leuprolide acetate: lupron^{R} Abbott lab), and ovarian stimulation with r-FSH (follitropin alpha: Gonal-f^{R}).
Results: We found that the number of eggs retrieved correlated with AMH levels. However, at the upper ranges, no significant difference was found in the number of eggs retrieved in the high AMH versus the very high AMH groups. Likewise, an increase in the number of viable embryos was seen as the AMH level increased. There were no significant differences found in the fertilization rates of the groups. The very high AMH group had a significantly higher OHSS rate than any of the other AMH groups ($P<0.05$). The OHSS rate was not significantly different between the other AMH groups. There was no difference found in the overall pregnancy rates between the groups however, when looking at the pregnancy rate from frozen cycles the low AMH group had a higher frozen cycle pregnancy rate then the medium AMH group.

No significant differences were found in the outcome variables when sub-stratifying by AFC except that the number of viable embryos was higher in the medium AFC than in the low AFC in the low AMH group (8.2±1.5 vs. 3.5±0.6, $P<0.05$) and the pregnancy rate for fresh cycles was higher in the medium AFC versus the high AFC in the high AMH group (87.5% vs. 57.1%, $P<0.05$).
Conclusions: The data suggests that the characteristics of polycystic ovarian syndrome do not have an effect on the outcomes of egg donor ART cycles.

ABSTRACT #O2

Radiologic Imaging Patterns of Gynecologic Patients: Does Physician Specialty Matter?

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Objective: To study the patterns of imaging by gynecologists and non-gynecologists (family physicians and others) following a pelvic ultrasound in women aged 45 and older, prior to a surgical intervention.

Methods: Provincial databases of health care utilization were linked to establish patterns of imaging and surgical outcomes between 2006 and 2008. Women 45 and older without any surgical or imaging history met the inclusion criteria for this study.

Results: 193, 261women met the inclusion/ exclusion criteria; of those, 19, 125 underwent a laparotomy. 18,632 women underwent surgery for a gynecologic indication. 87% of women had imaging initiated by a non-gynecologist with the reminder initially imaged by a gynecologist. Comparing percentages of further imaging incurred by patients as categorized by initial imaging physician, non-gynecologist vs. gynecologist, additional imaging differed as follows: repeat pelvic ultrasound 42% vs. 24%; abdominal ultrasound 30% vs. 12%; CT abdomen/pelvis 13% vs. 4%; MRI pelvis 4% vs. 1.5%. Time to surgery also increased in malignant cases based on imaging ordered: uterine malignancy mean time to surgery with pelvic ultrasound alone was 138 days vs. 213 days when CT scan and MRI was ordered; for malignant adnexal disease time to surgery increased from 100 days to 180 days ($P<0.001$).

Conclusions: here is an important discrepancy between gynecologists and non- gynecologists with regards to patterns of imaging involving gynecologic pelvic pathology. Educational interventions are needed to reduce potentially unnecessary imaging tests, which lead to treatment delay of serious underlying conditions including cancer.

Funded by: Division of Gynecologic Oncology, Sunnybrook Health Sciences Centre.

ABSTRACT #O3

Radical Vaginal Trachelectomy- Fertility Outcomes and Significance of the Lower Uterine Segment Presence in the Superior Margin of the Pathologic Specimen.

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Objective: To report if the presence of lower uterine segment (LUS) in the superior margin of the pathological trachelectomy specimen is associated with preterm birth following vaginal radical trachelectomy (VRT) for early-stage cervical cancer.

Methods: Review of 143 prospectively recorded patients treated by a laparoscopic pelvic lymphadenectomy (PLN) and VRT from January 2000 to December 2011 with regards to their cervical pathology and reproductive outcomes. Pathology was re-reviewed to identify the presence of LUS in the superior margin of the trachelectomy specimen.

Results: The median age was 31.5 years old, and 66% were nulliparous at time of surgery. Stage distribution was; 1A1 (14%), 1A2 (29%), and 1B1 (57%). No adjuvant treatment was administered to 90.1% of the patients. 52 pregnancies occurred, of which 30 (58%) reached the third trimester. The presence of the LUS in the superior surgical margin was identified in 60 patients (42 %). When the groups were compared based on the absence or presence of LUS: 77% vs. 70% of the patients reported attempted conception and 43% vs. 27% were successful respectfully. The incidence of a gestation greater than 24 weeks was 37% vs. 20% (OR=0.42 [95% CI 0.19-0.92], P=0.03) and the term pregnancy incidence was 27% vs. 20% (OR=0.37 [95% CI 0.15-0.92], P=0.03) in favor of the patients without LUS.

Conclusions: The presence of LUS in the superior margin of the trachelectomy specimen is associated with a higher likelihood of preterm birth.

Funded by: not applicable.

ABSTRACT #O4

Prenatal Diagnosis and Clinical Outcomes in Pregnancies Complicated by Breus' Mole

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ABSTRACT AVAILABLE IN HARDCOPY VERSION ONLY

ABSTRACT #O5

LOX, TIMP, MMP and ADAMTS2 Enzymes Expression in Vaginal Tissue of Premenopausal Women with and without Pelvic Organ Prolapse

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Hypothesis /Aims: Evidence suggests that abnormalities of connective tissue structure or its repair mechanism may predispose women to Pelvic Organ Prolapse (POP). We reported earlier that the Lysyl oxidase (LOX) family gene and protein expression involved in the maturation of collagen and elastin was decreased in the vaginal tissue of premenopausal women with severe POP in the proliferative phase of the menstrual cycle. Now we examined the expression of proteins involved in elastin and collagen metabolism, namely LOX, LOXL1-4, TIMP 1-4, and MMP1,2,7,9,12,14 in the vaginal tissue of premenopausal women with advanced POP and asymptomatic healthy controls in the secretory phase of the menstrual cycle. We also hypothesized that ADAMTS-2, -3 and -14 , extracellular procollagen-N-proteinases that cleave the N-propeptides of procollagens I, II, III in vivo , genes and proteins are differentially expressed in women with severe POP compared to healthy premenopausal women.

Methods: Premenopausal Caucasian women undergoing total hysterectomy for benign conditions were recruited as controls (POP-Q = 0) while women with advanced POP (POP-Q stage ≥ 3) were recruited as patients. Secretory phase of the menstrual cycle was confirmed by histology report. Exclusion criteria: steroids therapy, malignancy, previous pelvic surgery, connective tissue diseases. During surgery, 1 cm^2 of full thickness vaginal tissue was obtained, total RNA and protein were extracted and analyzed by RT-PCR and Western Immunoblot, respectively. Mann-Whitney test ($P<0.05$) was used for statistical analysis.

Results: We recruited 40 Caucasian premenopausal women (20 patients and 20 controls). ADAMTS-2, but not ADAMTS-3 and ADAMTS-14, mRNA was expressed in all vaginal biopsies and was significantly increased in all patients with POP compared with all controls. Four bands corresponding to pro and mature forms of the active and inactive isoforms of ADAMTS2 were detected on Immunoblot: 130 kDa, 100 kDa, 58 kDa and 34.5 kDa. The 58 kDa protein was significantly decreased in patients vs controls only in the proliferative phase of the menstrual cycle ($P=0.027$). We also noted that both (pro and mature) forms of inactive ADAMTS-2 protein were noticeably more abundant than their active counterparts. 18 women were in the secretory phase of the menstrual cycle (8 patients and 10 controls). LOX, LOXL1-4 gene were expressed in vaginal tissue biopsies, however only LOX was significantly increased ($P=0.0028$). We detected a significant increase in MMP2 and MMP14 mRNA levels in patients with POP compared to controls ($P=0.029$, $P=0.008$ respectively). Immunoblot analysis for LOX and MMP14 indicated a significant increase of the 35kDa form of LOX in vaginal tissue of patients compared to controls ($P=0.04$) however two isoforms of MMP14 were expressed equally. MMP-2 and -9 gelatinase activities were significant increased in vaginal biopsy samples of patients compared to controls .

Conclusion: We identified differential expression of proteins that may contribute to altered collagen and elastin biogenesis and subsequent defective assembly of pelvic tissues in patients with severe POP . Hormonal status might influence the expression of enzymes regulating the ECM biogenesis in vaginal tissue. **Funded by:** Physicians' Services Incorporated Foundation
Mount Sinai Hospital Research Fund

ABSTRACT #O6

Reduced Coq10 Gene Expression in Cumulus Cells with Aging

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Objective: There is evidence that older infertility patients have abnormal oocyte mitochondrial activity and reduced production of ATP, which in turn limits normal oocyte chromosomal disjunction and subsequent embryo development. Coenzyme Q10 is a crucial player in the electron transport at the mitochondria and has been shown to be reduced with aging. We have shown previously that the expression of CoQ10 synthesis genes in GVs is reduced with aging and treatment with CoQ10 improved the oocyte mitochondrial performance, ovulation and pregnancy rates. The cumulus cells, as the nourished cells of the oocyte can produce CoQ10 and deliver it, just as others substrates like cholesterol or pyruvate. The objective of this study was to evaluate whether CoQ10 synthesis in the cumulus cells alter with aging in mice and human.

Material and Methods: 10 aged mice (9 months old) of ICR strain were treated with 0.042 mg/kg CoQ10 for 12 weeks and were compared to 10 aged matched vehicle-treated mice and 10 young females. Dams were subjected to superovulation and retrieved oocytes were stripped from their cumulus cells (CC). These cells were count per oocyte and examined for mRNA expression of genes participating in CoQ10 synthesis pathway.

Results: The number of CC per oocyte were decreased with aging, but significantly less in the CoQ10 treated group (3050±236, 1472±144 and 2218±276 in young, old and CoQ10-treated old groups, respectively; $P<0.001$). The expression of most of the genes involved in CoQ10 synthesis was reduced in the aged group with significantly reduction in Coq6 and Pdss2 genes ($P<0.008$ and $P<0.013$, respectively). Preliminary results of mitotracker green staining of CC also reveal increased levels of mitochondrial staining with aging.

Conclusion: CoQ10 deficiency was found in CC, which we believe impaired their ability to rescue the oocyte from a mitochondrial energy deficiency state. We are currently analyzing whether this altered synthesis of CoQ10 with aging can be found in CC of humans by measuring CoQ10 levels in follicular fluid and expression of the CoQ10 synthesis genes in cumulus cells of women undergoing IVF/ICSI.

ABSTRACT #O7

Risk of Preeclampsia in HIV-Positive Pregnant Women Receiving HAART: A Matched Cohort Study

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Objective: We sought to determine whether HIV-positive women receiving HAART are at higher risk for preeclampsia than HIV-negative women. Secondary outcomes included comparing the risks of preterm birth, low birth weight, and small for gestational age birth in these women.

Methods: In this retrospective matched cohort study, we compared the pregnancy outcomes of HIV-positive women treated with HAART with those of HIV-negative women who gave birth at Mt. Sinai Hospital, Toronto, Ontario. Data were ascertained through chart review. Univariate and multivariate logistic regression models were used to compare pregnancy outcomes between the two groups.

Results: Ninety-one HIV-positive pregnant women receiving HAART and 273 HIV-negative pregnant women were identified. After adjusting for confounding factors, there was no difference between HIV-positive and HIV-negative women in the odds of preeclampsia (3.3% vs. 5.1%; adjusted odds ratio [aOR] 0.59; 95% confidence interval [CI] 0.11 to 3.08), preterm birth (15.6% vs. 11.4%; aOR 1.70, 95% CI 0.79 to 3.66) or small for gestational age infants (20.2% vs. 8.8%; aOR 2.08, 95% CI 0.89 to 5.24). HIV-positive women treated with HAART had increased odds of giving birth to a low birth weight infant compared to HIV-negative women (20.2% vs. 9.9%; aOR 2.91; 95% CI 1.47 to 5.78).

Conclusion: In this cohort, HIV-positive women on HAART did not demonstrate a higher risk of preeclampsia, preterm birth, or small for gestational age infants; however, they did have a higher risk of having low birth weight infants.

ABSTRACT #O8

Brief Family History Questionnaire for Identification of Lynch Syndrome in Women with Newly Diagnosed Endometrial Cancer

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ABSTRACT AVAILABLE IN HARDCOPY VERSION ONLY

ABSTRACT #O9

Effect of *Lactobacillus rhamnosus* GR-1 (GR-1) on Cytokines and Chemokines in Maternal Plasma, Amniotic Fluid and Intra-uterine Tissues of Pregnant CD-1 Mice.

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Objective: To determine the effect of GR-1 on cytokine and chemokine secretion profiles in pregnant CD-1 mice.

Methods: In two groups of pregnant mice, adaily dose of either GR-1 at 10^8, 10^9 or 10^{10} colony forming units (cfu) or saline was orally administered for 7 days from gestational day (gd) 9-15. The first group of mice (n=20) was monitored until term (gd 20). The second group of mice (n=31) was sacrificed on gd 16. Twenty-one cytokines and chemokines in maternal plasma (MP), amniotic fluid (AF) and intra-uterine tissues (myometrium, decidua, placenta, fetal membrane) were measured using Bioplex. Serum progesterone concentrations were determined using EIA.

Results: Oral administration of GR-1 did not alter either the gestational length or the MP progesterone level. However, GR-1 at 10^9cfu caused a significant increase in IL-6, IL-17, TNFα, and IL-10 concentrations in the MP. No effect was seen at 10^9cfu in the AF. A similar significant increase in IL-6, IL-17 and TNFα was detected in the AF but at a higher dose (10^{10} cfu) except for IL-10. GR-1 at 10^{10} cfu caused a significant increase in the chemokines KC and MIP-1β in the AF. There was no effect of GR-1 on MP chemokines.At 10^9cfu, GR-1 significantly decreased TNFα, IL-10, MIP-1β, RANTES, and IL-3 expression in the myometrium andsignificantly increased these cytokines, with the exception of RANTES, in the placenta. In addition, IL-2, IL-5, IL-9 and IL-17 in the placenta were increased after treatment with 10^9cfu of GR-1. In the fetal membranes, GR-1 at 10^9cfu caused a significant elevation in IL-10, RANTES, and IL-3 expression. No change in either cytokines or chemokines concentrations was observed in the decidua. Th2/Th1 ratios (IL-10/IL-1α, IL-10/IL-1β, IL-10/IL-6, IL-10/IL-12p40 and IL-10/TNFα were increased by GR-1 (10^9cfu) in the fetal membranes and the IL-10/IL-1α ratio was significantly increased in the placenta at the same dose of GR-1. However, these ratios were significantly decreased by GR-1(10^9cfu) in the myometrium.

Conclusions: GR-1 administered orally to pregnant CD-1 mice alters the innate immunity, leading to differential cytokine and chemokine profiles in the MP, AF and intra-uterine tissues. Compared to MP, a higher dose of GR-1 is required to induce changes in cytokines and chemokines in the AF. Th2 dominance was observed in the fetal membranes and placenta while Th1 dominance was observed in the myometrium. These findings support our previous *in vitro* studies and provide further evidence that *Lactobacillirhamnosus*can counter inflammation-associated preterm labour.

Funded by: CIHR

ABSTRACT #O10

Multidrug Resistance in the Developing Blood-Brain-Barrier (BBB): Interactions between Cytokines and Glucocorticoids (GCs)

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Objective: P-glycoprotein (P-gp) protects the developing fetal brain from a wide range of xenobiotics present in maternal circulation. Cytokines (released during infection) inhibit P-gp, but it is unknown how cytokines can affect fetal brain susceptibility in pregnancies complicated by infection. Infection accounts for ~40% of preterm labour (PTL) risk, for which pregnant women receive synthetic GCs (sGCs). P-gp is stimulated by sGCs, but it is unknown how prenatal sGC exposure (with cytokines) alters fetal BBB multidrug resistance. We hypothesized that: 1) cytokines inhibit P-gp function in brain endothelial cells (BECs); 2) sGC exposure alters subsequent BEC P-gp response to cytokines.

Methods: Brain microvessels (BMVs) and BECs were isolated from gestational day (GD) 50, 65 and postnatal day (PND) 14 male guinea pigs. BMVs and BECs were also isolated from GD50 fetuses exposed *in utero* to dexamethasone (sGC; 1 mg/kg), or vehicle (VEH) on GD48/49. Confluent BEC cultures were treated with 1-10,000 pg/mL of interleukin-1β (IL-1β), interleukin-6 (IL-6), or tumor necrosis factor α (TNF-α) for 1-24h, and P-gp function was assessed (calcein-AM; 1 μM). P-gp and IL-6 receptor (IL-6R) protein were measured in BMVs.

Results: IL-1β, IL-6 and TNF-α all reduced P-gp function in BECs derived from PND14 ($P<0.01$). These inhibitory effects were not seen in cells derived from GD50 fetuses, but were present in GD65 BECs ($P<0.01$). In contrast to naive GD50 BECs, GD50 DEX-exposed fetal BECs displayed enhanced responsiveness to the inhibitory effects of cytokines ($P<0.01$). Prenatal DEX exposure increased P-gp and IL-6R protein in BMVs, by 2 to 3-fold, respectively.

Conclusions: Our data suggest that a developmental window exists for cytokine regulation of P-gp function. This window is widened by prenatal exposure to sGCs. Near-term, the P-gp-mediated fetal BBB protection is reduced during infection, potentially leaving the fetal brain susceptible to teratogens. Prenatal sGC exposure appears to further promote this susceptibility. Greater consideration may be needed when administering sGCs for risk of PTL due to infection; particularly to women on medications that are known P-gp substrates.

Funded by: Canadian Institutes for Health Research.

ABSTRACT #O11

Trends in Menstrual Concerns and Suppression in Adolescents with Cognitive and Physical Challenges

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Objectives: Disabled young women and their families face challenges with the anticipation or onset of puberty and menarche. Given recent changes and trends in the availability and prescribing practices of methods for contraception, our study aims to demonstrate any changes in options and decision-making for menstrual suppression in the disabled adolescent population in a recent 5 year cohort compared to a historical cohort at the same hospital. Published data from 1998 to 2003 indicate a preference for Depo-medroxyprogesterone acetate (DMPA) in 59% and oral contraceptive pills (OCP) in 17% of postmenarchal patients.
Methods: This is a retrospective cohort study of all cognitively and physically challenged patients seen in consultation or follow-up for menstrual concerns at the Pediatric Gynaecology Clinic at a tertiary hospital between 2006 and 2011. Data was collected from standardized intake and follow-up forms, and dictated clinic letters. Research ethics board approval was attained.
Results: Three hundred physically and/or cognitively disabled patients from 7.3 to 18.5 years of age (mean 12.1 $\pm$ 1.6) were included. Caregiver concerns included menstrual suppression, hygiene, caregiver burden, behaviour, mood, dysmenorrhea, menstrual regulation and/or contraception or sexual abuse risk. Forty-five percent of patients had both cognitive and physical disabilities; 52% had only cognitive impairments, 4% had only physical impairments. Sixty-eight percent were dependent upon caregivers for activities of daily living, 35% incontinent of urine, feces, or both, 34% nonverbal, 17% wheelchair-bound, and 7% nourished by feeding tube. Thirty-two percent of patients were seen for premenarchal counseling. Postmenarchal patients were seen, on average, 15 months after menarche. The most commonly selected initial method of suppression was the extended or continuous OCP (42.3%) followed by patch (20.0%), expectant management (14.9%), DMPA (11.6%), and levonorgestrel intrauterine system (LNG-IUS) (2.8%). The average number of methods prescribed to reach caregiver satisfaction was 1.5. Sixty-six percent of patients or caregivers were satisfied with and continued the initial selection for menstrual suppression. The most common reasons for discontinuation of method included break-through bleeding with all methods, decreased bone marrow density from DMPA, or difficulties with patch adherence. Of those who changed methods, second-choice selections included oral contraceptive pill (42.5%) followed by LNG-IUS under general anesthesia (19.2%), DMPA (17.8%), and continuous transdermal patch (13.7%).
Conclusions: Since the publication of findings relating decreased bone mineral density to long-term usage of DMPA and the emergence of new contraceptive options, the use of extended or continuous oral contraceptive pills has surpassed the use of DMPA for menstrual suppression. While LNG-IUS is not commonly selected initially, the device is becoming an increasingly accepted and successful management option for menstrual suppression in disabled adolescents.

ABSTRACT #O12

Interleukin-1β (IL-1β)-Stimulated Inflammatory Gene Expression in Fallopian Tube Epithelial Cells is reversed by Glucocorticoids

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Objectives: The most common and lethal subtype of epithelial ovarian cancer (EOC) is serous carcinoma. Recent studies indicate that high-grade serous ovarian carcinoma (HGSC) may originate from the fallopian tube epithelium (FTE).Risk factors for EOC are linked to local inflammatory reactions such as endometriosis, pelvic inflammatory disease and lifetime ovulatory years. The relevance of inflammation in EOC is further supported by the protective effect of NSAID and OCP use, parity and breastfeeding. Ovulation is an acute inflammatory event during which the FTE is bathed in follicular fluid containing pro- and anti-inflammatory molecules such as IL-1 and cortisol. It is hypothesized that an altered ability of adjacent FTE cells to resolve the local pro-inflammatory environment associated with ovulation may contribute to HGSC. The inflammatory response of FTE cells *in vitro* has not yet been investigated. We sought to determine if exposure of FTE cells to IL-1β induces an inflammatory response and whether glucocorticoids oppose this effect.

Methods: Immortalized human FTE OE cells were treated with IL-1β, dexamethasone (DEX), IL-1β + DEX, or vehicle. Total RNA was extracted and hybridized to Illumina HT-12 v4 Expression BeadChips to obtain gene expression signatures. Protein lysates obtained were resolved by SDS-PAGE and immunoblotted for COX-2 and tubulin.

Results: ANOVA with Benjamini-Hochberg false discovery rate ($P<0.05$) indicated 450 probes as differentially expressed. A Tukey's post-hoc test was then used to examine differences between groups. IL-1β up-regulated a number of genes consistent with pro-inflammatory signaling. DEX reversed the effect of IL-1β on several genes including cytokines and pro-inflammatory proteins such as COX2. Up-regulation of COX2 by IL-1β and reversal by DEX was verified by Western Blot analysis. Verification of additional genes by real-time RT-qPCR is underway.

Conclusion: These findings support the hypothesis that pro-inflammatory signaling is induced in FTE cells during ovulation and this signaling is suppressed by glucocorticoids. Identification of signaling molecules involved in the inflammatory response of FTE may provide targets for prophylaxis in patients at high risk of developing HGSC.

Funded by: CIHR

ABSTRACT #O13

Effect of VEGF Overexpression by Concepti on Maternal VEGF in Mice

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Objective: Vascular endothelial growth factor (VEGF) is a potent angiogenic factor expressed by all organs, including the highly vascular placenta. It increases in the maternal circulation during pregnancy, but its source and function are unknown. It was hypothesized that if the placenta was the source of increased VEGF in the maternal circulation during pregnancy, then circulating VEGF in wildtype mothers carrying $Vegf^{hi}$ concepti would be elevated relative to controls.

Methods: Male $Vegf^{hi}$ mice were mated with wildtype (WT) CD1 females to obtain pregnancies where approximately half the concepti carried the $Vegf^{hi}$ transgene. Maternal plasma, maternal organs and regionally-enriched placental samples (junctional zone, labyrinth, and chorionic plate) were collected at E17.5 from WT pregnancies and from CD1 female mice (aged 8-12 weeks) mated with $Vegf^{hi}$ males. $VEGF_{120/164}$ protein was measured in the maternal circulation, organs, and the placenta by ELISA.

Results: When WT female mice were mated with $Vegf^{hi}$ males, placentas overexpressed VEGF protein compared to WT pregnancies ($P<0.05$). However, litter size (13.6±1.4 vs. 13.9±2.1 in WT, $p>0.05$; N= 8 and 10 respectively) and maternal body weight (63±2 vs. 61±2 g in WT, $p>0.05$; N=8 and 16 respectively) in the $WTxVegf^{hi}$ cross were not different compared to WT pregnancies. Even though VEGF was overexpressed in half the concepti, and consequently their placentas, we surprisingly found that maternal systemic arterial circulating levels of VEGF decreased relative to controls (303±62 vs. 599±48 pg/ml in WT, $P<0.05$; N=7 and 14 respectively). WT females mated with $Vegf^{hi}$ males had kidney and decidua VEGF levels that were not different than controls. However, ovarian VEGF levels were significantly decreased (320±68 vs. 536±57 pg/mg of total protein in WT, $P<0.05$; N=10 in both groups).

Conclusion: Contrary to our hypothesis, we did not obtain evidence supporting the placenta as a direct contributor to maternal plasma VEGF. However, conceptus VEGF appears to indirectly influence maternal plasma VEGF possibly by affecting ovarian VEGF production.

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ABSTRACT #O14

The Safety of Methimazole and Propylthiouracil Use in Pregnancy

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Objective: Methimazole (MMI) and propylthiouracil (PTU) are antithyroid drugs commonly used in the treatment of hyperthyroidism. Hyperthyroidism, one of the most common endocrinological abnormalities in pregnant women, can severely complicate the pregnancy course and outcome. Both MMI and PTU are associated with adverse effects. While MMI has traditionally thought to be more teratogenic, PTU is now known to be hepatotoxic.
The aim of this study is to systemically review the literature regarding the effects of PTU and MMI on the mother and the fetus, when prescribed to hyperthyroid pregnant women. Evaluation of maternal and fetal risk of PTU and MMI exposure, will help confirm if one drug is safer over the other in pregnant women.

Methods: A systematic search was conducted in various search-engines sources including original population-based studies, case-series, case reports, electronic databases and textbooks. The effects of prenatal exposure to the main anti-thyroid therapies - PTU and MMI on pregnancy outcome, was classified into several adverse subgroups. Only articles in English were included. Scientific abstracts and reports with undetermined interpretation of results were excluded as well. Exclusion criteria were: Non-English publications, studies including other anti-thyroid than PTU and MMI, and scientific abstracts without further manuscript publications.

Results: Our search detected 24 studied that matched our criteria. Four out of themwere population-based studies, while 20 were case-series or case reports. The four population-based studies consisted of an overall total of 554 pregnant women exposed to MMI and PTU during pregnancy – 340 treated with MMI and 214 with PTU. There was insufficient data pertaining to MMI related teratogenic features as well as to PTU-induced hepatotoxicity, in order to provide a quantitative maternal and fetal risk associated with MMI and PTU. However, based on these studies we were able to assess the qualitative maternal and fetal risk of such treatments.

Conclusions: MMI has significant teratogenic effects when the fetus is exposed to the drug in the first trimester, while PTU has severe hepatotoxic sequela. Thus, optimally, PTU should be administered during the first trimester and switched to MMI for the remainder of the pregnancy.

POSTER ABSTRACTS

ABSTRACT #P-A1

VEPH1 Inhibits Canonical TGF-β Signalling in Ovarian Cancer Cells by Impeding Nuclear Accumulation of SMAD2.

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ABSTRACT AVAILABLE IN HARDCOPY VERSION ONLY

ABSTRACT #P-A2

Pathways Associated with Differential Accumulation of Ascites in High Grade Serous Ovarian Cancer: A Search for Targeted Therapy to Control Ascites.

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ABSTRACT AVAILABLE IN HARDCOPY VERSION ONLY

ABSTRACT #P-A3

Modulation of Androgen Receptor (AR) signaling by Ventricular Zone-expressed PH Domain-Containing Protein Homolog 1 (Veph1) in Ovarian Cancer Cells.

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ABSTRACT AVAILABLE IN HARDCOPY VERSION ONLY

ABSTRACT #P-A4

Impact of BRCA1/2 Mutation Status on Inflammatory Signalling by Fallopian Tube Epithelial Cells in Culture in Response to Follicular Fluid Exposure – Work-in-Progress.

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Introduction: Recent theories on the pathogenesis of epithelial ovarian cancer suggest that high-grade serous type ovarian carcinomas (HGSC) originate from the distal fallopian tube epithelia (FTE). Studies suggest that ovulation is a micro-inflammatory event, of which a delayed resolution may lead to cellular transformation and precursor lesions within the fallopian tube epithelia. HGSC is the most aggressive and common histological subtype of ovarian cancer, and is the only subtype to be associated with *BRCA1/2* mutations. Preliminary *in vivo* data suggest that the resolution of pro-inflammatory signalling may be delayed in germline carriers of BRCA1 mutations, which if true, could contribute to the predisposition to HGSC by these mutations.

Objective: To determine if BRCA1/2 mutation status affects pro-inflammatory signalling by FTE cells in primary culture following their exposure to periovulatory follicular fluid.

Methods: Surgical fallopian tube tissue samples are obtained from consenting patients undergoing bilateral salpingo-opherectomy at Mount Sinai Hospital. Human follicular fluid was collected at the time of oocyte retrieval from 14 IVF patients undergoing controlled ovarian hyperstimulation. FTE cells were dissociated and seeded onto collagen IV coated 0.4μm transwells and grown to confluence. Cultures were then exposed to follicular fluid or medium alone for 24 hours. Cells were harvested 0, 12, 24, 36, 48, 72, 96, and 120 hours after removal of follicular fluid and cellular RNA was extracted for subsequent gene array sequencing.

Results: The majority of recovered cells in primary culture have a cobblestone appearance consistent with an epithelial phenotype. Immunohistochemical staining is consistent with the presence of both ciliated and secretory epithelial cells with few menenchymal cells. To date, 18 samples have been collected with a time course experiment completed on 13 samples. Of these, 7 were derived from control patients, 1 from *BRCA1* carriers, and 6 from *BRCA2* carriers.
Conclusions: Immunohistochemical staining of FTE cells grown on collagen IV reflect the cell types present in the fallopian tube epithelium, and exhibit an epithelial morphology. Gene expression studies to test our hypothesis will be initiated once we have collected at least six cases each of BRCA1, BRCA2, and control patients.

Funded by: CIHR, The Richard Venn and Carol Mitchell Graduate Studentship in Women's Health (to A.L)

ABSTRACT #P-A5

Sentinel Lymph Node Biopsy in Vulvar Cancer: A Health Technology Assessment for the Canadian Health Care Context

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Objectives: Inguinofemoral lymphadenectomy for vulvar cancer is associated with a high incidence of groin wound complications and lymphedema. Sentinel lymph node biopsy (SLNB) is a morbidity-reducing alternative to lymphadenectomy. The objective of this health technology assessment is to review the literature to determine the clinical effectiveness, cost effectiveness, and organizational feasibility of SLNB in the Canadian context.

Methods: A review of the English-language literature from January 1992 to October 2011 was performed across five databases and six grey literature sources. Predetermined eligibility criteria were used to select studies, and results in the clinical, economic and organizational domains were summarized. Included clinical studies were evaluated for methodologic quality using the Newcastle Ottawa Scale (NOS).

Results: Of the 825 reports identified, 89 observational studies met the eligibility criteria. Overall study quality was poor with a median NOS score of 2 out of 9 stars. Across all studies, the detection rate of the sentinel lymph node (SLN) was 82.2% per groin and the false negative rate (FNR) was 6.3%. The groin recurrence rate after negative SLNB was 3.6% compared to 4.3% after negative lymphadenectomy, and complications were reduced after SLNB. No economic evaluations were identified comparing SLNB to lymphadenectomy. Safe implementation of SLNB requires appropriate patient selection, detection technique, and attention to the learning curve.

Conclusions: Although study quality is poor, available data suggests implementation of SLNB may be safe and feasible in Canadian centres with adequate procedural volumes, given careful patient selection, technique, and ongoing quality assessment. Additional high quality evidence for this modality would increase confidence in the safety and efficacy of SLNB. Cost effectiveness remains to be elucidated.

ABSTRACT #P-A6

Effects of Veph1 on FoxO-regulated SOD2 in Epithelial Ovarian Cancer Cells in Response to Oxidative Stress

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ABSTRACT AVAILABLE IN HARDCOPY VERSION ONLY

ABSTRACT #P-B1

Transforming Growth Factor-B1 Regulates Multidrug Resistance at the Developing Blood-Brain Barrier

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Objective:P-glycoprotein (P-gp), a drug transporter responsible for mediating multidrug resistance at the developing blood-brain barrier, increases in activity during late gestation. The mechanism of this upregulation remains unclear. Astrocytes may have a prominent role in this upregulation as studies have shown that P-gp mRNA increases in brain endothelial cells (BECs) co-cultured with astrocytes. Transforming growth factor-β1 (TGF-β1) is a cytokine secreted by astrocytes during development and is critical in regulating cellular proliferation, differentiation, ECM production and apoptosis. Recent studies have shown the neuroprotective effectsof TGF-β1. Very little work has been done on the neuroprotective effect of blood/peripheral- and astrocyte-derived TGF-β1 during fetal and neonatal brain development. In the present study, we hypothesized that TGF-β1 increases P-gpactivity at the developing blood-brain barrier.

Methods:BECs were isolated from postnatal day (PND) 14, gestational day (GD) 65and 50 male guinea pigs. To assess the effect of peripheral TGF-β1, BECs weregrown on 96-well cell culture plates. Varying doses of TGF-β1 (10^0-10^4 pg/ml) were added to the luminal side of BECs for 2, 4, 8 and 24 hours. Following TGF- β1 treatment, P-gp function was measured via calcein-acetoxymethyl ester assay. Cell viability was measured by trypanblue staining.

Results: Preliminary results demonstrate that TGF-β1 exposure to the luminal side of PND14 BECs elicited a significant increase in P-gp function at 2 ($P< 0.05$), 4 ($P< 0.05$), and 8 hours ($P< 0.05$). Peak responses were seen at 8 hours with approximately a 45% increase in P-gp function on BECs treated with 10^4pg/ml of TGF-β1. At 24 hours of exposure, there was no significant change in P-gp function. Trypan blue staining indicated no significant cell death in BECs exposed to 10^3 or 10^4pg/ml TGF-β1 for 24 hours.

Conclusions: These preliminary results indicate that the effect of TGF-β1 exposure on the luminal side of PND14 BECs is to elicit a short-term increase in P-gp function. These data also suggest that TGF-β1 may mediate astrocyte-induced upregulation of P-gp function. Further experiments are being undertaken to investigate the role of astrocyte-derived (basolateral exposure) TGF-β1 in P-gp regulation.In addition, the role of TGF-β1 on P-gp function in the blood-brain barrier through late gestation will also be determined.

Funded by: Canadian Institutes for Health Research.

ABSTRACT #P-B2

Capillary Rarefaction, a Phenomenon that Antedates Essential Hypertension Is Not Present in Low Birth Infants at Birth

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Objective: Low birth weight infants are at a higher risk of developing essential hypertension and cardiovascular morbidity in later life. A reduction in skin capillary density (capillary rarefaction) is a hallmark of essential hypertension, and has been consistently shown to precede the onset of hypertension. We hypothesized that low birth weight infants would have significant capillary rarefaction at birth.

Methods: 44 low birth weight infants born to normotensive mothers were studied at birth. 33 were born preterm (birth weight: 1823±446g), and 11 were born at term (birth weight: 2339±177g). These were compared with 71 infants born at term with normal weight (birth weight: 3333±519g). We used orthogonal polarized spectroscopy to measure basal (functional) and maximal (structural) skin capillary densities.

Results: Low birth weight infants, whether born preterm or at term, had significantly higher functional capillary density (mean difference of 10.5 capillaries per millimeter squared; 95% CI: 6.6–14.4 capillaries per millimeter squared; $P<0.0001$) and higher structural capillary density (mean difference of 11.1 capillaries per millimeter squared; 95% CI: 7.6–14.5 capillaries per millimeter squared; $P<0.0001$) when compared with normal weight term infants.

Conclusions: Low birth weight infants born to normotensive mothers do not have capillary rarefaction at birth, but instead show a significantly higher capillary density. These results suggest that microcirculatory abnormalities observed in individuals of low birth weight occur in postnatal life rather than during their intrauterine existence. Whether the increased skin capillary numbers observed in these babies at birth is a reflection of neovascularization secondary to intra-uterine starvation remains to be established.

ABSTRACT #P-B3

Decidual Neutrophils: A Novel Angiogenic Population in the 2nd Trimester.

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Objective: The maternal decidual leukocyte populations play crucial roles in the uterine vascular remodeling accompanying normal placentation. Our multicolour FACS study of these populations over the 1st and 2nd trimesters identified a novel and significant population of neutrophils specific to the 2nd trimester (15-20% of all CD45 leukocytes). The aim of this study was to further phenotype the decidual neutrophil (DN) population in comparison to peripheral blood (PBN) and to determine if the decidua could drive PBN recruitment and differentiation.

Methods: 2nd trimester leukocytes were isolated from either decidual tissues or peripheral blood by mechanical mincing or histopaque centrifugation respectively. FACS analysis using Anti CD66b, CD15 (neutrophil markers), CD45 (common leukocyte antigen), CD181, CD182, CD183 and CD184 (chemokine receptors) was performed. Matching decidual biopsies were immunostained for CD66b, neutrophil elastase, and cytokeratin and HLA-G. We also tested the potential of decidual derived IL-8 to stimulate 1) extravasation of primary 2nd trimester PBN in vitro, and 2) the upregulation of angiogenic growth factors.

Results: The DN differ from PBN in that they express high levels of CD66b whilst the IL8 receptors CD181 and 182 are decreased. Conversely CD183 and 184 are increased in DN. Immunostaining confirmed the presence of neutrophils within decidua basalis only and not the decidua paretalis (n=10 in each group). Aggregates of neutrophils were seen within the decidual stroma in areas containing EVT. Neutrophils were observed adhered to endothelium and infiltrating the vascular wall. We also show that 2nd trimester decidua conditioned medium (DCM) can stimulate PBN to invade and transverse a monolayer of endothelial cells, and that this was inhibited by 60% following neutralisation of IL8. Furthermore 5h of DCM treatment upregulated VEGFA, CCL2 and ICAM1 mRNA levels in 2nd trimester PBN indicating the angiogenic function of DN.

Conclusion: This study indicates the peripheral blood origin of DN and identifies decidual Il-8 as a primary recruiting stimulus for these cells. The presence of DN in the 2nd trimester decidua basalis together with the production of angiogenic factors, similarly to the N2 tumor associated neutrophils, suggests a role for the DN in the stabilisation of transformed arteries in the uteroplacental bed.

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ABSTRACT #P-B4

Activation of PPAR-g and HO-1 via Rosiglitazone in BeWo cells Recapitulates the *in vivo* Molecular Pathway

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Objective: Severe preeclampsia (sPE) is a hypertensive pregnancy disorder characterized by maternal vasculopathy and impaired fetal growth that leads to perinatal death or long-term morbidity from prematurity. The placental pathology is characterized by highly abnormal differentiation of the syncytiotrophoblast (SCT) layer, which is in contact with the maternal blood. The peroxisome proliferator-activated receptor-gamma (PPAR-g), a steroid nuclear receptor and transcription factor, plays a role in physiologic SCT differentiation in mice and humans. We recently demonstrated that activation of PPAR-g with rosiglitazone, a selective agonist, ameliorated disease features in a rat model of sPE. Furthermore, we showed that an inhibitor of PPAR-g promotes features of sPE in these animals via its downstream target, heme oxygenase-1 (HO-1). We tested the hypothesis that PPAR-g promotes HO-1 transcription in the human choriocarcinoma-derived cell line, BeWo.

Methods: BeWo cells were cultured over 48 hours at 37^{o}C under 20% O_2 tension. Cells were treated with rosiglitazone alone or in combination with T0070907, PPAR-g antagonist, or SnPP, HO-1 activity inhibitor. Appropriate vehicle and media controls were also included. HO-1 mRNA levels were assessed by qRT-PCR.

Results: Rosiglitazone (10µM) upregulated the HO-1 expression over 2 days of culture (2.98 foldvs vehicle, $P<0.001$; n= 4). This effect was not diminished by co-administration of a T0070907 (500nM) with rosiglitazone (2.70 fold, $P<0.005$, n=4). Furthermore, rosiglitazone-induced HO-1 expression was unaltered by the co-administration of SnPP (2.91 fold, $P<0.005$, n=4).

Conclusions: Rosiglitazone promotes HO-1 expression in BeWo cells by stimulating PPAR-g transcriptional activity. Since HO-1 promotes vasorelaxation via generation of CO, its upregulation by rosiglitazone offers a pathway relevant to the prevention or treatment of sPE.

Funded by: CIHR and Department of Obstetrics and Gynaecology, Mount Sinai Hospital (Bernard Ludwig Studentship)

ABSTRACT #P-B5

GSK3β reduces Mcl-1 Phosphorylation in Preeclamptic Placentae

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Objective: Myeloid cell leukaemia factor 1(Mcl-1) is an anti-apoptotic Bcl-2 family member, that plays a key role in regulating trophoblast cell fate. Mcl-1 is a short-lived protein whose stability is tightly regulated through mechanism(s) involving proteolytic caspase cleavage and phosphorylation leading to Mcl-1 ubiquitination and proteosomal degradation. Glycogen Synthase Kinase-3β(GSK3β) is central to Mcl-1 phosphorylation; however when total GSK3β itself gets phosphorylated; it becomes inactive thereby preventing the post-translational modification of Mcl-1. We have previously reported an altered Mcl-1 expression in preeclampsia (PE) and have shown that in PE, decreased Mcl-1 levels are in part due to active caspase cleavage. Herein, we examined the mechanism(s) involved in the phosphorylation of Mcl-1 (pMcl-1) in placentae from normotensive and PE pregnancies.

Methods: Placental tissues collected from pregnancies complicated by severe early onset PE (n=17), and preterm age-matched controls (PTC) (n=10) were used. pMcl-1, total and phospho-GSK3β protein levels were measured by immunoblotting. Mcl-1/GSK3β association was assessed by immunoprecipatation. The effect of hypoxia/oxidative stress on Mcl-1 phosphorylation and total/phospho-GSK3β was assessed by treating choriocarcinoma JEG3 cells with the nitric oxide donor sodium nitroprusside (SNP; 2.5 mM and 5.0 mM) and by maintaining the cells at 3% O_2 with or without proteosomal inhibitor MG132.

Results: Phospho-Mcl-1 and total Mcl-1 protein levels were significantly ($P<0.05$) reduced in preeclamptic placentae relative to normotensive controls and this associated with decreased GSK3β protein expression. In stark contrast, phospho-GSK3β levels were markedly increased in PE. Immunoprecipitation experiments revealed a decreased Mcl-1/GSK3β association in preeclamptic placentae compared to PTC. Similar to PE, following SNP and 3% O_2 treatments, GSK3β and phospho-Mcl-1 were decreased and this associated with increased expression of phospho-GSK3β. When cells were treated with a specific GSK3β inhibitor (GSK-3 Inhibitor IX), phospho-Mcl-1 levels significantly decreased suggesting a contribution for GSK3β in Mcl-1 phosphorylation in trophoblast cells.

Conclusions: Oxidative stress-induced phosphorylation of GSK3β is in part responsible for a reduction in Mcl-1 phosphorylation in preeclamptic placentae thereby contributing to the altered Mcl-1 expression found in this disease.

Funded by: CHIR and Canada-Hope Fellowship

ABSTRACT #P-B6

Soluble VEGFR-1 (sFlt-1) and Hypoxia Decrease VEGFR-2 Expression in the Human Placenta

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Objectives: Vascular endothelial growth factor receptor 2 (VEGFR-2), the primary receptor for VEGF, is crucial for normal endothelial function and is reduced in placenta from patients with preeclampsia (PE). sFlt-1, which binds and inhibits VEGF, is increased in PE and is positively regulated by low oxygen. Our **objective** was to examine the effect of sFlt-1 on VEGFR-2 expression and signaling in the human placenta.

Methods: Placental samples were collected from early onset PE (n=27) and control (n=16) pregnancies. First trimester villous explants were cultured at 3% or 20% O_2 in the presence of sFlt-1 (n=4). VEGFR-2 protein and mRNA expression were measured by western blot and quantitative real-time PCR analyses respectively. Protein interaction was examined by co-immunoprecipitation (Co-IP) and co-localization by immunofluorescence (IF) for VEGFR-2 and sFlt-1.

Results: VEGFR-2 transcript and protein levels were significantly decreased in PE placentae compared to controls (1.82 and 1.85fold, respectively). An inverse correlation was observed for VEGFR-2 and sFlt-1 levels in both singleton and twin placentae from patients with PE. IF analyses revealed co-localization of VEGFR-2 and sFlt-1 in placental vasculature and Co-IP analyses confirmed VEGFR-2 and sFlt-1 interaction only in PE placentae compared to age-matched controls. VEGFR-2 transcript and protein levels from explants cultured in 3% O_2 (known to be associated with increased sFlt-1 expression) were significantly decreased compared to those incubated at 20% O_2 (5.9 and 12.47 fold, respectively). Also, VEGFR-2 transcript levels were significantly decreased in placentae from 8 to 11 weeks gestation (low oxygen environment) compared to 12 to 17 weeks (2.05 fold). We next explored whether sFlt-1 directly affects VEGFR-2 expression. Treatment of first trimester placental explants with sFlt-1 resulted in significantly decreased levels of VEGFR-2 (2.03 fold) and downstream signaling proteins phospho-ERK (1.60 fold) and phospho-Akt (1.64 fold).

Conclusions: Our findings show a novel hypoxia-induced down-regulation of VEGFR-2 in the human placenta. sFlt-1, which is known to be increased in hypoxic conditions, directly attenuates VEGFR-2 expression and signaling. Direct interaction between sFlt-1 and VEGFR-2 may represent an important mechanism in VEGFR-2 regulation, especially in preeclampsia that is associated with a high level of sFlt-1.

Funded by: The Deans Fund, University of Toronto. Department of Ob/Gyn, Sunnybrook Health Sciences Centre.

ABSTRACT #P-C1

Dual Specificity Phosphatase 9 (DUSP9) Regulation in Severe Early Onset Pre-eclampsia and in a Placental Villous Explant Model

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Objective: 1) To determine the effect of DUSP9 down-regulation in placentas of patients with severe pre-eclampsia (sPE) on downstream targets and whether this down-regulation is epigenetically mediated. 2) To silence DUSP9 expression in cell and tissue based models and study downstream targets. 3) To investigate the role of hypoxia on DUSP9 expression.

Methods: Phosphorylation of target proteins ERK1/2 and p38 was assessed with ELISA (Pre-term (PT) controls N=8, sPE N=8, severe growth restriction N=6). Epityper™ was used to determine methylation status of the DUSP9 promoter in sPE and PT control placentas (N=4/4). DUSP9 was silenced with siRNA in BeWo cells and in explanted first trimester placental villi. Expression was confirmed via qRT-PCR and phosphorylation of ERK1/2 was assessed via ELISA. Explants were subjected to hypoxia (3% O_2) to determine the impact on DUSP9 expression.

Results: DUSP9 is decreased in sPE placentas compared to those with severe growth restriction. We could not demonstrate hypermethylation and thus epigenetic mediation of this down-regulation. The ratio of phosphorylated to total ERK1/2 showed a trend to an increase in sPE, and no change for p38. In the tissue and cell based models DUSP9 expression was reduced (62/61%) in response to siRNA (N=4/4). ERK1/2 phosphorylation was not significantly altered in response to DUSP9 silencing in either BeWo cells or in explanted placental villi. These explants did however show a significant decrease in DUSP9 expression by 74±20% in response to hypoxia.

Conclusions: DUSP9 dephosphorylates MAP kinase proteins thus reducing cellular proliferation, a process which is significantly altered in sPE. DUSP9 down-regulation could not be explained with epigenetic promoter analysis. Hypoxia did however prove to be a negative regulator of DUSP9 expression. This down-regulation might be related to local hypoxic mechanisms governing stability, or from patchy necrosis of the syncytiotrophoblast layer. Further study of cytotrophoblast proliferation in DUSP9 silenced explants is ongoing.

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ABSTRACT #P-C2

Developing an *in vitro* Model o Kidney Differentiation as a Tool To Help Us Understand Kidney Developmental Defects

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Objective: The focus of our project is to develop an in vitro model ofkidney development to help us understand kidney normal differentiation anddevelopmental defects such as renal agenesis. We are interested in the specific interaction between embryonic kidney cells and the extracellular matrix, as well as the growth factors that are required for the maintenance and activation of various transcription factors involved in development of the kidney. Our primary objective is to understand how changes in gene expression as a direct result of deviations in growth factor secretion can lead to kidney development defects. The long-term goal is to use embryonic stem cell differentiation with co-culture on decellularized kidney matrices to determine if kidneys can be derived from embryonic stem cells and eventually used in the treatment of kidney diseases due to abnormalities of gene expression during development.

Methods: We are currently testing the ability of human embryonic stem cell lines (CA1, CA2) and mouse ES cell lines to differentiate into the mesodermal germ layer. Specifically, CA-1 and CA-2 embryonic stem cells have been grown on collagen type IV and gelatin coated plates, mouse ES cells have been grown on gelatin coated plates, over a course of 3 to 4 days with media changes occurring every other day. The same basal differentiation media is used for both types of embryonic stem cells which contain varying concentrations and combinations of BMP-4, FGF2 and Activin A. Brachyury, an early mesoderm marker, was used to detect for mesodermal differentiation. Furthermore, we are also determining if co-culturing with decellularized kidney matrix enhances differentiation.

Results: Mesoderm has been obtained through the use of several culture conditions from the CA-1 and CA-2 human embryonic stem cell lineages, however, efficiency and cell survival rates differed in each condition. We have also been able to determine that adult and fetal kidney cells can be supported by the decellularized kidney matrix.

Conclusion: In order to understand how developmental defects arise in the fetal kidney, we must first understand the developmental pathways that allow for kidney development, thus we have conducted our research and experiments with the objective of understanding signaling pathways and growth factors that are involved in producing renal progenitors from embryonic stem cells. In addition, combining ECM co-culture with specific growth factors given exogenously throughout culture should help us to understand kidney. We hope that we may be able to use this knowledge and apply it to better understand how atypical gene expression and anomalies in these pathways can give rise to developmental defects and aid in the development of cell based therapies for the treatment of kidney diseases, including renal agenesis which affects 1 in 5000 newborns.
Funded by: Province of Ontario Research Grant

ABSTRACT #P-C3

Pro-Inflammatory Cytokines and Chemokines Induced by Mechanical Stretch of Myometrial Cells Promote Neutrophil Infiltration by Enhanced Adhesion and Transendothelial Migration

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Objective: Spontaneous labour at term is associated with increased cytokine production, expression of adhesion molecules and leukocyte invasion into the myometrium. We previously demonstrated an association between uterine occupancy, the increased myometrial production of MCP-1, concurrent macrophage influx into the rat myometrium and the initiation of labour *in vivo*. We **hypothesize** that mechanical stretch induces pro-inflammatory cytokine secretion by human myometrial smooth muscle cells (SMC) which facilitates macrophage/neutrophil transendothelial migration (TEM) into the myometrium via upregulation of adhesion molecules and/or enhancement of their migratory characteristics.

Methods: 1) To test this hypothesis we cultured human myometrial SMC line (hTERT-HM) on flexible-bottomed collagen I-coated culture plates and applied static mechanical stretch using the Flexcell-5 strain unit for 24 hours (h). Stretch-conditioned media (SCM) and total RNA were collected and analyzed with multiplex human cytokine assays (Bio-Rad) and Real-Time PCR respectively. 2) Next we examined the activation states of both primary human neutrophils and human uterine myometrial microvascular endothelial cells (UtMVEC-Myo) after stimulation with SCM. The mRNA expressions of neutrophil activation markers (CD11a, CD11b, CD44) as well as endothelial cell adhesion molecules (E-selectin, ICAM-1, VCAM-1 and PECAM-1) were investigated by Real-Time PCR. 3) Adhesion assay and TEM assay were performed by seeding UtMVEC-Myo cells onto gelatin-coated 96-well microplate or 3-μm transwell inserts to examine whether SCM promote the adhesion and TEM of primary human neutrophils.

Results:1) Multiplex assay revealed the list of cytokines whose levels were significantly elevated by 24h stretch: IL-6, IL-8, VEGF and GRO-α. 2) Stimulation with SCM for 4 hours significantly increased endothelial E-selectin, ICAM-1 and VCAM-1 mRNA expressions while stimulation with VEGF alone induced VCAM-1 expression only. 3) Neutrophil adhesion assay showed a significant 2.42-fold increase in neutrophil attachment to endothelial cells after treatment with SCM as compared to control media. 4) SCM significantly increased transmigration of primary neutrophils in TEM assay. In a separate set of experiments we demonstrated that neutrophils transmigrated towards IL-8 and GRO-α stimuli in a dose-dependent manner. Altogether, these data indicate that VEGF acts as an endothelium activator, whereas IL-8 and GRO-α operate primarily as leukocyte recruiters. Stretch-induced activation of multiple cytokines and chemokines (SCM) resulted in the more prominent endothelium activation and subsequent extravasation of neutrophils.
Conclusion: Overall these results support our hypothesis that mechanical stretch can induce cytokine secretion capable of promoting peripheral leukocyte entry into the myometrium, which in turn, promotes a localized myometrial inflammation and the onset of labour.
Funding: CIHR (MOP-37775)

ABSTRACT #P-C4

Characterization of *In Vitro* P-gp Transport in Human Placental Tissue Culture

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Objective: Acute and chronic infections are common during pregnancy and there is evidence that infection can alter the activity ofdrug transporters, such asP-glycoprotein (P-gp). Specifically, studies have shown that cytokines inhibit P-gp mediated drug efflux activity in liver cells. However, knowledge of the relationship between infection and drug transporter activity and expression in the placenta is limited. The objective of this study wasto characterize P-gp transport in the human placenta using an *in vitro* culture model.The establishment of this model system will provide a means to study transporter function and expression under various treatment conditions, such as infection.

Methods: Term placentae were collected within 30 min of delivery from women with healthy pregnancies at Mount Sinai Hospital. Placental tissue was biopsied (8 mm^3) for measurement of P-gp activity and the remainder tissue was cultured for a 6-day period. Placental tissue explants were cultured at 37 °C (21% O_2, 5% CO_2). Culture medium was collected and replaced every 24h across a 6-day period. Lactate dehydrogenase (LDH) and human chorionic gonadotropin (hCG) released into the culture medium was measured to assess explant viability and syncytiotrophoblast function. P-gp activity was measured as accumulation of 1.5uM digoxin (a P-gp specific substrate; ^3H-digoxin was used as a tracer) at 10, 30, 60, 120 and 180 min. P-gpactivity was measured in fresh tissue on day 0 and after 6 days of culture, to assess whether explants express higher levels of P-gp and activitybefore or after the culture period.

Results: There was an increase in digoxin (P-gp substrate) in fresh placental fragments over time, with a plateau phase reached at 120 min. Preliminary results (n=3) indicate a decreased rate of digoxin accumulation (i.e. increased P-gp activity) after 6 days of culture compared to fresh placental tissue (day 0).

Conclusions: Cultured explants appear to have increased P-gp activity after a 6-day culture period. This *in vitro* placental explant model provides a means to measurechanges in P-gpfunction, owing to the increase of P-gp activity on day 6 of culture. Furthermore, different treatments, such at cytokines to mimic infection, may be used to test their effects on P-gp function and expression. This is important; as changes in P-gpmediated placental drug function may have adverse effects on the developing fetus.

Funded by: Canadian Institutes for Health Research.

ABSTRACT #P-C5

First Trimester Uterine Natural Killer Cells Migrate in Response to Secreted Cytokines in Trophoblast-Conditioned Media

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Objective: Spiral artery remodeling is a crucial step in the early implantation process and plays a significant role in ensuring adequate blood flow to the intervillous space during pregnancy. Using an *in vitro* placental-decidual co-culture model developed in our laboratory which recapitulates the early fetal-maternal interface, our more recent investigations show that this remodeling is mediated by a rapid infiltration and disruption of the vascular wall by decidual immune cells, particularly uterine Natural Killer (uNK) cells and macrophages. Importantly, while uNK infiltration requires the presence of placental tissue, it occurs prior to extravilloustrophoblast (EVT) cell invasion. Therefore, we hypothesise that placentally-secreted factors, rather than direct EVT contact, may recruit the uNK and/or macrophages into the vessel wall.

Methods: Primary EVT were isolated from first trimester placenta (GA = 6-8 weeks) and cultured on Matrigel-coated plates to confluence. HTR-8 cells were grown to confluence in 6-well tissue culture plates. Both cell types were then cultured in serum-free media for 48 hours, after which media was collected and stored at -20°C for subsequent multiplex ELISA assay of chemokine/cytokine secretion by EVT cells and assessment of uNK invasion and migration in response to EVT-conditioned media (EVT-CM). Primary uNK cells were isolated from first trimester decidua (GA = 6-12 weeks) using collagenase enzyme digestion and CD56 magnetic beads to isolate a pure uNK population. Isolated cells were labelled with YoYo nuclear dye and placed in 3µm cell invasion chambers pre-coated with collagen IV. uNK cells were left to migrate for 18 hours, following which migrated cells were collected and total fluorescence was assessed using a multi-well plate fluorometer (488nM).

Results: Multiplex ELISA assay detected numerous cytokines present in trophoblast-conditioned media. Levels of IL-6, IL-8, IL-9, IL-15, IL-17a, Eotaxin, GM-CSF, VEGF, and IP-10 were reproducibly higher in EVT-CM compared to control serum-free media. In preliminary invasion experiments, HTR8-CM stimulateduNK invasion and IL-8 (100ng/ml) stimulated low levels of uNK invasion, while VEGF (50ng/ml) had no effect. Further experiments will assess uNK invasion in response to remaining cytokines detected by multiplex assay in EVT-CM.

Conclusions: Extravilloustrophoblast cells secrete a distinct set of cytokines which successfully induce uNK invasion in early pregnancy. Whether specific EVT-secreted cytokines mediate the uNK invasion process alone or in concert is under further investigation – results will be validated by the addition of neutralizing antibodies to EVT-CM.
Funded by: Physicians' Services Inc. and CIHR (IHD-86232)

ABSTRACT #P-C6

Glucose Sensing in mHypoA-GnRH/GFP Immortalized Hypothalamic Neurons

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Objective: To investigate the direct cellular and molecular effects of glucose levels on the reproductive axis, using a novel non-clonal mHypoA-GnRH/GFP immortalized cell line.

Methods: We have generated an immortalized adult-derived neuronal cell line using primary cultures from transgenic mice expressing green fluorescent protein (GFP). These cell lines consist of the entire populations of Gonadotropin-Releasing Hormone (GnRH) neurons within the hypothalamus. Primary hypothalamic cultures were immortalized using simian virus (SV40) large T antigen and a neomycin resistance gene. Following immortalization, cells were FAC-sorted based on GFP fluorescence with greater than 95% purity. Utilizing one-step RT-PCR we will verify the presence of glucose processing machinery within our model. Quantitative RT-PCR will be used to measure changes in transcription of GnRH mRNA upon glucose stimulation. Western blot analysis will be employed to delineate signaling pathways involved in glucose sensing. Finally, enzyme linked immunoassay studies will be carried out to confirm secretion and we will begin analysis of the transcriptional mechanisms involved in GnRH regulation via transient transfection of the GnRH promoter tagged to a luciferase reporter gene.

Results: We have screened our cells using RT-PCR for the presence of cellular machinery responsible for glucose sensing in other tissues, including glucokinase, hexokinase, GLUTs, and the subunits of ATP-sensitive potassium channels (K-ATP; Sur1, Kir6.2). We have demonstrated that re-challenging GnRH neurons in media containing 5mM glucose following starvation in 0.5 mM glucose causes excitation of these cells and a significant increase in both c-Fos (15, 30, 60 min) and GnRH mRNA (1 hr, 2hr, 4 hr and 8 hr) levels. Furthermore, we have confirmed that the increase in GnRH mRNA levels following glucose re-challenge is metabolism and concentration dependent, via 2-deoxyglucose studies. Western blot analysis indicates that glucose acts through the second messengers AMP-activated protein kinase (AMPK) and acetyl-coenzyme A carboxylase, suggesting an AMPK dependant mechanism.

Conclusions: These studies will provide further insight into how nutrient status may influence neurons involved in reproductive function and will allow delineation of the molecular events involved in this process.

Funded by: BBDC, CIHR, CFI, CRC.

ABSTRACT #P-D1

The Prevalence of Reproductive Tract Infections (RTI) in Adolescents at Presentation to Colposcopy

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Objective: Reproductive tract infections (RTIs) are a major cause of female reproductive morbidity, are frequently asymptomatic, and rates in Canada are rising. Adolescents are at high risk for RTIs and rates of chlamydia (CT) and gonorrhea (GC) are consistently higher in adolescents compared with adults. Studies from the UK and Australia suggest that adolescents show higher prevalence of CT at presentation to colposcopy than adults, but there are no Canadian studies to date. Our primary objective was to determine the incidence of CT and GC at the time of first presentation to colposcopy in adolescents (<=25yo) and adults (>25yo). The secondary objective was to investigate associations between age, demographic and behavioral characterisitics, and incident RTIs.

Methods: We conducted a retrospective study of all new patients who presented to colposcopy at St. Michael's Hospital from January 2011 to 2012. We performed a univariate analysis with a chi squared test to investigate the associations between age, demographic and behavioral characteristics, and incident RTIs. A multivariate analysis is still pending.

Results: Between January 2011 and 2012 368 patients, 267 adults and 101 adolescents, were evaluated with a retrospective analysis. The incidence of CT was 3% in the adolescents and 0.4% in the adults. There were no positive GC swabs in either group. In the univariate analysis, a positive CT result, a previous history of CT, and condom use were all significantly higher in the adolescent group.

Conclusions: Our preliminary data show that the incidence of CT is higher in adolescents who present to colposcopy as compared to their adult counterparts. We thus recommend that routine STI screening be performed in all patients 25 years and under at first presentation to colposcopy.

ABSTRACT #P-D2

Effect Of EMR Implementation on Patient and Staff Satisfaction, and Chart Completeness in a Resource-Limited Ante-Natal Clinic in Kenya

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Objective: Electronic Medical Records (EMR) are thought to improve patient care through a variety of means. However, the study of EMR implementation in resource poor settings has been minimal. We conducted a study comparing patient/staff satisfaction and completeness of patient charts prior to EMR implementation (2009) and one year post EMR implementation (2011) at a busy antenatal clinic in Kenya. The purpose was to determine the effects of EMR on patient care in a resource-limited setting.

Methods: The study consisted of 3 parts: patient satisfaction questionnaire, staff satisfaction questionnaire, and a retrospective chart review. For patient surveys, 124 (2009) and 150 (2011) patients were interviewed during their clinic visit. Questions related to the complete time for their visit, their understanding of information presented, and overall satisfaction. For the chart review, charts of 250 patients were examined for completeness of key indicators used in antenatal care. Staff in the antenatal unit was also surveyed for overall satisfaction.

Results: The results showed that the self-reported time it took for women to complete their visits was very significantly reduced ($p = 0.000$) after implementation of EMR. The documentation of administered tetanus toxoid, HIV testing STI testing was significantly increased with EMR and positive trends were also seen in documentation of malaria prophylaxis.

Conclusions: Although greater sample numbers would help show more significant trends, this pilot study was able to demonstrate a positive impact of EMR on antenatal patient care in a resource limited setting. We demonstrated that EMR can be a valuable investment in resource-limiting settings.

Funding: Dr. Elva May Rowe Fund International Health Undergraduate Summer Research Scholarship, Medical Alumni Association for the University of Toronto, and the Comprehensive Research Experience for Medical Students (CREMS) Program.

ABSTRACT #P-D3

Maternal Experiences with Breastfeeding: A Comparison Between Women Who Are Exclusively Breastfeeding and Those Who Are Formula-Feeding at Six Weeks

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Objectives: The objective of this study was to examine barriers to breastfeeding in women exclusively breastfeeding compared to those who are complementary breastfeeding or exclusively formula-feeding at six-weeks postpartum.
Methods: All consecutive patients attending a six-week postpartum obstetrical clinic at St. Michael's Hospital were eligible. A survey was administered to assess demographic, pregnancy, breastfeeding and social support information. Consent was implied upon completion of the survey. Subjects were asked to rate their experience with 25 statements associated with lactational, psychosocial, nutritional, lifestyle, medical, milk-pumping and self-weaning barriers to breastfeeding on a 4-point Likert-type scale measuring agreement. Categorical variables were stratified into exclusively breastfeeding and formula-feeding groups and described using frequencies and percentages. Associations between categorical data were evaluated using a chi square test with a significance value of $P \leq 0.05$. Associations between current infant feeding practices and experience of barriers to breastfeeding were reported using odds ratios with 95% confidence intervals and analysis of maximum likelihood estimates where $P \leq 0.05$.
Results: Of 165 completed surveys (79%), 147 patients were evaluable and 18 not evaluable because of missing information. Of the evaluable patients, 55.8% were exclusively breastfeeding, 37.4% were complementary breastfeeding, and 7.4% were exclusively formula-feeding at six-weeks postpartum. Of those exclusively breastfeeding, most planned to continue for at least 7 months (66.2%). Most of the women who were formula-feeding started within the first 2 weeks postpartum (75.4%), with a majority clustered to within the first week. The patient population at St. Michael's Hospital is diverse, with 63% of our study population reporting a non-Caucasian ethnicity. This is an important consideration, as women born outside of Canada were more likely to formula-feed ($P<0.001$). Most women were married or in a common-law relationship (87.9%), and had at least some post-secondary education (82.5%). Women who underwent Caesarean deliveries or had infants who were born prematurely were more likely to formula-feed ($P=0.019$ and 0.043 respectively). There was no significant difference between exclusively breastfeeding and formula-feeding groups in their experience with most (18/25) of the barriers. Women who were formula-feeding cited insufficient milk production (odds ratio (95% C.I.): 31.08 (10.87-88.87)), trouble with milk flow (4.61 (2.00-10.59)), infant trouble with latch/suck (3.08 (1.97-6.34)), infant lack of satisfaction with breast milk (89.16 (19.83-400.92)), infant self-weaning (7.50 (1.58-35.62)), and maternal and health professional concerns regarding infant weight gain (6.88 (2.40-19.74) and 5.47 (1.70-17.60), respectively) significantly more than women who were exclusively breastfeeding.
Conclusions: It is recommended that breastfeeding interventions focus on counseling of lactational and nutritional issues for mothers during their postpartum hospitalization and shortly after their discharge to help provide the educational information and technical skills women need to overcome barriers to breastfeeding in the early months.

ABSTRACT #P-D4

A Survey of Postgraduate Training in Indigenous Women's Health in Obstetrics and Gynaecology

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Objectives: In 2005, the Royal College of Physicians and Surgeons Canada made improving the health of Canada's indigenous peoples a strategic priority. It mandated the introduction of indigenous health education into the postgraduate curriculum. Residents in Obstetrics and Gynaecology routinely care for aboriginal patients and therefore would benefit from formal teaching in: First Nations, Inuit, and Métis culture and history; the determinants of health among Canada's indigenous peoples; cultural safety training; and accessing resources available to this population. The purpose of this study is to assess the background knowledge of Obstetrics and Gynaecology residents across the country in indigenous women's health with respect to this specialty. Concurrently we aim to assess the resources and programming in place in Obstetrics and Gynaecology departments across the country at an administrative level by surveying program directors.

Methods: A 20-question multiple choice survey for residents was developed to assess baseline knowledge in aboriginal women's health in Obstetrics and Gynaecology in four key areas: general knowledge regarding Canada's indigenous peoples; the impact of the Residential School system; clinical experience in aboriginal women's health; and a self-assessment of competency in aboriginal women's health. A second multiple choice survey for program directors was developed to assess the curriculum content and the resources available to support this curriculum. Surveys were distributed to 495 residents and 19 program directors in accredited Obstetrics and Gynaecology programs at Canadian universities. The data was analyzed using an SPSS database.

Results: Very few residents had previous training in aboriginal women's health (<5%). General knowledge about Canada's aboriginal peoples was low with only 39% of residents knowing how many groups were recognized as aboriginal. Similarly residents had limited knowledge of the residential school system and its impact. Residents encountered aboriginal patients primarily in Obstetrics (>70%) and were aware of health issues that disproportionately affect aboriginal women in Canada (>90%) including antenatal care, STIs, sexual abuse, and cervical cancer. The majority of program directors do not have a formal curriculum for residents and they do have the resources available to support such a program.

Conclusions: A well-supported national curriculum in indigenous women's health needs to be a priority in post-graduate training programs in Obstetrics and Gynaecology.

ABSTRACT #P-D5

Canadian Women's Attitudes toward Noninvasive Prenatal Testing of Fetal DNA in Maternal Plasma

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Objective: Fetal DNA that is found in the maternal plasma has been proposed as a means for noninvasive prenatal screening and testing of fetal chromosomal and genetic abnormalities. Our study aims to determine the views, perceptions and attitudes of Canadian women to this new screening modality.

Methods: A specifically designed questionnaire was administered in the first half of pregnancy to women attending the outpatient antenatal clinic at a tertiary urban hospital. Demographic and socio-economic information was collected. Views and attitudes to current and new prenatal screening modalities were assessed using a five-point Likert scale. McNamer's test was used to compare individual responses regarding the two screening modalities and Cochran-Mantel-Haenszel analysis was used for univariate analysis of associations between categorical variables.

Results: 129 women enrolled in this study. Mean maternal age was 31.65 (+/- 4.84) and mean gestational age was 11.65 (+/-3.07). A majority of women were Canadian born, primiparous and Caucasian (63.6%, 55.8% and 53.55%). 45% of respondents had received prenatal counseling prior to the study. 88% of women state that they would perform prenatal screening via fetal DNA in the maternal plasma if available. When compared to conventional screening more women think that screening with fetal DNA in maternal plasma could be used in a negative way to select for desired traits (39.7% Vs. 27.6% P=0.02). On univariate analysis country of birth, ethnicity and age were associated with increased fear of misuse of this type of screening (P<0.05).

Conclusions: The use of fetal DNA in the maternal plasma is widely accepted in our Canadian population as a future method of non-invasive prenatal screening, despite recognition of certain ethical concerns. A significant concern was the potential use of prenatal screening information for eugenic selection. This information can be used when implementing new genetic screening programs.

ABSTRACT # P-D6

Assessment of Global Methylation of Human Sperm

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Objective: To determine the baseline state of global methylation of normal human sperm for comparison in future studies where pathological conditions.

Methods: The extraction of genomic sperm DNA methodology was optimized to overcome the highly condensed state of human sperm DNA. LUMA analysis was performed on 9 independent samples (n=2). LUMA is an assay that estimates genome-wide CCGG methylation at the internal CG using genomic DNA. Genomic DNA is cut using isoschizomers HpaII (methylation sensitive) and MspI (methylation insensitive), followed by sequencing by synthesis of the sticky ends. An amount of light is emitted for every C or G that is incorporated. By comparing the amount of light emitted using the HpaII vs. MspI restriction enzymes, one can estimate the global levels of methylation. There are limitations to this assay since it is biased towards areas that are CG-rich. There are also assumptions in the activity of the enzymes used, for example, HpaII is a better cutter where there are multiple recognition sites close together. Additionally, neither MspI nor HpaII will cut if the exterior C is methylated. We then used another methodology based on LINE-1 elements that estimates global CG methylation by assaying repetitive and presumably parasitic DNA. This assay uses bisulfite converted DNA and PCR amplifies a target sequence on the L1 retrotransposon. The L1 element is estimated to populate ~20% of the human genome.

Results: The LINE-1 and LUMA global methylation findings were comparable. The LUMA assay indicated that 'normal' human sperm exhibits an average global methylation of approximately 55% and the LINE-1 methylation analysis revealed an average global methylation of approximately 60%.

Conclusions: Previous work in human and animal models has indicated that global sperm methylation, specifically hypomethylation, may be a predictor of pregnancy outcome. Modern approaches to epigenetics may allow for this to become a clinical diagnostic test target in predicting infertility. In order to make any advances in this area a complete understanding of the general methylation status of human sperm DNA is requisite. Therefore, we determined the baseline "normal" methylation level of sperm. Interestingly, this level was lower than other cell types of the early embryo, as well as cultured human umbilical vein endothelial and aortic vascular smooth muscle cells. Future, studies will involve identifying human conditions that affect the degree of methylation in human sperm.

ABSTRACT #P-E1

Evaluation of Sperm Aneuploidy in Patients with Severe Oligozoospermia

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Objective: Sperm aneuploidy has been suggested as an indicator of spermatogenesis. Male infertility is associated with higher rates of sperm aneuploidy compared to men with proven fertility. Degree of aneuploidy in spermatozoa utilized for ICSI has been reported to contribute to chromosomal abnormalities in embryos. The purpose of this study was to evaluate sperm aneuploidy rates in patients with severe oligozoospermia undergoing ART treatment.

Methods: Following Institutional Research Ethics Board approval, 20 patients were recruited to the study. Following ICSI procedure, remaining aliquots of semen samples were assessed for chromosomes 18, X, Y aneuploidy by multicolor Fluorescence in-Situ Hybridization (FISH). Spermatozoa were decondensed with 0.5M NaOH and counterstained with DAPI. Statistical evaluation was performed with SPSS 19.0 software and results expressed as mean ± SD.

Results: Embryo transfer occurred in 19 cases (no fertilization in one case) with a pregnancy rate of 58% per transfer. Pregnancies were correlated to female partner's age and sperm aneuploidy (P <0.05). The rates of sperm aneuploidy were significantly lower in patents whose spouses became pregnant, when compared to patients with unsuccessful ICSI treatment; aneuploidy for chromosome 18 was 0.43% ± 0.29 vs. 0.75% ± 0.29, P <0.03; sex chromosomes 1.01% ± 0.43 vs. 3.1% ± 2.5, P <0.01; total aneuploidy for the three analyzed chromosomes 1.89% ± 0.80 vs. 4.58% ± 3.4, P <0.02. Most aneuploidies were disomies.

Conclusion: We observed higher levels of sperm aneuploidy in patients with severe oligozoospermia compared to individuals with normal semen parameters. Patient who did not achieve pregnancies after ICSI had two and a half fold increases in the level of sperm aneuploidy compared to pregnant ones. Only female age and sperm aneuploidy levels were predictive factors for pregnancy outcome in our group of patients (P <0.05). Our data supports the importance of sperm aneuploidy evaluation in patients with severe sperm abnormalities prior to ICSI treatment.

ABSTRACT #P-E2

Correlation of Telomere Length and DNA Damage in Human Spermatozoa

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Objective: Telomeres are repeating sequences of non-coding TTAGGG that cap the terminal regions of each chromosome, protecting DNA from degradation, recombination and fusion. Telomeres also participate in the organization of sperm nuclear architecture, which is necessary for normal fertilization and zygote development. Telomere length is established early in spermatogenesis and 5-10 kb longer in spermatozoa than somatic cells. Paternal heritability of telomere length is greater than maternal heritability, and long telomeres in spermatozoa are hypothesized to contribute to the maintenance of critical telomere length in the offspring which is necessary to support subsequent cellular divisions in early blastocyst development. Critically short telomeres have been shown to induce DNA damage and errors in cellular replication in various somatic cells. The purpose of this study is to evaluate the connection between telomere length and DNA damage in spermatozoa, and its possible relationship with male-factor infertility.

Methods: Telomere length assessment will be performed on two sets of spermatozoa: neat ejaculate processed by differential lysis to remove somatic cells, and highly motile spermatozoa separated via gradient wash centrifugation. Both types of samples will be subjected to telomere length assessment using terminal restriction fragment (TRF) analysis and single telomere analysis (STELA) at the XpYp chromosome to determine the overall distribution of telomere length and identify critically short telomeres within each semen sample. In addition, telomere length will be compared with data obtained via standard semen analysis and flow-cytometry based DNA Fragmentation Index (DFI) for DNA damage.

Results: This is a work-in-progress. At the time of submission, individual semen samples were divided and prepared using gradient wash centrifugation or the differential lysis procedure, DNA was then extracted and subjected to telomere length assessment to ensure that each separation technique yielded different populations of spermatozoa. Telomere assessment was also performed on fresh and frozen semen samples to assess telomere damage as a result of freezing, verifying whether or not frozen samples could be used in the study. Correlation between telomere length, parameters of standard semen analysis and DFI will be established.

Conclusions: If the results of this study reveal a correlation between telomere length, DNA damage, and sperm quality, the presence of critically shortened telomeres may help explain how sperm DNA damage arises, thus causing male-factor infertility. Shortened telomeres may have a negative effect on the establishment of critical telomere length in offspring, therefore limiting the subsequent cellular divisions intrinsic to early blastocyst development. The results of this study will contribute to our knowledge of male-factor infertility and the paternal contribution of embryo development.

ABSTRACT #P-E3

Neural Potential of First Trimester Human Umbilical Cord Perivascular Stem Cells

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Objective: To investigate the neuropotentiality of first trimester human umbilical cord perivascular stem cells (ftHUCPVCs) *in vitro*, with the ultimate goal of developing cell therapies targeting pathological states of the nervous system**.**
Methods: Using a modified human neurosphere protocol, spheres were derived from ftHUCPVCs and term derived human umbilical cord perivascular stem cells (tHUCPVCs) with either a ROC- or LIF-based media. Both, methods included FGF, B27 and heparin, and the LIF approach also included EGF. Spheres that formed after 5 days and were 50 μm or greater in diameter were counted. Spheres were then individually passaged and allowed to differentiate on Matrigel® for 7 days, prior to fixation and immunocytochemistry, or RNA extraction for quantitative PCR (qPCR) analysis.
Results: Ten ftHUCPVCs lines and four tHUCPVCs term lines were subjected to the modified human neurosphere protocol. No differences in sphere formation frequency were observed with the two methodologies, although variance between individual lines was apparent. Approximately 1.2% of ftHUC-PVC and 0.04% of tHUC-PVC cells were able to generate spheres after 5 days, representing a thirty-fold increase ($P<0.0001$). Spheres were then isolated and allowed to differentiate on Matrigel substrate. After 7 days, differentiated cultures were stained by immunocytochemistry for neural markers. All ftHUCPVCs-derived spheres exhibited extremely high expression of β3 tubulin, nestin, high expression neurofilament low expression of vimentin, and no positivity was seen for the glial marker GFAP. The differentiated ftHUCPVCs (from spheres) cultured under these conditions did not achieve the neuronal morphological criteria (i.e. processes > 3 lengths of the cell body). tHUCPVCs seldom formed spheres, but when one was evident and was differentiated it seldom expressed β3 tubulin. Interestingly, when undifferentitated cells were examined, vimentin or β3 tubulin expression was not observed, although expression of the glial markers GFAP and O4 were strong. Nestin and neurofilament were present in undifferentiated cells, spheres, and differentiated spheres. Spheres derived from primary tissue also strongly expressed nestin protein. qPCR (array and Taqman based) validated expression of nestin transcript in both undifferentiated cells and in spheres of ftHUCPVCs. As little to no spheres formed with tHUCPVCs, it was not possible to analyze these using qPCR.

Conclusions: These *in vitro* studies suggest that undifferentiated ftHUCPVCs have more therapeutic potential for neural pathologies where glial cells are needed, such as spinal cord injury. For neurodegenerative disease conditions, which require neurons, predifferentiation of ftHUCPVCs may be preferable, rather than employing tHUCPVCs. As a result of these findings, our ongoing studies are examining undifferentiated ftHUCPVCs in a rat model of spinal cord injury.

ABSTRACT #P-E4

The Impact of Vitamin D Status on Implantation and Clinical Pregnancy Rates Following *In Vitro* Fertilization

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Objective: The overall goal of the study is to investigate whether vitamin D (serum 25-OHD) levels, in infertile women are predictive of in vitro fertilization (IVF) outcomes. Specifically, to determine if vitamin D status impacts IVF cycle parameters and/or implantation and clinical pregnancy rates following IVF. The prevalence of vitamin D insufficiency in our population of infertile women will also be compared to previously published Canadian prevalence data.

Methods: Vitamin D status, as determined by serum 25OH-D levels, was prospectively evaluated in a cohort of undergoing IVF. 173 patients were recruited at the Centre for Fertility and Reproductive Health (CFRH) at Mount Sinai Hospital between April 2011 and November 2011. REB approval was obtained. Recruited patients underwent IVF cycles per standard clinical care. Serum 25OH-D samples were collected within one week of oocyte retrieval during an IVF cycle. Patients were divided into 3 groups based on serum 25-OHD levels: sufficient >75 nmol/L, insufficient 25-75 nmol/L and deficient <25 nmol/L. Groups were compared for the main outcome measures: IVF cycle parameters, endometrial quality, pregnancy rate and implantation rate.

Results (In progress): Study recruitment is completed and data analysis is in progress. Results and analysis will be presented at Research Day.

Conclusions: The goal of the study was to determine whether serum 25OH-D levels in infertile women are predictive of IVF outcomes and thereby provide insight into the mechanism of uterine receptively and embryo implantation. If vitamin D insufficiency can be shown to impair implantation in an infertile population, vitamin D supplementation could provide an easy and cost effective means of improving pregnancy rates. This would be very advantageous to couple suffering from infertility, as the inability to have a baby can be very psychologically stressful and very expensive to overcome.

Funded by: Reproductive Endocrinology and Infertility Division, Department of Obstetrics & Gynaecology, Mount Sinai Hospital

ABSTRACT #P-E5

Improved Survival of Umbilical Cord Derived Donor Cells in Bone Marrow Transplantation due to Trogocytosis

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Objective: Bone marrow transplantation (BMT) is a common procedure used to treat hematological disorders, such as leukemia and anemia. The hematopoietic stem cells (HSC) used for transplantation can be derived from umbilical cord blood, bone marrow or peripheral blood. With its ease of collection, high proliferative properties, and decreased risk of graft-versus-host disease and transmissible viral infections, umbilical cord blood is the preferred source of HSC for many patients. Like any source of HSC, graft survival and engraftment is always higher if HSC is donated from a related donor than an unrelated donor. Graft rejection is primarily due to major histocompatibility complex (MHC)-mismatch between the donor and recipient. Moreover, acute rejection of grafts is thought to be mediated by natural killer (NK) cells.

In our previous report, we transplanted human umbilical cord blood into NOD/SCID mice and observed that all surviving donor cells had acquired host MHC class I proteins. We speculate that these acquired proteins protect the donor cells from host's NK cell attack. In this study, we will expand on our previous study and further investigate the role of trogocytosis in the transplantation setting, and how donor cell survival is affected by the acquired MHC class I proteins. Ultimately, we hope to design a reduced intensity conditioning regimes that favours trogocytosis and improves graft survival and engraftment.

Methods: Human umbilical cord blood cells and mouse bone marrow cells were injected intravenously into sublethally irradiated NOD/SCID and NOD/SCID/gamma (NSG) mice. Bone marrow cells (BMCs) were retrieved from femurs at various time points, stained for recipient and donor MHC class I proteins, and analyzed using flow cytometry.

Results: Different patterns of transfer of surface proteins (trogocytosis) were observed when different immune-compromised mouse strains and donor cell sources were used. For instance, when umbilical cord blood cells or allogeneic mouse bone marrow cells were transplanted into NOD/SCID mice, we observed that all of the surviving donor cells had acquired host MHC class I protein. On the other hand, when donor cells were transplanted into NSG mice, not all donor cells were positive for host MHC class I protein.

Conclusions: In the T and B cell-deficient NOD/SCID mice, the involvement of all surviving donor cells in trogocytosis suggests that the transferred recipient MHC class I proteins confer protection from host's NK cells. In other words, the presence of NK cells in NOD/SCID mice generates a selective pressure for cells with host MHC class I proteins. The T, B and NK cell-deficient NSG mice lack this selective pressure and hence, survival of donor cells is not dependent on acquisition of host MHC class I proteins. A better understanding of trogocytosis in the bone marrow transplantation setting, and how host NK cells can influence cell survival can help us design pre-transplantation conditioning regimens that can improve graft survival while reducing conditioning-associated toxicity.

ABSTRACT #P-E6

3D Image Analysis of Chromatin Structure of Motile and Immotile Sperm Populations

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Objective: Human spermatozoa contribute a haploid set of DNA to the egg for embryo development. Sperm is known to have a well−organized chromatin structure that is highly compacted, keeping nuclear chromatin more stable. Improper organization and packaging could disrupt the structured sequence of fertilization. The purpose of our study was to evaluate structural differences in a randomly chosen chromosome (chromosome 17) between motile and immotile mature human spermatozoa using 3−D digital image morphometric and image analysis.

Methods: Fresh semen samples were centrifuged using a 90% density gradient medium to separate the motile and immotile populations. Cells were fixed using Carnoy's solution. Fluorescent in−situ hybridization (FISH) was used in combination with a NaOH decondensation technique, to label chromosome 17's centromere and chromocenter. The volume of sperm nucleus, centromere of chromosome 17 and total chromocenter were calculated along with the intra−nuclear position of chromosome 17's centromere.

Results: The table 1 shows the results comparing motile and immotile group.

	Motile	Immotile
Total number of cells	333	334
Volume of sperm head	70.715 ± 26.253	71.635 ± 18.106
Volume of chromosome 17 centromere	0.242 ± 0.167*	0.294 ± 0.231
Volume of chromocenter	1.539 ± 0.961*	2.021 ± 1.205
Distance between chromosome 17 and tail	2.966 ± 0.769	2.877 ± 0.877

*$P<0.05$ immotile population has significantly higher chromosome 17 centromere volume and chromocenter volume.
Observational data was collected to show that more than 85% of the time, the centromere of chromosome 17 was found in the medial region of the sperm head, in both motile and immotile sperm.

Conclusion: Our data indicates that using 3−D image analysis allows us to better understand the localization of chromosomes. It can be concluded that motile and immotile sperm show a significant difference in the compactness of the chromatin structure. Previously, it was known that the gradient wash separates motile and immotile cells. This study shows that the gradient wash may be separating cells based on the compactness of the chromatin structure. Immotile sperm appear to be prone to higher decondensation and disruption of the chromatin compactness.

ABSTRACT #P-F1

Outcome of Laparoscopic Two-Team Sling, Tension Free Transvaginal Tape (TVT) and Transobturator Tape (TOT) for Women with Recurrent Stress Urinary Incontinence: A Retrospective Cohort Study.

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Objective: The aim of this study is to review the success rate of laparoscopic two-team sling procedures in women with recurrent stress urinary incontinence versus Transobturator Tape (TOT) or Tension Free Transvaginal Tape (TVT) and to look at the immediate and the long-term complications associated with these procedures.

Methods: This is a retrospective cohort study with institutional ethics approval. Health records of patients who underwent laparoscopic two-team sling procedure,TVT or TOT for recurrent SUI in the Urogynaecology Unit at Mount Sinai hospital will be reviewed from Jan 2006 up to September 2010. Data to be collected will include results of urodynamic testing (stress urinary incontinence, bladder capacity, maximal urethral pressure and post void residual), degree of prolapse, age, parity, menopausal status, smoking, BMI, previous continent surgery, post-operative subjective cure (patient reports no leaking) and objective cure (negative cough stress test), intra- and postoperative complications. Patients managed by laparoscopic two-team sling procedure, TVT or TOT for primary SUI are excluded.

Results: Data collection is in progress. An updated abstract with results will be provided prior to presentation.

Conclusions: Pending.

Funded by: N/A

ABSTRACT #P-F2

Same-Day Discharge versus Overnight Stay after Laparoscopic Hysterectomy: A Prospective Assessment of Patient Safety and Patient Satisfaction [Work-in-Progress]

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ABSTRACT AVAILABLE IN HARDCOPY VERSION ONLY

ABSTRACT #P-F3

Maternal and Fetal Outcomes in Canadian Women after Bariatric Surgery (Work-in-Progress)

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Objective: This study is designed to compare perinatal outcomes in obese women who have undergone bariatric surgery with obese women who have not undergone surgery.

Methods: This will be a retrospective cohort study of all women who became pregnant after undergoing bariatric surgery and their newborns. These women will be matched by pregnancy BMI, age and parity to a control group. Maternal and neonatal hospital charts will be reviewed. Data collected will include maternal demographics (maternal age, prepregnancy weight and BMI, gravida, parity, years from surgery to conception, essential hypertension, type 2 diabetes mellitus, heart disease), pregnancy outcomes (pregnancy weight gain, delivery BMI, gestational diabetes, preterm rupture of membranes, pregnancy-induced hypertension, labour induction, mode of delivery, postpartum hemorrhage, postpartum infection) and fetal outcomes (gestational age, birth weight, apgars, congenital anomalies, intrauterine demise, NICU admission). Bariatric surgery complications will be assessed including nutritional deficits and supplementation, hyperemesis gravidarum, banding adjustments, maternal intestinal obstruction, and gestational hemorrhage. All data will be transferred into a computerized database. Data will be compared using Fisher exact test, independent Student's t test, and Mann-Whitney U test statistics, with $p < 0.05$ considered significant.

Results: As this is a work-in-progress, results are not yet available.

Conclusion: Not yet available.

ABSTRACT #P-F4

Female Genital Tract Graft-vs-Host Disease: A Current Retrospective Patient Review.

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Objective: Graft-vs-host disease (GVHD) is a complex, T-cell-mediated complication following hematopoietic stem cell transplantation. The aim of this study is to provide an up-to-date review of the literature regarding female genital tract GVHD and to describe our experience in a tertiary healthcare centre.
Methods: A current literature review and retrospective hospital chart analysis of patients referred to a specialized Menopause clinic in a tertiary healthcare centre were performed.
Results: A total of twenty-six articles was identified, comprised of four reviews, two observational studies, two retrospective studies, four case series, eleven case reports, and three poster sessions. The incidence of female genital tract GVHD ranged from 25% to 49%, with the majority of women developing this complication more than 100 days after transplantation. Risk factors for female genital tract GVHD were stem cells from peripheral blood progenitor cells, unrelated or HLA mismatched donor, older age of recipient, and positive CMV donor. Common symptoms reported were vulvar pain, vulvar pruritis, and dyspareunia. Examination findings were similar to lichen planus, such as vulvar erythema, vulvar erosions, vulvar scarring, narrowed introitus, labial fusion, vaginitis, vaginal scarring, vaginal adhesions, vaginal strictures, and/or vaginal stenosis. Medical treatment options were topical and/or systemic immunosuppressants and estrogen, topical superpotent corticosteroids, vaginal dilators, and regular intercourse. Surgery was reserved for the most severe cases.

In a specialized Menopause clinic in our tertiary healthcare centre, a preliminary retrospective hospital chart review shows that four patients have been followed for female genital tract GVHD. All presented with dyspareunia and two had GVHD affecting other organs. Other complaints included vaginal pruritis (n=2) and vaginal dryness (n=1). Examination revealed vulvar erythema (n=1), vaginal erythema (n=1), vaginal adhesions (n=1), and vaginal stenosis (n=2). To date, one patient has been treated successfully with dilators and topical estrogen, and now has regular intercourse.
Conclusions:

- Female genital tract GVHD remains under-recognized and poorly understood.
- Education of patients and clinicians and early, regular gynaecologic examinations are crucial to the identification, treatment, and prevention of progression of female genital tract GVHD.
- All patients should be followed in a dedicated centre to improve the quality of care.

Key References:

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ABSTRACT #P-F5

Identification of Factors that Influence Full Disclosure during a Gynaecology Appointment

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Objective: We sought to examine whether characteristics of the Gynaecologist (age, gender, level of education, ethnicity, type of health care worker, sexual orientation, marital status, and physical attractiveness), as well as the reason for appointment, are perceived barriers to honest patient communication.

Methods: A paper-based questionnaire was distributed to patients attending a Gynaecology or colposcopy appointment at St. Michael's Hospital, Toronto, Canada, between January 2011 and January 2012.

Results: Responses for 286 completed questionnaires were analyzed. The most common barriers included having a male physician (40.9%) and having medical history reviewed by a medical student (24.6%). Women under the age of 30 specifically identified male gender as a barrier, whereas older women did not ($P<0.05$). Open-ended responses revealed common themes to ameliorate communication, namely a professional and non-judgemental physician.

Conclusions: Physician gender and education level may be barriers to full disclosure from patients. Awareness of these factors is crucial to encourage complete communication and promote patient-centered care.

ABSTRACT #P-G1

Vitrification of Human Spermatozoa without Permeable Cryoprotectants

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Objective: The slow vapor method of cryopreservation is widely employed for human spermatozoa. The use of vitrification for preserving human spermatozoa is an attractive alternative. The objective of our study was to compare sperm motility, kinetics and DNA damage between semen samples cryopreserved by standard vapor freezing vs. vitrification protocols.

Methods: Semen samples from 11 patients presenting for infertility evaluations were washed by density gradient centrifugation and evaluated by CASA and the TdT-mediated dUTP nick end labeling (TUNEL) assay. Two freezing protocols were compared for each sample. Samples for slow vapor freezing were diluted 3:1 with commercial cryoprotectant medium and frozen by standard protocol (300 µl per CBS straw). Aliquots of samples for vitrification were diluted with a proprietary mixture developed in our laboratory for sperm vitrification, loaded into straws (10 µl, close system) and immediately plunged into liquid nitrogen. Following thawing at 37ºC, samples were re-evaluated by CASA and TUNEL.

Results: Mean sperm concentration of fresh samples was 89 x 106/mL ± 45 and motility of 61.8% ± 20. Mean motility of vitrified samples was 25.4% ± 13.6, which was almost two fold higher compared to motility of samples frozen by slow vapor protocol (14.6% ± 10.2), ($P < 0.05$). No significant differences were observed in sperm DNA damage (9.6 ± 4.4 vs. 9.5 ± 5.1, NS) or sperm kinetic characteristics such as average path velocity, straightness, amplitude of lateral head displacement and curvilinear velocity between two types of cryopreservation protocols. Seven oocytes were microinjected with the spermatozoa from one patient with severe oligozoospermia (5-12 spermatozoa in the sample): 5 oocytes with fresh motile spermatozoa (4/5 fertilized, four 6-8 cells embryos on Day 3), 2 oocytes with vitrified-thawed motile sperm (2/2 fertilized, two embryos on Day 3 at 5 cells and 8 cells stages); all cleavage embryos had Grade 2.

Conclusion: Our results demonstrate that human spermatozoa can be successfully vitrified in a small (10 µl) and in large (200 µl) sample volumes without the use of potentially toxic permeable cryoprotectants. The vitrification protocol showed significantly better results in preserving motility rates of spermatozoa when compared to slow vapor freezing. No significant differences were observed in post thaw sperm kinetic characteristics or on DNA damage in comparison to the standard slow freezing method.

ABSTRACT #P-G2

WITHDRAWN

ABSTRACT #P-G3

Can fewer eggs make more babies? Conversion of high-response gonadotropin intrauterine insemination cycles as a model for mild stimulation in vitro fertilization.

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Objective: Traditional in vitro fertilization (IVF) is a well-established treatment for infertility that involves ovarian stimulation aimed at producing at least ten mature follicles. Controlled ovarian hyperstimulation (COH) in combination with intrauterine insemination (IUI) has also been established as an effective treatment for infertility, but with a goal to produce four or fewer follicles. IUI cycles in which greater than four follicles are produced may be converted to IVF, in order to reduce the likelihood of multiple gestation and cycle cancellation. This represents a scenario in which response is less than anticipated for traditional IVF but IVF is performed regardless. Converting high response COH-IUI cycles to IVF cycles may offer us a novel model for IVF, which provides more gentle stimulation and comparable outcomes.

Methods: This retrospective case-control study evaluated 20 cases converted from COH-IUI cycles to IVF cycles. Those cases in which 4 to 10 eggs were produced were compared to IVF controls, matched for age and ovarian reserve. The study took place between January 2009 and December 2010 at a hospital-based fertility centre. The primary outcome measured was pregnancy rate per fresh embryo transfer. Other variables compared included average starting dose of gonadotropins, total dose of gonadotropins, number of mature follicles on day of hCG, estradiol level on day of hCG, number of oocytes retrieved, fertilization rate, number of transferable embryos, and the rate of multiple pregnancy and ovarian hyperstimulation syndrome.

Results: The average starting dose of gonadotropins and total gonadotropin dose was significantly lower for the cases than for the controls (84.4 $\pm$ 26.5 vs. 168.4 $\pm$ 45.1, $P<0.0001$, and 1120.8 $\pm$ 438.7 vs. 1502.9 $\pm$ 398.0, $P=0.04$). There were significantly fewer oocytes retrieved from the cases compared to the controls (6.6 $\pm$ 2.2 vs. 16.1 $\pm$ 7.1, $P<0.0001$), as well as significantly fewer transferable embryos (3.2 $\pm$ 1.9 vs. 8.2 $\pm$ 5.1; $P=0.0012$). Although the pregnancy rate showed a trend of being slightly lower for the cases than for the controls (44.4% vs. 61.1%), the clinical pregnancy rate showed a trend in the opposite direction, with the cases having a slightly higher ongoing pregnancy rate (33.3% vs. 27.8%).

Conclusions: This study demonstrates that, with proper selection of patients, mild ovarian stimulation in IVF produces comparable pregnancy rates to more aggressive treatment. This in turn will decrease the side effects and complications associated with higher dosing, with no compromise on outcome. The finding of a larger loss rate with aggressive stimulation may be explained by the recruitment of poorer quality eggs.

ABSTRACT #P-G4

First-Trimester Human Umbilical Cord Perivascular Cells (Fthuc-Pvcs) Can Differentiate towards the Hepatic Lineage using a Two-Step Induction and Maturation Approach

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Objective: Liver degeneration and disease is a leading cause of mortality in all geographic populations. Umbilical cord-derived stem cells have garnered interest as a cellular therapeutic in the context of regenerative medicine, and in particular for the treatment of liver disease. Here, we investigate the hepatic differentiation potential of first trimester human umbilical cord-derived perivascular cells (ftHUC-PVCs).

Methods: Three independent lines of ftHUC-PVCs at passage 3 were cultured to confluency in maintenance media including 10% FBS, bFGF (10 ng/mL) and EGF (10 ng/mL). A two-step protocol including an induction treatment (HGF (50 ng/mL) and bFGF (10 ng/mL) and a maturation treatment (OSM, 20 ng/mL) was adapted for this assay. To assess differentiation towards the hepatic lineage, we analyzed the morphological changes as well as the hepatic phenotype of the differentiated cells at day 8, 15, 22 and 32 using flow cytometric analysis of the hepatic marker alpha-fetal protein (AFP) and albumin. Immunocytochemistry was also performed for AFP. HUVECs and HEPG2 cells were used as negative and positive controls respectively for the hepatic markers. Functional assessment was done by performing an LDL-uptake assay at 4 weeks.

Results: In the initiation step, the cell size of ftHUC-PVCs increased noticeably, and cells started to lose the typical fibroblast-like bipolar morphologies observed in control undifferentiated cells. Round-shaped cells with a polygonal structure were gradually observed in the maturation phase. Flow cytometric analysis revealed that levels of AFP and albumin increased and was higher in induced ftHUC-PVCs when compared to undifferentiated ftHUC-PVCs throughout the induction and maturation phase time points analyzed. Importantly, 4 weeks following this induction, the majority of induced ftHUC-PVCs were positive for Dil-ac-LDL uptake, whereas undifferentiated cells were not.

Conclusions: ftHUC-PVCs have the potential to generate hepatocyte-like cells *in vitro* and may therefore be a good source of stem cells for liver regenerative therapy. We are planning *in vivo* studies in an immunocompromised mouse model to further examine this potential.

ABSTRACT #P-G5

Pilot Study: A Comparison of Ovarian Reserve in BRCA Positive Women Versus Age-Matched BRCA Negative Controls

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Objective: In the general population, the prevalence of BRCA1/2 mutations is estimated to be 1/400 to 1/800. BRCA gene mutations, whether breast or ovarian cancer has developed or not, has implications for women's medical, psychosocial and reproductive futures. It has been shown that mutations in the BRCA gene may be associated with lower than expected egg production in BRCA1 mutation positive women undergoing fertility treatments. Epidemiologic studies have begun to explore the extent to which BRCA mutations affect fertility and age of menopause of BRCA-positive women; however, objective markers of ovarian reserve have never been measured. The overall goal of this study is to determine if BRCA-positive women have a decreased ovarian reserve compared to women who are BRCA-negative or BRCA 1/2 negative but determined to be high risk by family history. Based on the known deleterious effect of the BRCA mutation on gametogenesis, we hypothesize that women who are BRCA1/2 gene carriers versus age-matched BRCA negative controls will have a decreased ovarian reserve as measured by AMH, FSH, LH and antral follicle count.

Methods: Ovarian reserve will be evaluated prospectively in a cohort of women undergoing screening at the Mount Sinai Familial Breast Cancer Clinic. Eligible women, based on inclusion and exclusion criteria, will be identified through monthly prescreening of clinic lists and accessing the genetic databases. These women will be approached between April 2012 and June 2013 by study co-investigators, physicians, genetic counsellors or nurse at their appointment, or self-recruited in response to study advertisements. Eligible women will be asked if they have family members who might be willing to participate. All interested women will then be provided with information on the study by a research assistant at the CFRH. Informed consent will be obtained by a research assistant at which time demographic information will be recorded and study participant identification numbers assigned. Women will be asked to call in on Day 1 of their menstrual cycle to the CFRH to book a transvaginal ultrasound for antral follicle count and blood work including an AMH, FSH, LH, and estradiol on Day 3 or 4 of their menstrual cycle.

Results: We are currently seeking REB approval and submitting applications for grants.

Conclusions: This is a study in progress thus at this time we do not have any conclusions to report. However, if we show definitively that ovarian reserve is decreased and these BRCA-positive women are predisposed to infertility, this may influence in the future the family planning of or expedite the initiation of expert infertility consultation of BRCA-positive women.

ABSTRACT #P-G6

Assessment of Global Methylation of Human Sperm

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Objective: To determine the baseline state of global methylation of normal human sperm for comparison in future studies where pathological conditions.

Methods: The extraction of genomic sperm DNA methodology was optimized to overcome the highly condensed state of human sperm DNA. LUMA analysis was performed on 9 independent samples (n=2). LUMA is an assay that estimates genome-wide CCGG methylation at the internal CG using genomic DNA. Genomic DNA is cut using isoschizomers HpaII (methylation sensitive) and MspI (methylation insensitive), followed by sequencing by synthesis of the sticky ends. An amount of light is emitted for every C or G that is incorporated. By comparing the amount of light emitted using the HpaII vs. MspI restriction enzymes, one can estimate the global levels of methylation. There are limitations to this assay since it is biased towards areas that are CG-rich. There are also assumptions in the activity of the enzymes used, for example, HpaII is a better cutter where there are multiple recognition sites close together. Additionally, neither MspI nor HpaII will cut if the exterior C is methylated. We then used another methodology based on LINE-1 elements that estimates global CG methylation by assaying repetitive and presumably parasitic DNA. This assay uses bisulfite converted DNA and PCR amplifies a target sequence on the L1 retrotransposon. The L1 element is estimated to populate ~20% of the human genome.

Results: The LINE-1 and LUMA global methylation findings were comparable. The LUMA assay indicated that 'normal' human sperm exhibits an average global methylation of approximately 55% and the LINE-1 methylation analysis revealed an average global methylation of approximately 60%.

Conclusions: Previous work in human and animal models has indicated that global sperm methylation, specifically hypomethylation, may be a predictor of pregnancy outcome. Modern approaches to epigenetics may allow for this to become a clinical diagnostic test target in predicting infertility. In order to make any advances in this area a complete understanding of the general methylation status of human sperm DNA is requisite. Therefore, we determined the baseline "normal" methylation level of sperm. Interestingly, this level was lower than other cell types of the early embryo, as well as cultured human umbilical vein endothelial and aortic vascular smooth muscle cells. Future, studies will involve identifying human conditions that affect the degree of methylation in human sperm.

ABSTRACT #P-H1

SSEA-4 Expression Marks a Highly Proliferative and Multipotent Subpopulation of First Trimester Human Umbilical Cord-Derived Perivascular Stem Cells

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Objective: The identification and purification of subpopulations of cells with enhanced clonogenic activity and differentiation potential within heterogeneous stem cell cultures is of major interest in the field of stem cell therapy research. We have recently identified comparable expression of stage-specific embryonic antigen 4 (SSEA4) in first trimester human umbilical cord-derived perivascular stem cells (ftHUC-PVCs). Here, we investigated whether SSEA4 could be used as a marker for the enrichment of a subpopulation of ftHUC-PVCs with enhanced therapeutic potential.

Methods: SSEA4(+) and SSEA4(-) cells were prospectively isolated from three different ftHUC-PVC lines using fluorescence-activated cell sorting (FACS). Their clonogenic capacity and capacity to differentiate towards adipogenic and osteogenic lineages were compared in culture assays. We also investigated the effect of serum-free culture conditions on SSEA4 expression, and correlated this to proliferative ability and multipotency by measuring population doubling times through passaging and by performing adipogenic and osteogenic differentiation assays.

Results: We observed a reversibility in SSEA4 expression in SSEA4(+) and SSEA4(-) cultures. A constant frequency of SSEA4 expressing cells (20-30%) was maintained with passaging (P1-P9) in both cultures. BrdU assay and FACS isolation revealed that the SSEA4(+) population displayed a faster cell cycle, increased ability to form clones, and increased differentiation towards mesenchymal lineages, when compared to SSEA4(-) controls. SSEA4 expression in ftHUC-PVCs is irreversibly lost after culturing in serum-free media conditions, leading to decreased proliferation and loss of multipotency.

Conclusions: Our data suggest that 1) a heterogeneous population of progenitor and committed cells can be distinguished in part by SSEA4 expression 2) the dynamic and reversible SSEA4 expression in ftHUC-PVC cultures is required for the maintenance of their proliferative activity and multipotency; 3) SSEA4 can be used as a marker for the enrichment of a subpopulation of adult progenitor cells with increased therapeutic potential.

ABSTRACT #P-H2

NLRP5 Regulates Autophagy in Preimplantation Embryos. (Work-in-Progress)

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ABSTRACT AVAILABLE IN HARDCOPY VERSION ONLY

ABSTRACT #P-H3

Real-Time PCR Array-Based Gene Expression Profiling of Human Umbilical Cord-Derived Perivascular Cells.

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Objective: Human umbilical cord-derived perivascular cells (HUC-PVCs) are a recently characterized source of mesenchymal stromal cells that have gained interest in the field of cellular therapeutics. This study is the first to examine the gene expression profile of first trimester-derived (ft) HUC-PVCs and term (t) HUC-PVCs using gene arrays. This study explores the advantages and limitations of such an approach as well as the possibilities of extending QPCR-based profiling to serum and media testing. This system is marketed as the most reliable and accurate tool for analyzing the expression of a focused panel for genes. It utilizes SYBR Green-based real-time PCR. Our aim was to evaluate this gene array system for studying the transcriptional expression profile of these cells in comparison to several other cell lines.
Methods: We applied QPCR arrays to evaluate the gene expression of several independent ftHUC-PVC lines, tHUC-PVC lines, the teratocarcinoma cell line (NTERA2), human embryonic stem cell lines (H11 and H9 line) and the fetal foreskin fibroblast (HS68) cell line. We used 2 different Human RT^{2}Profiler^{TM} PCR Arrays to analyze the differential expression of genes: the Cell Lineage and Identification array (PAHS-508) containing gene markers for specific cell types throughout cellular lineage progression and the Stem Cell array (PAHS-405) which profiles the expression of genes related to the identification, growth and differentiation of stem cells, including those involved in signaling pathways important for stem cell specific maintenance. Real-time PCR using Taqman® assays for numerous pluripotency genes and cell lineage markers found on the arrays were also performed on all aforementioned cell lines.
Results: Gene expression profiles, encompassing over 150 different genes, were determined for the aforementioned cell lines. Expression of several genes shifted in ftHUCPVC cells grown under serum versus serum free conditions. Inclusion of growth factors, such as FGF, to the media, also altered the expression profiles of ftHUCPVCs. These results were validated using real-time PCR Taqman® assays, flow cytometry and immunocytochemistry. Several interesting expression patterns were found and will be presented.
Conclusion: We found the PCR array system to be a valuable tool to explore the gene expression profile of ftHUC-PVCs, tHUC-PVCs, hES cells and other cell lines of interest. It is an efficient research method for profiling pathway-focused sets of genes using quantitative real-time PCR and allows dynamic expression profiling of cells exposed to varying culture conditions. In addition, it is a time saving and cost effective way to generate large quantities of informative data that can be used to narrow the scope of research to a smaller number of target genes that relate to growth and differentiation potential in stem and progenitor cell populations. Protein array studies on these cell lines are underway in order to correlate relative protein expression with this transcript data.

ABSTRACT #P-H4

Role of Bim in Oocyte Survival

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Objective: Clinically, girls and young women with cancer who undergo whole-body radiation therapy lose many primordial follicles via apoptosis. Females are born with a certain number of primordial follicles, making up the ovarian reserve that eventually produces one ovulated egg each menstrual cycle. Therefore, their irreversible depletion leads to infertility later in life. Although primordial follicles are extremely sensitive to radiation, the death pathway has not been clearly elucidated in oocytes. This project aims to uncover the role of Bim, a pro-apoptotic Bcl-2 protein, in primordial follicle oocyte death induced by irradiation in animal model.

Methods: Ovarian tissue was collected from neonatal females which underwent gamma-radiation and western blot an analysis for Bim expression was performed. Using a Bim whole-body knock-out mouse model, ovaries were collected from day 4 pups, gamma- irradiated and processed for sectioning 48 hours later. Numbers of primordial and primary follicles in irradiated (100 rads) and non-irradiated ovaries in both KO and WT mice were counted and compared.

Results: Results show an increased expression of Bim protein in ovarian lysates few hours after irradiation. Preliminary results show higher baseline numbers of primordial follicles in KO mice but comparable primordial death rates as WT after irradiation. Further experimental adjustments including decreasing the radiation dosage and time interval between irradiation and sectioning will be made to see if knocking-out Bim confers protection from death to primordial follicles.

Conclusions: Bim levels are induced by gamma irradiation, followed by rapid death of oocytes in primordial follicles, however its inactivation does not provide a protection to protect the oocytes from death.

Funded by: Department of Obstetrics and Gynaecology, University of Toronto.

ABSTRACT #P-H5

Central Mechanisms for the Direct Inhibitory Effects of Gonadotropin-Inhibitory Hormone (GnIH) on Gonadotropin-Releasing Hormone (GnRH) using Novel Hypothalamic Cell Models

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Objective: Reproduction is coordinated by the actions of specific neuropeptides and peripheral hormones, all of which converge on the gonadotropin-releasing hormone (GnRH) neurons, which reside at the pinnacle of the hypothalamic-pituitary-gonadal (HPG) axis. Recently, a novel hypothalamic neuropeptide, gonadotropin-inhibitory hormone (GnIH), has emerged as a potent inhibitory modulator of neuroendocrine function. In mammals, GnIH appears to be localized in the dorsomedial hypothalamus and displays similar inhibitory functions as the avian form, though its distinct role in the HPG axis is not well established. To date, there is a paucity of studies focusing on the regulation of hypothalamic GnIH, as well as its potential direct regulation of GnRH neurons. Therefore, we sought to evaluate the direct central mechanisms of GnIH on GnRH neurons, as well as delineate the signaling events initiated by the GnIH/GPR147 system.

Methods: We have generated immortalized, clonal, rodent cell lines derived from both embryonic and adult hypothalamic primary culture. Using semi-quantitative RT-PCR, we classified a subset of cell lines that exhibit strong GnIH expression, as well as receptors for glucocorticoids (GR) and estrogen (ERβ and GPR30). We have also verified the presence of mammalian GnIH in two cell lines, rHypoE-19 and -23, using an anti-RFRP antibody (PAC 1365; generously provided by Dr. L.J. Kriegsfeld, UC Berkeley). In addition, we have generated a new cell model of GnRH neurons, the mHypoA-GnRH/GFP, which were immortalized and FAC-Sorted from an adult GnRH-GFP mouse to generate a non-clonal cell line representative of the entire GnRH neuronal population. Real time RT-PCR and Western blot analysis were used to delineate the direct GnIH-mediated effects on GnRH neurons. Future studies will explore the effects of GnIH on GnRH secretion.

Results: In the newly established cell model of GnRH neurons, the mHypoA-GnRH/GFP, we confirmed the presence of the GnIH receptor, GPR147. Furthemore, using real time RT-PCR we have demonstrated that GnIH treatment (100 nM) directly represses GnRH mRNA expression by approximately 40% at 1 and 4 hours ($P<0.05$). Current studies using the GPR147 antagonist, RF9, and Western blot analysis are being used to delineate the direct GnIH/GPR147-mediated mechanisms controlling GnRH transcription. Preliminary evidence suggests that RF9 can attenuate the inhibitory actions of GnIH on GnRH expression.

Conclusions: We anticipate that these novel hypothalamic GnIH cell models can be used to further define the cellular mechanisms by which GnIH input and signaling mediates mammalian reproduction through the modulation of GnRH.

Funded by: CIHR, CFI, CRC, and OGS.

ABSTRACT #P-H6

Utilizing Two Different Extraction Methodologies to Determine a Correlation Between Sperm DNA Damage and Sperm Protein Profile.

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Objective: The objective of this study was to examine the relationship between sperm protein profile and sperm concentration, motility and DNA damage in patients undergoing fertility evaluation.

Methods: Following Institutional Research Ethics Board approval, semen samples from 41 patients undergoing infertility evaluation were assessed by Computer Aided Semen Analysis (CASA). Sperm DNA damage was evaluated by flow cytometry based technique with acridine orange stain, expressed as DNA Fragmentation Index (DFI). Sperm proteins were extracted by two methods: 1) NP-40 a non-ionic detergent to separate acrosome and membrane protein from insoluble nuclear protein; 2) RIPA buffer. Protein samples were separated using SDS−electrophoresis gel and visualized by staining with Gelcode and scanning using the Li−cor Odessey scanner.

Results: In this preliminary study, clear differences in sperm proteins with molecular weight (< 17KDa) were observed in patients with abnormalities in standard semen parameters in comparison to normozoospermic patients with. The correlation between levels of sperm DNA damage and proteins profile were also noticeable.

Conclusions: Non−ionic detergent NP40 is a suitable method of protein extraction from human ejaculates. Semen quality and levels of DNA damage are associated with differences in protein content. Further investigation is required to characterize these proteins and to determine whether these proteins are nuclear or DNA binding proteins.

ABSTRACT #P-I1

Effects of Prenatal Synthetic Glucocorticoid Exposure on Hypothalamo-Pituitary-Adrenal (HPA) Function in Juvenile Offspring

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Objectives: Approximately 10% of pregnancies in North America end in preterm labour. Affected women are often treated with synthetic glucocorticoids (sGC) at 24-34 weeks gestation to promote fetal lung maturation. However, animal models have demonstrated that prenatal sGC exposure modifies hypothalamic-pituitary-adrenal (HPA) function in first (F_1) and second (F_2) generation adult offspring. Little is known about the impact of sGC on HPA-function in juvenile animals. We hypothesised that prenatal sGC treatment results in substantial alterations in basal and activated HPA-function in juvenile F_1 offspring.

Methods: Pregnant guinea pigs were treated with betamethasone (BETA; 1mg/kg) or saline (control) at gestational days 40/41, 50/51 and 60/61. Juvenile offspring were exposed to a mild stressor in the form of a novel open-field environment for 30 minutes on post-natal days (PND) 19 and 24, to assess HPA-responsiveness to challenge. Salivary cortisol sampling was undertaken at 0, 30, 60 and 120 minutes. Circadian variation in basal salivary cortisol was assessed at PND26, with samples taken at 8am, 12pm, 4pm and 8am the following morning. Salivary cortisol provides a non-invasive index of free circulating plasma cortisol and was measured using enzyme-linked immunosorbent assays.

Results: Cortisol levels increased significantly following exposure to the open field stressor, although response latency varied markedly amongst different combinations of sex and treatment. BETA females produced a greater peak cortisol response compared to controls at PND19 (30 minutes; $p < 0.05$). A similar relationship was identified in males at PND24. At PND26, BETA females exhibited an increase in cortisol production at 12pm ($p < 0.01$), with no increase in controls. In contrast, cortisol levels showed no significant circadian variation in BETA males, but were significantly elevated at 4pm in controls ($p < 0.05$). In both sexes, control animals showed no change in basal cortisol with advancing post-natal age. However, BETA females exhibited a significant reduction in basal cortisol at PND24 compared to PND19 ($p < 0.05$), whilst a comparable reduction was identified in BETA males at PND26 compared to PND19 ($p < 0.01$).

Conclusions: Antenatal sGC exposure caused significant and sex-specific alterations in basal and activated HPA-function in juvenile F_1 offspring. We are currently defining the molecular mechanisms that underlie the alterations in HPA-function following sGC exposure. Given that a very large number of children have been antenatally exposed to sGC, often repeatedly, these findings have the potential to be of major clinical relevance.

Funded by: Canadian Institutes for Health Research.

ABSTRACT #P-I2

Umbilical Cord Diameter Percentile Curves and their Correlation to Birth Weight and Placental Pathology

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ABSTRACT AVAILABLE IN HARDCOPY VERSION ONLY

ABSTRACT #P-I3

Number and Activation Status of Uterine Natural Killer Cells Suggest a Novel Role in the Second Trimester of Pregnancy

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Introduction: Human uterine (u)NK cells represent the most abundant immune cell population in the deciduas. The $CD56^{bright}CD16^{-}$ NK subset is distinct from peripheral blood NK cells expressing unique marker with immunomodulatory potential. UNK cells play a critical role in mediating spiral artery remodelling in the first trimester, required for optimal blood to the placenta. Studies suggest later in pregnancy, uNK cell numbers are reduced within the deciduas. However, the only studies in the second trimester invade semi-quantitative analysis on histochemical sections.

Objective: In this study we used quantitative flow cytometry to determine both the number and activation status of uNK cells throughout the first and second trimester.

Methods: Decidual samples were obtained from informed consented healthy women undergoing elective pregnancy termination during the early phase pregnancy (6-20 weeks of gestation). Decidual tissue was macroscopically identified, rinsed and then disassociated to enrich mononuclear cells. Live/dead staining was applied to eliminate staining artifacts from analysis. Multi-color flow cytometry was performed to investigate uNK ($CD45^{+}CD56^{+}CD16^{-}$) population and their activatory receptors (CD244, CD314, CD335, CD336, CD337, NKp80).

Results: In the early gestation stage (6-20wk), 68% of CD45 positive decidual leukocytes were CD56+CD16- uNK cells. There was no difference in the proportion of the uNK population between first (6-12wk) and early second (13-20wk) trimester. More than 95% of uNK cells were strongly positive for CD335 and CD244. Interestingly, CD336 expression was presented in 15% uNK but at varying levels between patients across the first and second trimester. With increasing gestational age uNK expression levels of CD337 and CD314 were slightly upregulated. Interestingly, in second trimester uNK the activating receptor NKp80 expression level was significantly increased (49% at 13-20wk; 2 fold, $P<0.05$), in comparison with that in first trimester (27% at 6-12wk).

Conclusion: Flow cytometry analysis of uNK cells provided detailed phenotypic characterization of uNK cells from first to mid second trimester. Surprisingly we found that the number of uNK remained elevated through the second trimester. Our observation of an increase in NKp80 which has been suggested as triggering cytotoxicity raise the possibility of novel functions for uNK in the second trimester.

ABSTRACT #P-I4

Antenatal Dexamethasone Exposure in Mice Does Not Affect Levels of SNAT Proteins in the Placental Microvillous Membrane

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Objective: Objective: Synthetic glucocorticoids (sGCs), which are administered to women threatened with preterm labour, differentially regulate the placental system A amino acid transporter in vitro. The system A transporter is composed of three independent proteins (SNAT1, SNAT2 and SNAT4) which are encoded by the Slc38a1, Slc38a2 and Slc38a4 genes. Recently, we demonstrated that sGC treatment administered in mid-gestation reduced murine system A mediated transport at term. This reduction in transporter function was not mediated by altered gene expression, as DEX did not affect Slc38a isoforms (Audette *et al.*Endocrinol 2011). The molecular mechanisms underlying sGC-induced reductions in system A activity are not known. We hypothesized that maternal sGC treatment down-regulates SNAT protein expression at the placental microvillous membrane in late gestation.

Methods: C57BL/6 pregnant dams were treated with dexamethasone (DEX; 0.1mg/kg, n=6) or saline (n=6) on embryonic day (E)13.5 and E14.5. Placental tissue was collected on E18.5 (term E19.5). Protein levels of SNAT1, SNAT2 and SNAT4 (Santa Cruz) were measured in total placental homogenates and in isolated microvillous membrane using western blot. Alkaline phosphatase activity was used to verify enrichment of placental microvillous membrane.

Results: Alkaline phosphatase activity demonstrated similar fold enrichment between vehicle (17.00±1.6) and DEX (20.49±5.5) treated placentae. Protein levels of SNAT1, SNAT2 and SNAT4 were demonstrated in placental homogenates however, were not affected by DEX treatment ($p>0.05$). Similarly, SNAT1, SNAT2 and SNAT4 demonstrated in microvillous membrane vesicles were also unaffected by DEX treatment ($p>0.05$).

Conclusions: Previously we have demonstrated that antenatal sGC treatment in mid-gestation reduces murine placental system A transport prior to term - where reduction in transporter activity is not mediated by alterations in Slc38a gene transcription. Our current results show that sGC treatment does not alter SNAT protein levels in the placenta or microvillous membrane. This suggests that alternative post-translational modifications may reduce transporter function.

Funded by: Canadian Institutes for Health Research

ABSTRACT #P-I5

Transabdominal Amnioinfusion in Premature Preterm Rupture of Membranes: A Systematic Review and a Meta-Analysis

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ABSTRACT AVAILABLE IN HARDCOPY VERSION ONLY

ABSTRACT #P-I6

Anti-Mullerian Hormone as a Marker of Fertility in IVF and IUI Therapy: A Pilot Study.

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Objective: The primary objective of this study was to determine the ability of serum AMH level to predict the odds of a women becoming pregnant while undergoing IVF or IUI fertility treatments.

Methods: This is a retrospective chart review pilot study with institutional ethics approval. Serum AMH, follicle stimulating hormone, estradiol, and luteinizing hormone were measured on cycle day three of 26 women undergoing IVF and 8 women undergoing IUI therapy at First Steps Fertility between January 2009 and February 2012. Patients were arranged into 2 groups, pregnant and non-pregnant, and AMH and FSH levels were analyzed.

Results: Of the patients involved in this pilot study 18 became pregnant compared to 16 who did not. The pregnancy group on average had higher AMH levels (18.5 pM/l vs. 15 pM/l) and lower FSH levels (6 mIU/ml vs. 7.1mIU/ml) compared to the non-pregnant group. Low AMH levels according to age occurred in 44% vs. 61%, elevated FSH occurred in 12.5% vs. 0%, normal AMH occurred in 44% vs. 11%, normal FSH occurred in 87.5% vs. 100% and high AMH occurred in 12% vs. 28% in the non-pregnant and pregnant groups respectively.

Conclusions: The results from this pilot study show mixed results of the ability of AMH to predict fertility in women undergoing IVF and IUI therapy. As a group women who became pregnant had a higher AMH average but a lower percentage of women with normal or high AMH levels. A larger group should be investigated to identify the ability of AMH to predict pregnancy results in IVF or IUI therapy.

ABSTRACT #P-J1

A Review of Laparoscopic Sacrocolpopexy: Surgical Outcomes, Complications and Failures

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Background: Pelvic organ prolapse is an extremely common problem occurring in up to 50% of parous women. It is estimated that 10% of women will have surgery for prolapse in their lifetime. Currently, the gold standard of management for vaginal vault prolapse is the abdominal sacrocolpopexy. A Cochrane review has shown that it is associated with a lower rate of recurrence compared to other forms of vaginal vault suspension. As minimally invasive surgery is becoming more available, the open abdominal sacrocolpopexy is becoming replaced with the laparoscopic approach. There are very few studies comparing open versus laparoscopic sacrocolpopexy, however it would appear that the outcomes are similar and that the laparoscopic sacrocolpopexy is associated with decreased hospital stay and decreased patient discomfort. Available studies suggest that the cure rate ranges from 78-95%.

Objective: The objective of this study is to perform an audit of laparoscopic sacrocolpopexies done at Sunnybrook Health Sciences Centre (SHSC). Our primary objective is to determine objective success of the operation and to record intra-operative and post-operative complications. Our secondary objective is to determine if there were any failures and if there are any risk factors associated with failure.

Methods: A retrospective chart review of all laparoscopic sacrocolpopexies done between June 2010-December 2011 at Sunnybrook hospital will be performed. Pre-operative and post-operative prolapse grading will be recorded. Objective success will be considered as a vaginal vault grade ≤2. Intra-operative and postoperative complications including rates of urinary incontinence, dyspareunia and mesh erosion will be determined. Any failures will secondarily be analyzed to determine if there were any risk factors associated with the failure including age, BMI, surgical technique and prior prolapse surgery. All data will be collected in Excel and analyzed using SAS.

Results: No results are available at the time of abstract submission.

Conclusions: No conclusions are available at the time of abstract submission.

ABSTRACT #P-J2

Attitudes and Expectations of Canadian Women in Labour towards Point of Care HIV Testing on the Labour and Delivery Unit

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Objective: To assess attitudes and opinions surrounding point of care HIV testing among Canadian women, and to determine predictors for acceptance of testing.

Methods: A survey assessing acceptability and attitudes towards rapid HIV testing was distributed on the Labour and Delivery unit in an academic hospital in Toronto, Canada during the summer of 2011. Information collected included demographics, health and pregnancy history, willingness to undergo rapid HIV testing while in labour, and barriers to testing. HIV testing was not performed.

Results: Responses for 92 completed questionnaires were analyzed. The average age of respondents was 32 years and all were HIV-negative. 12% of patients reported having at least 1 risk factor for HIV transmission. 59% of women were willing to be tested at the time of survey completion, and these women stated that they would accept any of saliva, urine, or serum testing. If found to be positive, 98% would accept antiretroviral treatment and 96% would formula feed their infants. Of the women who were not willing to be tested (41% of respondents), their reasons for refusal include "don't want to know" (39%) and being in "too much labour pain" (29%). Regardless of willingness to be tested, social stigma and reaction from partners were the most frequently cited barriers to testing (64% and 69% respectively).

Conclusions: Canadian women in labour are willing to undergo rapid HIV testing via urine, saliva or serum. If found to be positive, women are willing to undergo treatment as well as formula feed in order to prevent mother to child transmission of HIV.

ABSTRACT #P-J3

Cervico-Vaginal Inflammatory Changes in IUCD Users: A Pilot Study

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Objective: To determine whether the presence of an intrauterine contraceptive device (IUCD) changes the cervico-vaginal cytokine profile and further characterize the pro- or anti-inflammatory factors present.

Methods: The proposed pilot study will be a prospective study with institutional ethics approval in progress. Twenty women attending a general Gynaecology clinic at St. Michael's hospital will be followed over a 1-month period. During the initial visit, participants will be asked to fill out a demographics questionnaire. Vaginal swabs for bacterial vaginosis (BV) and cervico-vaginal swabs for cytokine analysis will be taken prior to IUCD insertion. At the 1-month follow-up visit, a second questionnaire inquiring about problems with the IUCD will be administered. As per standard of care, the IUCD strings will be checked to confirm placement if seen at the external cervical os and repeat swabs will be done for both BV and cytokine analysis. Each participant will therefore act as their own control. The primary outcomes are changes in the cervico-vaginal cytokine profiles in the presence of an IUCD and characterizing any associated cytokine changes with or without confirmed BV. Secondary outcomes include the prevalence of women who have clinical evidence of BV prior to insertion of an IUCD or acquire the infection at the 1-month follow up, and the incidence of expulsion, abnormal bleeding, pain and pelvic infections at the follow-up visit.

Results: The research study is currently in progress.

Conclusions: The research study is currently in progress.

ABSTRACT #P-J4

Prevalence of Unidentified/Subclinical Hypothyroidism in Two Urban Prenatal Populations: Can Predisposing Maternal Risk Factors be Identified?

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Objective: (1) To determine the prevalence of subclinical hypothyroidism as evidenced by elevated TSH levels in two urban prenatal populations (Toronto & Calgary).
(2) To identify predisposing maternal risk factors in order to increase the detection rate of subclinical hypothyroidism in pregnancy.

Methods: This study is a retrospective chart review of consecutive new prenatal patients who presented between Jan-Dec 2011 for prenatal care to two staff obstetricians in Toronto or Calgary. Institutional ethics approval was obtained at both sites. Screening blood work included TSH testing. Current recommendations state that the TSH level should not exceed 2.5mIU/L in the first trimester and 3.0mIU/L in the second and third trimesters. Patients with abnormal TSH results were managed according to the current standard of care. Charts of all patients have been reviewed and maternal demographic data and characteristics including obstetric history, maternal age, BMI, blood pressure, ethnicity, smoking, and relevant past medical history recorded. This information is readily available from the Ontario Antenatal Record and the Alberta Prenatal Record.

Results: We have identified 107 patients in Toronto and 168 patients in Calgary for a total of 275 charts. The prevalence of elevated first trimester TSH (>2.5mIU/L) was found to be 16% (17/107) in Toronto and 23% (28/120) in Calgary. The prevalence of elevated TSH in the second and third trimesters (>3.0mIU/L) was found to be 17% (8/48) in Calgary. Data analysis is currently in progress looking for associations between increased TSH levels in pregnancy and maternal characteristics including age, BMI, previous history of preterm delivery or spontaneous abortion, nulliparity, smoking in pregnancy, and Vitamin D levels.

Conclusions: Pending.

(Subclinical hypothyroidism is found in 1.0-4.6% of pregnancies and is associated with multiple adverse outcomes for both mothers and neonates. Current recommendations for targeted case finding fails to detect 30% of those with overt or subclinical hypothyroidism because they are classified as low-risk. High-risk patients are those with a personal or family history of thyroid disease, history of recurrent miscarriage or preterm delivery, type 1 diabetes, other autoimmune disorders, or symptoms/signs suggestive of thyroid dysfunction. By looking at a broad range of maternal characteristics we hope to find correlations that may inform patient selection for improved "targeted case finding" and thereby increase the detection rate of subclinical hypothyroidism in pregnancy.)

ABSTRACT #P-J5

Outcomes from a Radical Hysterectomy Training Program in a Low Resource Setting in Africa.

Samantha Young [M](1), Peter Itsura(2), Hellen Muliro(2), Brendan Charles(3), Astrid Christoffersen-Deb(1), Rachel Spitzer(4), Barry Rosen(3), Elkanah Omenge Orango(2).
(1)University of Toronto (2)Department of Reproductive Health, Moi Teaching and Referral Hospital, Moi University (3)Gynaecology-Oncology, Princess Margaret Hospital (4)Department of Obstetrics and Gynaecology, Mount Sinai Hospital, University of Toronto

Objective: This project aims to evaulate the safety of Radical Hysterectomy surgery performed by gynaecologists in a low resource setting in Kenya after completion of a surgical training program.

Methods: Surgical notes from thirty three radical hysterectomies performed by the trainees over 18 months were reviewed. Intraoperative complications, postoperative complications and postoperative voiding were used as surrogate measures to assess the safety of this surgical procedure. These results were compared with published data on complication rates in both a low and high resource setting using chi-square analyses.

Results: At presentation, 18 of the radical hysterectomy patients had operable lesions (FIGO Stage ≤IIA); 15 more received neoadjuvant chemotherapy for downstaging prior to surgery. Of 33 radical hysterectomies performed, 3 (9.1%) resulted in one or more complications. One patient had a major intraoperative hemorrhage requiring transfusion of 8 units of blood and ligation of the external iliac vein. Postoperative complications included 1 fascial dehiscence, 1 deep vein thromboemolism, 1 wound infection and 1 fistula. 31 (93.9%) patients voided on their own by postoperative day 5 and all others by postoperative day 10. The complication rates were not statistically different ($p > 0.05$) to those documented in either a high-resource or low-resource settings.

Conclusions: Radical hysterectomy in this setting is a high risk but high reward procedure. The preliminary analyses have shown immense promise for the continuation of the training program and proof of its effectiveness. As screening increases in low resource settings, more early stage cancers will be identified and more women can be eligible for curative surgery.

ABSTRACT #P-J6

Power, Passenger, Passage…and Physician?: Changing Obstetrical Practice as a Determinant of the C-Section Rate at a Toronto Community Hospital

Gregory Handrigan[M](1), Brenda Woods (2), Leke Badmos (2), Kellie Murphy(3), Melissa Tai (2)
(1) Undergraduate Medical Education, Faculty of Medicine, University of Toronto, (2) Family Birthing Centre, Toronto East General Hospital, (3) Maternal Fetal Medicine, Mount Sinai Hospital.

Objective: Caesarean section (C/S), while a lifesaver in high-risk childbirths, comes at a cost to mother and baby as well as to the healthcare system. In spite of this, the C/S rate in Canada has nearly doubled in the past 20 years, and it continues to rise, surpassing the WHO recommended rate of 15%. The high C/S rate at Canadian hospitals has been anecdotally attributed to mothers choosing elective C/S over vaginal delivery as the preferred mode of delivery. Such belief has prompted health economists to suggest de-listing C/S as an OHIP-insured service. Recent research points to changing physician practice as an important determinant of the rising C/S rate. Obstetricians today perform more primary c-sections for relative indications, such as failure to progress (FTP) and atypical fetal heart rate patterns (AFHR).

In this pilot study, we developed a new audit tool to investigate indications for C/S at Toronto East General Hospital (TEGH). In particular, we investigated whether differences in obstetrical practice impacts the C/S rate. We hope, in the long-term, that interventions aimed at potentially modifiable determinants will lower the C/S rate at TEGH.

Methods: We retrospectively reviewed birthing summaries of deliveries performed at TEGH for a three-month period during 2001 and 2011 for delivery type, maternal age/comorbidities, indications for delivery and other variables. Ethics approval was granted by the TEGH Research Ethics Board.

Results: The C/S rate at TEGH increased from 24.1% in 2001 to 26.3% in 2011. This trend was driven largely by an increase in primary C/S indicated by FTP and/or AFHR. Currently, at TEGH, these two indications account for over 90% of primary C/S performed due to failed labour. We noted considerable variation in C/S rates and assisted vaginal delivery rates among obstetricians at TEGH.

Conclusions: The rising C/S rate at TEGH is associated with changes in obstetrical practices related to the management of FTP and AFHR. We recommend open, collegial review to promote uniform practice patterns and management of labour towards achieving a lower C/S rate at TEGH. In view of the malpractice climate, decrease in C-sections performed for AFHR will be difficult to achieve.

ABSTRACT #P-K1

Effects of Placental VEGFA Deficiency on Pregnancy in Mice

Han Li [G](1), Dawei Qu (1), Hoon-Ki Sung (1), Andras Nagy(1,4), S Lee Adamson(1,2,3)**.** (1) Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Depts of (2) Physiology, (3)Obstetrics & Gynaecology, and (4)Molecular Genetics, University of Toronto.

ABSTRACT AVAILABLE IN HARDCOPY VERSION ONLY

ABSTRACT #P-K2

The Impact of the International Association of Diabetes and Pregnancy Study Groups (IADPSG) Diagnostic Thresholds for Gestational Diabetes Mellitus (GDM) on the Incidence of GDM in a Canadian Inner-City Multi-Ethnic Population.

Karli Mayo [R](1), H Vandenberghe (2), R Kedar(3), H Berger(3).
(1) Department of Obstetrics & Gynaecology, University of Toronto (2) Department of Laboratory Medicine & Biochemistry, St. Michael's Hospital (3) Maternal Fetal Medicine, Department of Obstetrics & Gynaecology, St. Michael's Hospital

Objective: The International Association of Diabetes and Pregnancy Study groups (IADPSG) recently published new diagnostic criteria for Gestational Diabetes (GDM). Based on these new criteria the incidence of GDM is expected to increase significantly. The objective of this study is to calculate the impact of these new criteria on the incidence of GDM in a Canadian inner city, multi-ethnic population.

Methods: The results of the 1-hour 50g GCT and the fasting plasma glucose (FPG), 1-hour and 2-hour results of the 75g OGTT were recorded from all pregnant women at St. Michael's Hospital Toronto in the years 2008 to 2010. For the purpose of this study GDM was defined as at least one abnormal glucose value on the 75g oral glucose tolerance test (OGTT) or a result ≥ 10.3 mmol/l after a 1-hour 50g glucose challenge test (GCT). The expected incidence of GDM based on the proposed IADPSG thresholds was compared to the incidence of GDM according to the thresholds outlined in the 2008 Canadian Diabetes Association (CDA) guidelines.

Results: During the study period, 6368 patients performed the 50g GCT, of them 1192 (18.7%) screened positive. An additional 201 (3.16%) had glucose concentrations ≥10.3mmol/L and were diagnosed with GDM. After performing a 75 gram OGTT the cumulative incidence of GDM was 10.63% and 13.45% according to CDA and IADPSG thresholds respectively.

Conclusions: If adopted, the new IADPSG thresholds increase the incidence of GDM by 26.5%. The impact on health care resources and patient health perception needs to be taken into consideration.

ABSTRACT #P-K3

Altered Mechanisms of Acid Sphingomyelinase Regulation and Processing in Preeclampsia

Megan Melland-Smith [G](1,2,3), Martin Post(4), Isabella Caniggia(1,2,3)
(1)Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Departments of (2)Obstetrics and Gynaecology and (3)Physiology, (4)Hospital for Sick Children, University of Toronto.

Objective: Sphingolipids act as bioactive mediators in several pathophysiological processes by regulating cell fate. In particular, ceramides (CERs) are key effectors in pathways initiated by diverse stress stimuli. CERs metabolism is tightly controlled by balancing its synthesis and breakdown via the action of specific enzymes. Acid SphingoMyelinase (ASM) causes sphingomyelin (SM) hydrolysis and subsequent CERs generation. ASM is synthesized as a precursor in the endoplasmic reticulum (ER) with 6 N-linked oligosaccharide chains which are essential for trafficking to the lysosomes and enzyme activation. The objective of this study was to examine CERs and ASM expression, function and processing in placentae from preeclamptic (PE) and normotensive control pregnancies.
Methods: Protein and mRNA expression levels of ASM were assessed by Western Blot analysis and immunofluorescence (IF) in preterm control (PTC), term control (TC) and PE placentae using antibodies against ASM, calreticulin, an ER resident protein and lysotracker used to identify lysosomes. ASM enzyme activity was evaluated using a fluorogenic enzyme coupled assay. Human villous explants and choriocarcinoma JEG-3 cells were treated with sodium nitropursside (SNP, a nitric oxide donor) or kept at either 3% or 20% O_2 and ASM post-translational modification was analyzed using the glycosylation inhibitors peptide-N4-aspargine amidase F (PNGaseF) and/or tunicamycin. In addition, ASM glycosylation was examined by immunoprecipitation followed by western blotting with concanavalin A, a lectin that binds sugars on the protein surface. Lipid analysis in normal and PE placental tissue and in SNP-treated cells was performed using high power liquid chromatography linked to mass spectometry (MS/MS).
Results: MS/MS revealed a significant increase in CERs and SM levels in PE relative to PTC and TC and this associated with an increase in ASM precursor protein expression. Similarly, exposure of explants and JEG-3 cells to SNP increased CERs and both active ASM and its precursor levels. Decrease ASM enzyme activity was detected in PE relative to PTC placentae and SNP treated explants and JEG-3 cells. Tunicamycin reversed the SNP-induced active ASM expression while increasing that of its precursor. In addition, de-glycosylation using PNGase F reduced active ASM and its precursor in PTC and to a lesser extent in PE lysates. Furthermore, treatment with concanavalin A indicated that ASM undergoes glycosylation and that this post-translational modification event was disrupted in PE. IF analysis in sections from PE and PTC placentae showed co-localization of ASM with calreticulin. Similarly following SNP exposure we observed ASM accumulated in the ER while its signal was absent in the lysosomes.

Conclusion: To conclude, in PE, disruption of ASM expression, processing and its glycosylation affects enzyme trafficking and this is due to the oxidative stress status typical of this pathology. Altered ASM expression/activity in PE results in CERs and SM accumulation thereby contributing to increased trophoblast cell death. (**Funded by:** CIHR and OGS)

ABSTRACT #P-K4

Transgenerational Effects of Antenatal Synthetic Glucocorticoid Treatment on Learning and Memory

Vasilis Moisiadis [G](1), Alisa Kostaki(1), Jeff Emack(1), Stephen G. Matthews(1,2,3).
(1)Departments of Physiology, (2)Obstetrics and Gynaecology and (3)Medicine, Faculty of Medicine, University of Toronto.

Objective: Approximately 10% of pregnant women are at risk of preterm delivery. The majority of these women receive treatment with synthetic glucocorticoids (sGCs) to reduce the risk of infant respiratory distress syndrome. We have shown that prenatal sGC exposure alters stress responsiveness and locomotor activity in first (F_1) and second (F_2) generation offspring. Increased locomotor activity in F_1 offspring is associated with altered hippocampal NMDA receptor expression and hippocampal long-term. In the present study, we hypothesized that maternal exposure to sGC results in impaired learning and memory in F_1 and F_2 offspring.

Methods: Pregnant guinea pigs (F_0; n=8-10/gp) were subcutaneously injected with betamethasone (BETA; 1mg/kg) or vehicle (VEH; saline) on gestational days (gd) 40/41, 50/51 and 60/61. Adult F_1 female offspring from each group (n=7-8/gp) were mated with control males. F_1 and F_2 offspring underwent behavioral testing in a Morris Water Maze (a test for learning and memory) on postnatal days 35 (juvenile) and 70 (adult). Latency to find a hidden platform, retention of platform location and search strategy were analyzed.

Results: All groups effectively learnt the location of the hidden platform. However, there was no effect of prenatal (F_0) sGC exposure on latency to find the platform in juvenile or adult offspring in either generation. There were also no significant differences in memory of the platform location (probe trial) between any of the groups. However, both juvenile and adult female F_1 offspring whose mothers received sGCs during pregnancy used a different strategy to search for the platform's location during the probe trial ($P<0.05$), indicating a greater ability to adapt to changing conditions (i.e. removal of the platform during the probe trial).

Conclusions: In conclusion, while antenatal treatment with sGCs has strong transgenerational effects on locomotor activity and neuroendocrine function, there appears to be little effect of this treatment on measures of learning or memory. Together, these results suggest that the processes of memory and learning are resilient to the effects of prenatal exposure to sGCs.

Funded by: Canadian Institutes for Health Research.

ABSTRACT #P-K5

Kick-Starting Action: Canadian Women's Understanding of Fetal Movement Guidelines

Susan Pakenham [R](1), Andrea Copeland(2) and Dan Farine(3).
(1)Department of Obstetrics and Gynaecology, University of Toronto; (2)Faculty of Science, Queen's University; (3)Department of Obstetrics and Gynaecology, Mount Sinai Hospital, University of Toronto

Objective: To determine if obstetrical patients in a large tertiary-care centre receive counselling, understand the guidelines, and seek timely assessment in the event of decreased fetal movement.

Methods: We surveyed a convenience sample of pregnant women (N = 206) at term between July and October 2011. After collecting demographic and provider information, we assessed patient familiarity with fetal movement counting, including sources, timeliness, counting protocols and response to decreased fetal movement.We calculated incidence rates, measures of association and statistical significance by $\chi 2$ testing.

Results: The majority of patients (147/206 = 71.4%) relied on their care provider for information and 44.1% of patients were very familiar with fetal movement counting. A majority, 57.8% (119), received timely information, although 8.1% (27) received information late in pregnancy or not at all. Quite consistently amongst subgroups (low vs. high risk pregnancy, nullipara vs. multipara, patients of varied providers), one-third (34.7%, 70/202) of patients had NO or INCORRECT knowledge of the Canadian guidelines, 35.1% (71/202) had knowledge of fetal movement counting and what to do, while 30.2% (61/202) who knew how to monitor fetal movements did not know how to respond to decreased movement.

Conclusion: Recent literature shows a substantial drop in stillbirths with timely intervention for decreased fetal movement. Only one-third of our patients were both informed and would have sought further investigation for decreased movement. Reinforcing the significance of fetal movement counting in educational papers can remind care providers about the importance of informing all patients about this simple, inexpensive and successful monitoring protocol.

ABSTRACT #P-K6

The PPAR-γ agonist Rosiglitazone Reverses sFLT1 Hyper-secretion from First Trimester Placental Villi in a GCM1-Dependent Manner

Sascha Drewlo [PD](1), Fergus McCarthy(2), Khrystyna Levytska(1), Louise Kenny, PhD(2), John Kingdom(1). (1)Samuel Lunenfeld Research Institute, Mount Sinai Hospital, (2) University College Cork, Anu Research Centre, Ireland.

ABSTRACT AVAILABLE IN HARDCOPY VERSION ONLY

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F1	Hassonah, Seham	F	Drutz
G4	Hong, Seok-Ho	O	Librach
O10	Iqbal, Mahid	G	Matthews
J2	Iqbal, Salikah	R	Yudin
C4	Javam, Mohsen	G	Matthews
D4	Jumah, Naana	R	Shah R
G6	Kenigsberg, Shlomit	O	Librach
O11	Kirkham, Yolanda	F	Ornstein
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A4	Lau, Angela	G	Brown TJ
B6	Lee, Dennis K	O	Nevo
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P/O #	Name	Category	Supervisor(s)
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*University of Toronto Trainee Category: G=Graduate Student; F=Clinical Fellow; M=Medical Student (UG=Undergraduate Student); PD=Post-Doctoral Fellow; R=Resident; O=Other (ie not a University of Toronto trainee)

Presenters by Abstract # and Session

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A3 Kollara, Alexandra
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E3 Teichert, Anouk-Martine
E4 Garbedian, Kimberley
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F3 Po, Leslie K
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G2 Withdrawn
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G4 Hong, Seok-Ho
G5 Daniel, Ariadne
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H4 Cao, Sarah S
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J2 Iqbal, Salikah
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K1 Li, Han
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K5 Pakenham, Susan
K6 Drewlo, Sascha

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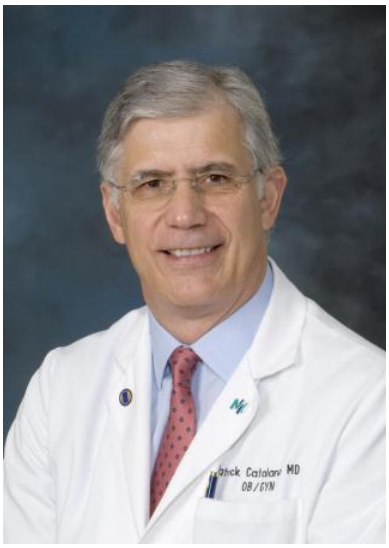

Patrick Catalano MD
2012 Henderson Lecturer

Patrick Catalano MD is Professor and former Chair of the Department of Reproductive Biology at Case Western Reserve University/MetroHealth Medical Center. He received his medical degree from the University of Vermont College of Medicine and is certified in general Obstetrics and Gynecology and Maternal-Fetal Medicine. Doctor Catalano's interests include obesity, diabetes and metabolism in pregnancy. His research includes the longitudinal evaluation of women before and throughout pregnancy to determine the short- and long-term effects of maternal obesity and diabetes on both the mother and her fetus.

Associated with several professional organizations, Dr Catalano's memberships include the American Congress of Obstetrics and Gynecology, the Society of Maternal-Fetal Medicine, Society for Gynecologic Investigation, American Diabetes Association and the Perinatal Research Society. Dr Catalano has chaired the American Diabetes Association Council on Pregnancy and Women's Health and co-chaired the NICHD Scientific Vision Group on Pregnancy; currently he sits on the Maternal-Fetal Medicine Division of the American Board of OB/GYN. Having sat on the Institute of Medicine (IOM) committee to review the weight gain in pregnancy guidelines, he currently sits on the IOM committee tasked with disseminating the Guidelines.

Dr Catalano has received the Norbert Freinkel Award from the American Diabetes Association, the Jorgen Pedersen Award from the Diabetes in Pregnancy Study Group of the European Association for the Study of Diabetes, and the Agnes Higgins Award from the March of Dimes. He has over 140 peer-reviewed publications and has received continuous National Institute of Health funding since 1987.

Obstetrics & Gynaecology
UNIVERSITY OF TORONTO

Research Day, Friday, May 4, 2012 – Location and Map

Location: Research Day will take place at the **JJR Macleod Auditorium & Stone Lobby** in the **Medical Sciences Building,** University of Toronto, 1 King's College Circle, M5S 1A8 from 8:00 a.m. to 6:30 p.m. This is in the heart of the University, just west of Queen's Park/Avenue Road and north of College Street, in between the Museum and Queen's Park subway stations.

The **JJR Macleod Auditorium** is attached via a sheltering roof to the north end of the **Medical Sciences Building,** doors visible to the left once you climb the stairs and walk towards the main building.

By car: By car you may approach the building from the main College St. entrance west of Queen's Park, up King's College Road to King's College Circle or from Wellesley St. West. There is pay parking on Hart House Circle and around King's College Circle. The Medical Sciences Building is south of the Wellesley St entrance on King's College Circle.

By foot: You may take the same approach walking. If approaching from the north, you can walk on the west side of Queen's Park Circle and take the pedestrian pathway just north of Wellesley that leads you to Hart House and then walk south to the Medical Sciences Building.

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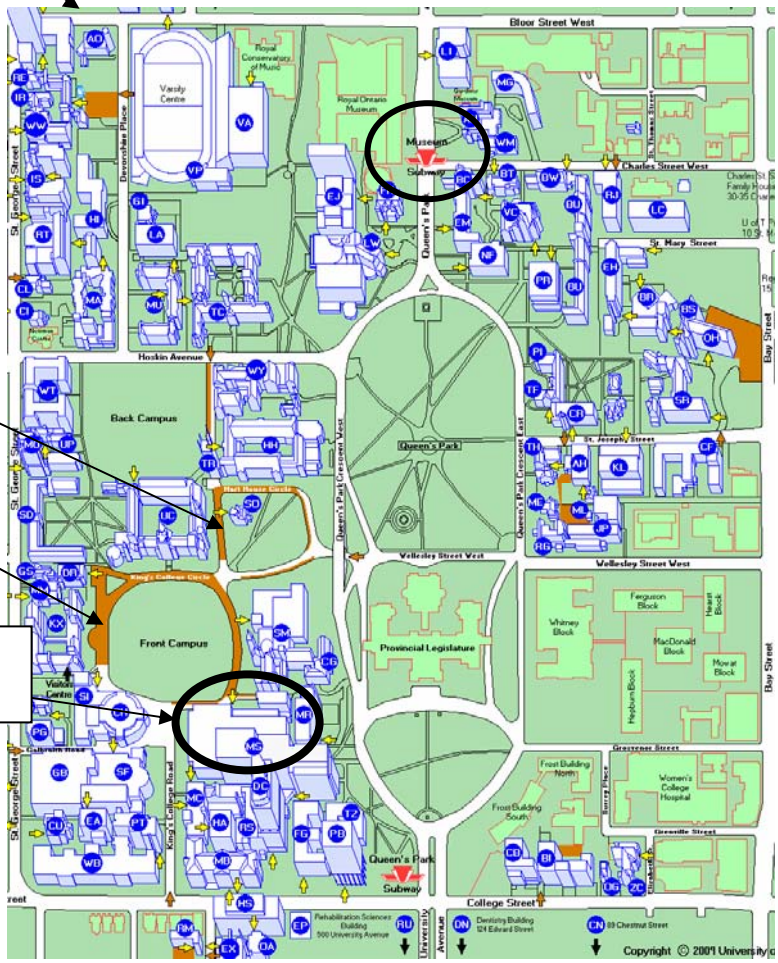
By subway: If coming from the **south**, go to **Queen's Park** and walk along the north side of College St. to King's College Road, then north to King's College Circle and then east along the circle to the Medical Sciences Building. If coming from the **north**, go to **Museum** and exit on the **west side** of Queen's Park/Avenue Road, then walk south and take the walkway to Hart House just north of Wellesley and then south along both circles to the Medical Sciences Building.

See Map on Next Page

JJR Macleod Auditorium and Stone Lobby, Medical Sciences Building
University of Toronto, 1 King's College Circle, M5S 1A8

Bloor Street



Museum Subway Station

Hart House Circle

King's College Circle

Wellesley Street

Medical Sciences Building

College St.

Queen's Park Station

Obstetrics & Gynaecology
UNIVERSITY OF TORONTO

RESEARCH DAY CONTACT INFORMATION
(To accompany abstract submission by email)
29th Annual Research Day
Friday, May 4, 2012

[This is a Word document – please type in the appropriate responses, save under your name, i.e. Jones Contact Information.doc and email, along with your abstract, to: helen.robson@utoronto.ca by **Monday, March 5, 2012**.]

Abstract Title:

Category (Gynaecologic Oncology, Gynaecology, Maternal-Fetal Medicine/Obstetrics, Paediatrics and Adolescent Gynaecology, Reproductive Sciences, or Urogynaecology):

Preference – PLEASE DISCUSS WITH YOUR SUPERVISOR.
(Oral, Poster, or None):

Do you wish to **withhold your abstract** from **online publication** by reason of intellectual property rights? (eg. an impending patent) Yes/No:

Name of Trainee:

Mode of Address (Mr., Miss, Ms, Mrs., Dr. and include whether M.D. or Ph.D.):

If you receive an award, how would you like your name to appear on the certificate? (eg. Josephina M Doe MD or Josie Doe MD or JM Doe MD):

Affiliation (Hospital, Institute. Department or UT):
Name of Supervisor:
Email address of Supervisor:

University of Toronto Training Status (at submission and Research Day) Please include ALL that apply, eg. a resident also doing a graduate programme should include both.
(Graduate Student = G; Resident = R; Clinical Fellow = F; Post-Doctoral Fellow = PD; Medical Student = M):
If not a U of T trainee, please explain status:

Contact Info for Trainee **before** Research Day (**email,** address, telephone, fax, pager number):

Home Address if not as above(**email,** address, telephone):

Please complete this form, save it under your last name, i.e. Jones Contact Information.doc and email to Helen Robson, helen.robson@utoronto.ca along with your abstract, by Monday, March 5, 2012. Thank you.
Documents and information also at: http://www.obgyn.utoronto.ca/Research/ResearchDay.htm

Obstetrics & Gynaecology
UNIVERSITY OF TORONTO

Call for Abstracts
29th Annual University of Toronto Department of Obstetrics and Gynaecology Research Day, Friday, May 4, 2012

Dear Faculty, Staff, Trainees and Guests:

The 29th Annual Research Day of the University of Toronto Department of Obstetrics and Gynaecology will take place from 8:00 a.m. to 6:30 p.m. on **Friday, May 4, 2012** at Hart House, University of Toronto, 7 Hart House Circle, M5S 3H3.

We are very pleased to welcome the Henderson Lecturer this year, Dr Patrick Catalano, Professor, Reproductive Biology, MetroHealth Medical Center/Case Western Reserve University, whose interests include obesity and diabetes and their effects on mother and fetus in pregnancy. His topic for the Henderson Lecture is: *Maternal Obesity and Pregnancy: Much Ado about Something.* Please see our website for a short biography.

This year's **abstracts** for oral and poster presentations are **due on Monday, March 5, 2012.** Please note that those submitting abstracts are asked for their preference of oral or poster presentation**. Please confer with your supervisor to ensure only one request for an oral comes from each supervisor.**

Please go to our website at http://www.obgyn.utoronto.ca/Research/ResearchDay.htm for the following information and links for **abstract submission**:

Call for Abstracts
Abstract Requirements and Template (required for submission)
Contact Information Form (required for submission)
Instructions for Oral Presenters (coming soon)
Instructions for Poster Presenters (coming soon)
Awards Criteria
Research Day Poster
Research Day Booklet (coming soon)
Research Day Programme (coming soon)
Location (coming soon)

If you have any questions with regard to these documents or the process, please contact me at helen.robson@utoronto.ca.

We look forward to another excellent Research Day, an opportunity to exhibit and share all the cutting-edge research in the department!

Best regards,

Helen Robson
Consultant; Research Coordinator

Obstetrics & Gynaecology
UNIVERSITY OF TORONTO

FINAL INSTRUCTIONS FOR POSTER PRESENTERS

University of Toronto Department of Obstetrics and Gynaecology
Research Day, Friday, May 4, 2012

Thank you for submitting your abstract for Research Day. Your abstract has been chosen for a poster presentation. Please see the details below.

Location: Research Day will take place at the **JJR Macleod Auditorium & Stone Lobby** in the **Medical Sciences Building,** University of Toronto, 1 King's College Circle, M5S 1A8. This is in the heart of the University, just west of Queen's Park/Avenue Road and north of College Street, near the Museum and Queen's Park subway stations. A map and directions are available on our website (see below).

Time: Research Day will begin with breakfast at 8:00 a.m. on Friday, May 6, 2011 and end with a wine and cheese reception and award presentation from 5:30 to 6:30 p.m.

Registration: Please register first, before you do anything else, in the lobby outside the JJR Macleod Auditorium between 8:00 and 8:25 a.m., to receive your nametag, abstract booklet and any further instructions.

Poster boards: We will provide each presenter with a 3' high by 6' wide board and velcro for attaching the poster. Boards will be numbered to correspond to the poster numbers published in the abstract book distributed at the meeting.

Set-up for Posters: ALL POSTERS WILL REMAIN UP ALL DAY IN THE STONE LOBBY. Please mount your posters before the programme begins at 8:25 a.m.
Tear-down: Directly after the last poster session, between 4:05 and 4:20 pm.

Poster Session I: The morning session will start with a general walkabout from 9:45 to 10:05 a.m., followed by a Poster Tour from 10:05 to 11:05 a.m..
Poster Session II: The afternoon session will start with a general walkabout from 2:35 to 3:05 p.m., followed by a Poster Tour from 3:05-4:05 p.m.
Poster Tours: Each group will be led by two Chairs, and we have tried to mix basic scientists with clinicians. We ask that you be present the entire time and join the others in your group in the tour. Please be prepared to give a **3-5 minute presentation**, with 5 minutes for discussion/questions. **Please note that strict adherence to timing is essential and we will ring a bell to end each presentation.**

Awards: In order to be eligible for an award, you must be a U of T trainee and present your own work. Your work and presentation will be judged by the Chairs of your poster tour and one other Judge for the JW Knox Ritchie Research Awards. There will be 5 awards, with a monetary component, based on level of training (Graduate Student, Resident, Clinical Fellow, Post-Doctoral Fellow, Medical Student) rather than type of presentation. Please see judging criteria on our website. These awards will be presented at the wine and cheese reception between 5:25 and 6:30 p.m.

***Please see http://www.obgyn.utoronto.ca/Research/ResearchDay.htm for information or contact Helen Robson at* helen.robson@utoronto.ca**

Obstetrics & Gynaecology
UNIVERSITY OF TORONTO

INSTRUCTIONS FOR ORAL PRESENTERS

University of Toronto Department of Obstetrics & Gynaecology
Research Day, Friday, May 4, 2012

Thank you for submitting your abstract for Research Day. Your abstract has been chosen for an oral presentation. Please see the details below.

Location: Research Day will take place at the **JJR Macleod Auditorium & Stone Lobby** in the **Medical Sciences Building,** University of Toronto, 1 King's College Circle, M5S 1A8. This is in the heart of the University, just west of Queen's Park/Avenue Road and north of College Street, near the Museum and Queen's Park subway stations. A map and directions are available on our website (see below).

Time: Research Day will begin with breakfast at 8:00 a.m. on Friday, May 4, 2012 and end with a wine and cheese reception and award presentation from 5:30 to 6:30 p.m.

Registration: Please register first, before you do anything else, in the lobby outside the JJR Macleod Auditorium between 8:00 and 8:25 a.m., to receive your nametag, abstract booklet and any further instructions.

Oral Session Times: There will be three oral sessions, two in the morning (8:30-9:45 a.m. and 11:10-12:10) and one in the afternoon (1:20-2:35 p.m.).

Presentation: Each oral presentation is allowed 15 minutes: **10 minutes** for the presentation and 5 minutes for questions**. Please note that we will adhere strictly to these time limits!**

Audiovisual Support: All presentations will be placed on the Department's laptop in advance of Research Day. **Your presentation must be PC-compatible.**
* You have the choice of bringing your presentation in on a USB key, or emailing it Cherryl Bird, Departmental Assistant, **as early as Monday, April 30, 2012, but NO LATER THAN WEDNESDAY, May 2, 2012.**
By email: Please email **in pdf format only** to c.bird@utoronto.ca **OR**
In person: To 92 College St, 2nd floor.
If you foresee any difficulties, please contact Cherryl ahead of time.
Please provide your own backup (ie USB key) for Research Day.

Awards: In order to be eligible for an award, you must be a U of T trainee and present your own work. Your work and presentation will be judged by the Chair of your oral session and two other Judges for the JW Knox Ritchie Research Awards. There will be 5 awards, with a monetary component, based on level of training (Graduate Student, Resident, Clinical Fellow, Post-Doctoral Fellow, Medical Student), rather than type of presentation. (Please see judging criteria on our website.) These awards will be presented at the wine and cheese reception between 5:30 and 6:30 p.m.

***Please see http://www.obgyn.utoronto.ca/Research/ResearchDay.htm for information or contact Helen Robson at* helen.robson@utoronto.ca**

Obstetrics & Gynaecology
UNIVERSITY OF TORONTO

RESEARCH DAY CONTACT INFORMATION
(To accompany abstract submission by email)
29th Annual Research Day
Friday, May 4, 2012

[This is a Word document – please type in the appropriate responses, save under your name, i.e. Jones Contact Information.doc and email, along with your abstract, to: helen.robson@utoronto.ca by **Monday, March 5, 2012**.]

Abstract Title:

Category (Gynaecologic Oncology, Gynaecology, Maternal-Fetal Medicine/Obstetrics, Paediatrics and Adolescent Gynaecology, Reproductive Sciences, or Urogynaecology):

Preference – PLEASE DISCUSS WITH YOUR SUPERVISOR.
(Oral, Poster, or None):

Do you wish to **withhold your abstract** from **online publication** by reason of intellectual property rights? (eg. an impending patent) Yes/No:

Name of Trainee:

Mode of Address (Mr., Miss, Ms, Mrs., Dr. and include whether M.D. or Ph.D.):

If you receive an award, how would you like your name to appear on the certificate? (eg. Josephina M Doe MD or Josie Doe MD or JM Doe MD):

Affiliation (Hospital, Institute. Department or UT):
Name of Supervisor:
Email address of Supervisor:

University of Toronto Training Status (at submission and Research Day) Please include ALL that apply, eg. a resident also doing a graduate programme should include both.
(Graduate Student = G; Resident = R; Clinical Fellow = F; Post-Doctoral Fellow = PD; Medical Student = M):
If not a U of T trainee, please explain status:

Contact Info for Trainee **before** Research Day (**email,** address, telephone, fax, pager number):

Home Address if not as above(**email,** address, telephone):

Please complete this form, save it under your last name, i.e. Jones Contact Information.doc and email to Helen Robson, helen.robson@utoronto.ca along with your abstract, by Monday, March 5, 2012. Thank you.
Documents and information also at: http://www.obgyn.utoronto.ca/Research/ResearchDay.htm

Obstetrics & Gynaecology
UNIVERSITY OF TORONTO

RESEARCH DAY ABSTRACT REQUIREMENTS:

PLEASE SUBMIT ONLY ONE ABSTRACT. You may submit work in progress. *Please help us to streamline the process of submission and printing by following the guidelines below.*

Format: Word
Margins: top, left, right and bottom all 1 inch
Font: Times New Roman
Font Size: 12
Spacing: Single-spaced
Length: Maximum of **ONE** page
Format: Do not justify or centre.
Structured abstract required with headings:

Objectives
Methods
Results
Conclusions

Template: Please use the attached template for format re titles and names.

Training Status: Graduate Student = G; Resident = R; Clinical Fellow = F; Post-Doctoral Fellow = PD; Medical Student = M
Your training status should be incorporated into the author line. Please see template.

Spelling: Please check your spelling and grammar.

Tables are allowed as long as the total length is within the one page limit**.**

Graphics, if you have them, should be incorporated into your poster and **not** your abstract.

Contact information sheet: Please make sure your contact information is correct, with current information and also your permanent address after Research Day, just in case there is a need to communicate with you after the event.

Submitting: Please use the template for your **abstract** and **save under your last name,** i.e. Jones Abstract.doc. Please complete the **Contact Information form** and **save under your last name,** i.e. Jones Contact Information.doc. Please **email both** documents to Helen Robson at **helen.robson@utoronto.ca by Monday, March 7, 2011. You will receive an acknowledgement of your submission.**

If you have any questions, please contact Helen Robson at helen.robson@utoronto.ca Thank you.

Documents and information on Research Day are also available at:
http://www.obgyn.utoronto.ca/Research/ResearchDay.htm

EXAMPLE: **ABSTRACT #** ***[Leave this line as is]***

Assessment of the Fetal Heart Prior to 15 Weeks' Gestation ***[Title is in bolded Title case.]***
Fionnuala McAuliffe[F](1), Edgar Jaeggi(2), Lisa Hornberger(2)***.[Only the first author is bolded, with designation re training status in square brackets]***
(1)Maternal-Fetal Medicine Division, Department of Obstetrics & Gynaecology, Mount Sinai Hospital, (2)Department of Cardiology, Hospital for Sick Children, University of Toronto.
[space]
Objective: We sought to document fetal cardiac anatomy by ultrasound prior to 15 weeks' gestation. ***[Heading bolded – main question, objective or hypothesis.]***
[space]
Methods: This is a prospective observational study with institutional ethics approval. Following informed written consent, fifty-seven women underwent transabdominal … ***[Heading bolded – study design, participants, outcome measures]***
[space]
Results: In all cases we obtained the four chamber view and assessed ventricular function. The tricuspid and mitral valves were seen in 52 (92% of cases… ***[Heading bolded -- summary of data]***
[space]
Conclusions: The fetal heart can be examined early in pregnancy and a significant proportion of major structural defects identified. . . ***[Heading bolded – summary and interpretation/significance of findings]***

Funded by: ***[Heading bolded, source of funding, only if applicable]***

Obstetrics & Gynaecology
UNIVERSITY OF TORONTO

JW Knox Ritchie Research Award Criteria

Principles:

1. Only a trainee (clinical fellow, graduate student, post-doctoral fellow, medical student or resident affiliated with the University of Toronto Department of Obstetrics and Gynaecology) is eligible for an award.
2. The submitter must be a trainee at the time of submission and at Research Day.
3. If the trainee is in more than one category, i.e. resident and graduate student, both those categories should be noted in the submission.
4. Each trainee may submit only **one** abstract.
5. Work in progress is welcomed and **is eligible** for an award.
6. Trainees must be present during the poster session for the entire period.
7. The trainee is eligible for an award only if he/she presents his/her own work.
8. Those in the **Other** category are not eligible for an award.
9. There will be 5 awards, with a monetary component, based on level of training (Graduate Student, Resident, Clinical Fellow, Post-Doctoral Fellow, Medical Student), rather than type of presentation.
10. Oral = Poster for evaluation purposes.
11. Each presentation is judged by at least 2 people, one or two chairs and one or two judges.
12. Any judge with a conflict in his/her session will cede to an alternate judge for marking.
13. **The winners of these awards are candidates for the APOG (The Association of Professors of Obstetrics and Gynaecology of Canada) Best of the Best competition**.

Judging Criteria:

The following information will be provided on the judging form. Each criterion is marked from 1-10 with 1 being the *lowest* and 10 being the *highest*, for a maximum total of 50 marks.

Originality = New topic or novel approach? (**Mark out of 10)**

Scientific Merit = Is the topic important and worth studying? Is this a useful examination? Does this research advance the field? (**Mark out of 10)**

Study Design and Analysis = Is the design, and are tests, appropriate and done properly? **(Mark out of 10)**

Interpretation and Conclusions = Does the candidate examine all data and inferences? Are there realistic and practical conclusions? **(Mark out of 10)**

Presentation = Is the presentation, oral or poster**,** well developed and explained? Is the poster easy to read? Is the candidate able to respond well to questions? **(Mark out of 10)**

Total = addition of criteria columns to a maximum of 50 marks