The 15th Annual Gilbert S. Greenwald Symposium on Reproduction and Perinatal Research

October 18-19, 2018

KU MEDICAL CENTER
The University of Kansas

Biography - Gilbert S. Greenwald

The Institute for Reproduction and Perinatal Research at the University of Kansas Medical Center hosts the Annual Gilbert S. Greenwald Symposium on Reproduction in honor and as a memorial to the life and research career of Gilbert S. Greenwald, PhD. Professor Greenwald had an illustrious career as a Distinguished Professor at the Medical Center and as an internationally recognized reproductive biologist.

Professor Greenwald received his doctorate from the University of California at Berkeley, followed by postdoctoral studies at the Carnegie Institute of Embryology in Baltimore. He then moved to his first faculty appointment in the Department of Anatomy at the University of Washington. He joined the Departments of Obstetrics & Gynecology and Anatomy at the University of Kansas Medical Center in 1961 where he held an endowed chair in Research in Human Reproduction. He also served as chair of the Department of Physiology at the Medical Center for 16 years (1977-1993).

Professor Greenwald received numerous awards for his outstanding research accomplishments from several scientific societies. Among these is the Distinguished Service Award from the Society for the Study of Reproduction for his work as one of the founding members and early president of the Society, as well as Editor-in-Chief of its journal, Biology of Reproduction. Professor Greenwald also received the Carl Hartman Award for a career of outstanding scientific contributions to the field of reproductive biology.

The National Institutes of Health supported his research over his entire career. Professor Greenwald trained more than 50 graduate students and postdoctoral fellows and was instrumental in the career development of numerous faculty, including several currently holding leadership positions at the University of Kansas Medical Center and at other academic institutions throughout the world. He was a true scholar, a superb mentor, and a generous friend. Professor Greenwald passed away on August 26, 2004.

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Sincere thanks to our generous sponsors and volunteers for making this event possible.

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Beth Greenwald Jordan and Jerry Jordan
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School of Medicine Bohan Endowed Speaker Program
Institute for Reproductive Health and Perinatal Research
NIH R13 HD083029 (Katherine Roby, PI)
Department of Anatomy and Cell Biology
The University of Kansas Cancer Center

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EVENT SUPPORT STAFF:

Institute for Reproduction and Perinatal Research
Priscilla Nechrebecki, BS, Coordinator
Stacy Oxley, BA, Associate Director of Administration

Symposium History

Plenary Speakers

2004

Harry Weitlauf, MD
Texas Tech University
Osborn Address

James Cross, PhD
University of Calgary

B. Anne Croy, DVM, PhD
University of Guelph

Mary Hunzicker-Dunn, PhD
Northwestern University Feinberg School of Medicine

Kevin Osteen, PhD
Vanderbilt University

Richard Stouffer, PhD
Oregon Health & Science University

Neena Schwartz, PhD
Northwestern University

2005

Shyamal K. Roy, PhD
University of Nebraska
Osborn Address

Sally Camper, PhD
University of Michigan

Thaddeus Golos, PhD
Wisconsin Regional Primate Center

Matthew Hardy, PhD
Population Council

Joy Pate, PhD
Ohio State University

John Robinson, PhD
Ohio State University

2006

Geula Gibori, PhD
University of Illinois at Chicago
Osborn Address

Robert Braun, PhD
University of Washington

Susan Fisher, PhD
University of California-San Fransisco

Fred Karsch, PhD
University of Michigan

John Schimenti, PhD
Cornell University

Teresa Woodruff, PhD
Northwestern University

2007

John J. Eppig, PhD
The Jackson Laboratory
Osborn Address

Indrani Bagchi, PhD
University of Illinois-Champaign

E. Mitchell Eddy, PhD
National Institute of Environmental Health & Safety

Patricia Hunt, PhD
Washington State University

Mark S. Roberson, PhD
Cornell University

Carole R. Mendelson, PhD
The University of Texas Southwestern Medical Center

Bruce D. Murphy, PhD
University of Montreal

2008

David Page, MD
Howard Hughes Medical Institute
MIT, Boston, MA
Osborn Address

Jon Levine, PhD
Northwestern University
Evanston, IL

Ina Dobrinski, M.V.Sc., PhD
University of Pennsylvania
Philadelphia, PA

John Peluso, PhD
University of Connecticut
Farmington, CT

Miles Wilkinson, PhD
MD Anderson Cancer Center
Houston, Texas

Nasser Chegini, PhD
University of Florida
Gainesville, Fl

2009

Jerome Strauss III, MD, PhD, Virginia Commonwealth University
Osborn Address

Alberto Darszon PhD
National Autonomous University of Mexico

Louis DePaolo, PhD
Eunice Kennedy Shriver NICHD, NIH

Keith Latham, PhD
Temple University

Ajay Nangia, MD
University of Kansas Medical Center

2009 *(continued)*

Stephanie Seminara, MD
Massachusetts General Hospital, Harvard Medical School

Thomas Spencer, PhD
Texas A&M University

2010

Marco Conti, MD
University of California-San Fransisco
Osborn Address

Romana A. Nowak, PhD
University of Ilinois

Susan S. Suarez, MS, PhD
Cornell University

John Davis, PhD
University of Nebraska Medical Center

Sergio R. Ojeda, DVM
Oregon National Primate Research Center

Stephen A. Krawetz, PhD
Wayne State University

Gil G. Mor, MD, MSc, PhD
Yale University

Symposium History

Plenary Speakers

2011

Kenneth S. Korach, PhD, NIEHS/NIH
Keynote Lecturer

Blanche Capel, PhD, Duke University Medical Center

Aaron J.W. Hsueh, PhD, Stanford University School of Medicine

Asgi T. Fazleabas, PhD, Michigan State University

Yaacov Barak, PhD, University of Pittsburgh

Tony M. Plant, PhD, University of Pittsburgh

2012

R. Michael Roberts, PhD, University of Missouri-Columbia, Keynote Lecturer

Kyle Orwig, PhD, University of Pittsburgh

Bruce D. Murphy, PhD, University of Montreal

Francesco DeMayo, PhD, Baylor College of Medicine

Yoel Sadovsky, PhD, University of Pittsburgh

2013

Martin M. Matzuk, MD, PhD, Baylor College of Medicine and Ben Taub General Hospital, Keynote Lecturer

Frederick vom Saal, PhD, University of Missouri-Columbia

Mary Hunzicker-Dunn, PhD, Washington State University

Louis J. Muglia, MD, PhD, University of Cincinnati College of Medicine

Derek Boerboom, DVM, PhD, University of Montreal

Shoukhrat Mitalipov, PhD, Oregon Health and Science University

2014

W. Lee Kraus, PhD, University of Texas Southwestern, Keynote Lecturer

Marisa S. Bartolomei, PhD, University of Pennsylvania

Suzanne Moenter, PhD, University of Michigan

Kathy Sharpe-Timms, PhD, University of Missouri-Columbia

David Zarkower, PhD, University of Minnesota

2015

Bert W. O'Malley, MD, Baylor College of Medicine
Keynote Lecturer

William Kinsey, PhD, University of Kansas Medical Center

Amy Ralston, PhD, MIchigan State

Wei Yan, MD, PhD, University of Nevada School of Medicine

James A. MacLean, PhD, Southern Illinois University

Robert Taylor, MD, PhD, Wake Forest School of Medicine

Qinglei Li, PhD, Texas A&M University

2016

David A. Haig, PhD, Harvard University
Keynote Lecturer

Alex Bortvin, MD, PhD, Carnegie Institution for Science

Jon D. Hennebold, PhD, Oregone National Primate Research Institute

Sarah Kimmis, PhD, McGill University

Donald F. Conrad, PhD, Washington University

Deborah M. Sloboda, PhD, McMaster Univeristy

Kathleen M. Caron, PhD, University of North Carolina

2017

Kent Thornburg, PhD, Oregon Health and Science University - Keynote Lecturer

Hugh Clarke, PhD, McGill University

Diana Laird, PhD, University of California - San Francisco

Liang Ma, PhD, Washington University - St. Louis

James Pru, PhD, Washington State University

Eric Greer, PhD, Harvard Medical School, Boston Children's Hospital

Mellissa Mann, PhD, Magee-Womens Research Institute

Program Schedule

THURSDAY, October 18th — **University of Kansas Medical Center, 3901 Rainbow Blvd., Kansas City, KS 66160**

3:30-5:00 p.m.	**Registration Opens**, 1006 Wahl West (Auditorium)
4:15 p.m.	Welcome from **Greenwald Symposium Trainee Elevator Pitch Organizer Pavla Brachova, PhD,** 1006 Wahl West (Auditorium)
4:15 - 4:50 p.m.	**Trainee Elevator Pitches**, 1006 Wahl West (Auditorium)
5:00 - 5:01 p.m.	Welcome from **Center for Reproductive Sciences Director Warren Nothnick, PhD, HCLD**
5:01 - 5:02 p.m.	Welcome from **Greenwald Symposium Organizing Committee Chair Katherine Roby, PhD**
5:02 - 5:05 p.m.	Welcome/Opening Remarks from **School of Medicine Senior Associate Dean for Research and Graduate Education Peter Smith, PhD**
5:05 - 5:08 p.m.	Brief History of the Greenwald Symposium/Dr. Greenwald from **Paul F. Terranova, PhD, Emeritus Professor**
5:08 - 5:10 p.m.	Keynote Lecturer Introduction, **Clifford Mason, PhD, Assistant Professor**
5:10 - 6:15 p.m.	**Keynote Lecture: Sandra T. Davidge, PhD, University of Alberta** ***"Impact of Pregnancy Complications on Maternal and Offspring Cardiovascular Health"***
6:30 - 8:30 p.m.	**Reception and Poster Session**, 5202 Health Education Building (HEB), Ad Astra Room (Poster Session Begins at 7 p.m.)

FRIDAY, October 19th — **Kansas City Public Library - Central (Downtown), 14 West 10th St., Kansas City, MO 64108, Helzberg Auditorium, 5th Floor**

BRING IN YOUR PARKING TICKET

(Parking garage located on NW corner of 10th & Baltimore, just West of library - this is the only paid parking lot for our event)

8:00 - 8:30 a.m.	**Breakfast / Registration**
8:30 - 8:35 a.m.	Welcome/Announcements from **Katherine Roby, PhD,** Chair, Greenwald Symposium Organizing Committee

Session I

8:35 - 9:05 a.m. *(Q&A 9:00-9:05 a.m.)*	**Paul S. Cooke, PhD, University of Florida** *(Ashley Cloud, BS, introducing)* *"Mechanism of Action of Membrane Estrogen Receptor 1: Role of the Histone Methyltransferase EZH2"*
9:05 - 9:20 a.m. *(Q&A 9:17-9:20 a.m.)*	**Masanaga Muto, PhD, University of Kansas Medical Center** *(Warren Nothnick, PhD, HCLD, introducing)* *"Tissue Factor Pathway Inhibitor Regulation of Endovascular Trophoblast Cell Development and Uterine Spiral Artery Remodeling at the Placentation Site "*
9:20 - 9:35 a.m. *(Q&A 9:32-9:35 a.m.)*	**Caroline Pfeiffer, BS, University of Missouri** *(Vargheese Chennathukuzhi, PhD, introducing)* *"Biological Role of Prostaglandin Synthase 2 (PTGS2) on Early Conceptus Development in Pigs"*

Program Schedule

9:35 - 10:05 a.m. *(Q&A 10:00-10:05 a.m.)*	**Ramakrishna Kommagani, PhD, Washington University School of Medicine, St. Louis** *(Vincentaben Khristi, PhD, introducing)* *"The Gut Microbiota: A Central Player in Endometriosis*
10:05 - 10:30 a.m.	**Morning Break**
Session II	
10:30 - 11:00 a.m. *(Q&A 10:55-11 a.m.)*	**Rebecca A. Simmons, MD, University of Pennsylvania School of Medicine** *(Kaela Varberg, PhD, introducing)* *"Eating for Two: Effects of Maternal and Paternal Diet on the Offspring"*
11:00 - 11:15 a.m. *(Q&A 11:12-11:15 a.m.)*	**Kendra Clark, BS, Iowa State University** *(Fu-Sheng Chou, MD, PhD, introducing)* *"Lean Maternal Gestational Diabetes Mellitus Impacts the Ovarian Proteome Basally and in Response to a Stressor Later in Life"*
11:15 - 11:30 a.m. *(Q&A 11:27-11:30 a.m.)*	**Michele R. Plewes, PhD, University of Nebraska Medical Center** *(Lane Christenson, PhD, introducing)* *"Dynamic Regulation of the Mitochondrial Effector Dynamin Like 1 (DNM1L) and Steroidogenesis in the Bovine Corpus Luteum"*
11:30 a.m. - 12:00 p.m. *(Q&A 11:55 a.m.-12 p.m.)*	**Joan S. Jorgensen, DVM, PhD, University of Wisconsin** *(Rikki Nelson, BS, introducing)* *"Cooperation Between Irx3 and Irx5 Promote Primordial Follicle Maturation and Survival"*
12:00 - 12:45 p.m.	**LUNCH** (Speakers and Trainees go through food line first; Trainee Speaker Interaction is from 12-12:45 p.m.)
12:45 - 1:30 p.m.	**Mingle Time**
1:30 - 1:45 p.m.	**Trainee Poster Award Presentation, Katherine Roby, PhD**
Session III	
1:45 - 2:15 p.m. (*Q&A 2:10-2:15 p.m.)*	**Satoshi H. Namekawa, PhD, Cincinnati Children's Hospital Medical Center** *(Keisuke Kozai, PhD, introducing)* *"Epigenetics in Spermatogenesis from Stem Cells to Sperm"*
2:15 - 2:30 p.m. *(Q&A 2:27-2:30 p.m.)*	**Pavla Brachova, PhD, University of Kansas Medical Center** *(Ning Wang, PhD, introducing)* *"ADAR1 A-to-I RNA Editing in Mouse and Human Oocytes"*
2:30 - 2:45 p.m. *(Q&A 2:42-2:45 p.m.)*	**Philma Glora Muthuraj, M.V.Sc., University of Nebraska-Lincoln** *(Courtney Marsh, MD, MPH, FACOG, introducing)* *"Zika Virus Infection Induces Endoplasmic Reticulum Stress in Placental Trophoblast Cells"*
2:45 - 3:15 p.m. *(Q&A 3:10-3:15 p.m.)*	**Todd S. Macfarlan, PhD, NICHD (NIH)** *(Bhaswati Bhattacharya, MS, introducing)* *"The Impact of a Retroviral/Zinc Finger Gene 'Arms Race' on Mammalian Evolution"*
3:15 - 3:30 p.m.	**Closing comments - meeting adjourned**

KUMC Campus Map

15th Annual Gilbert S. Greenwald Symposium on Reproduction and Perinatal Research

The University of Kansas Medical Center, 39th & Rainbow campus

Parking is available in the P4 Garage at the northwest corner of the main campus.

Parking Instructions:
Take Adams St. off of Rainbow Blvd. to access the P4 Garage entrance. The gates will be open by 2:30 p.m. If the gates are not raised, use the call button and inform parking services that you are attending the Greenwald Symposium event.

1006 Wahl West (Auditorium):
Take the P4 Garage elevator up to the 5th level and walk across the walkway/bridge to access the Hemenway building. Continue walking south to the Health Education Building. Enter the Health Education Building via the exterior stairs. Once inside the HEB, you will be on the 1st floor - walk across the skywalk bridge over 39th Ave. When you enter the Orr Major building, turn left and walk past the Orr-Major elevators. 1006 Wahl West will be around the corner (to the left).

Health Education Building (HEB):
Walk back across the skywalk bridge to the HEB elevators. The evening's event will take place on the 5th floor, Ad Astra Room.

Event parking

Elevator

Event locations

Accessible parking spaces

Walking route to event locations

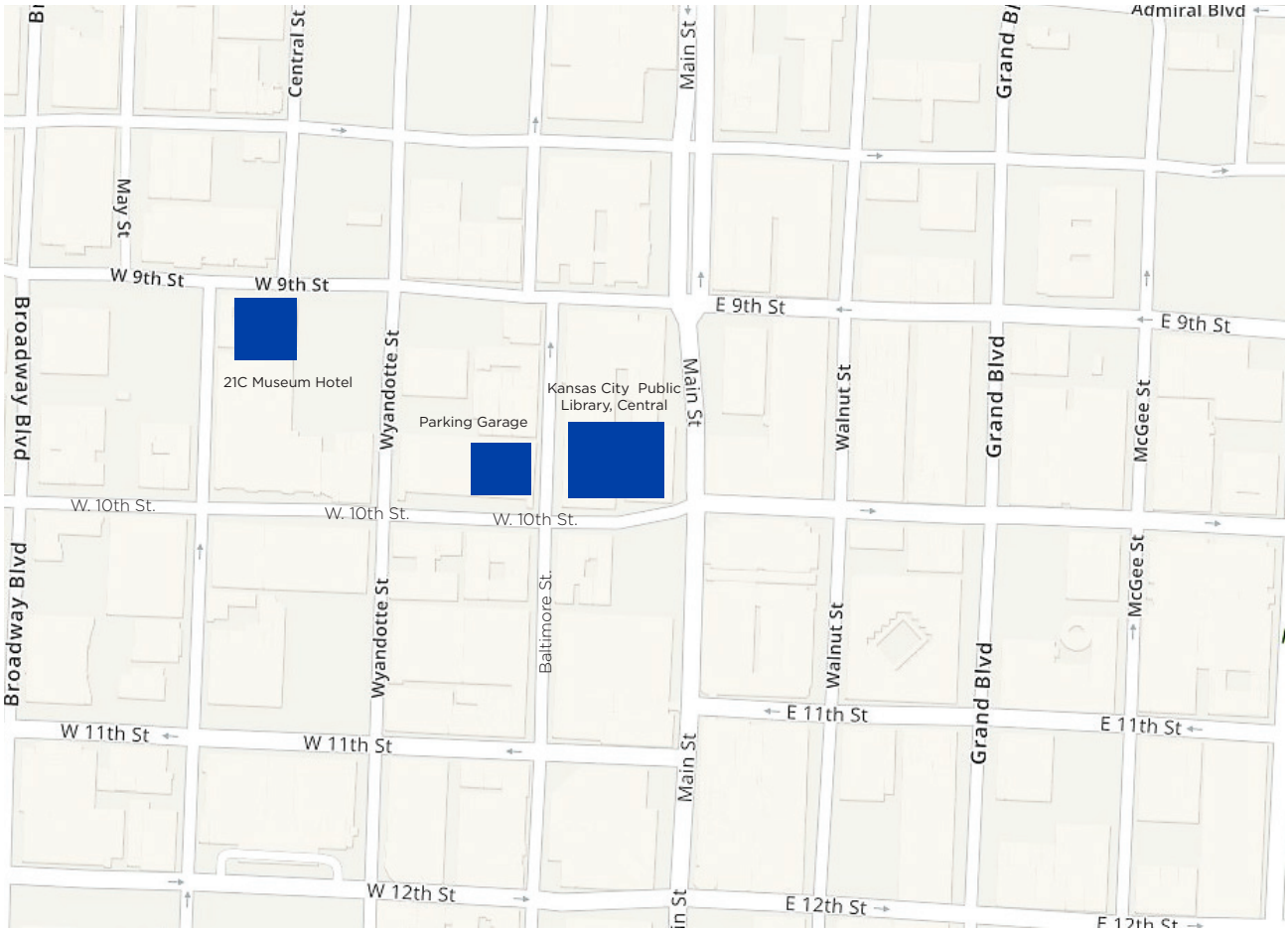
KU MEDICAL CENTER
The University of Kansas

Kansas City Map

The Kansas City Public Library, Central is located at 14 West 10th Street on the northeast corner of W. 10th St. and Baltimore in downtown Kansas City, Missouri.

The parking garage is west of the library, on the northwest corner of W. 10th and Baltimore. **Please enter the garage on Baltimore.** Parking for our event is free – let the attendant know you are with the Greenwald Symposium, and be sure to bring your parking ticket inside so we can validate it for you.

Enter the library at the main entrance on W. 10th
and take the elevator to the Helzberg Auditorium on the 5th floor.



Venue Information

The Kansas City Public Library - Central

The Kansas City Public Library system consists of a central library, nine branches, and an outreach services program serving a constituency of over 250,000 in Kansas City, Missouri. In addition to providing library services to residents, the Library also serves as a resource for the 1.7 million metropolitan residents of greater Kansas City.

In 2004, the Kansas City Public Library - Central moved into the former First National Bank building at 10th and Baltimore in downtown Kansas City, Missouri. The century-old building, a true masterpiece of craftsmanship with its marble columns, bronze doors and ornate mouldings, required remodeling and a fifth floor addition, but provided the framework for a modern and impressive urban library. The location features state-of-the-art technology, improved and increased services, meeting rooms, a screening room, a coffee shop and much more, all within the walls of a building originally constructed to convey a sense of strength and continuity. It is upon that foundation the Library places its vision for the next century to come.

Facts About the Library

•The Kansas City Public Library has ten locations.
•The Central Library is the largest facility, housing resources, special collections and administrative offices.
•More than 2,348,408 materials were checked out during the last fiscal year.
•The Inter Library Loan department loaned out 115,846 items last year to other libraries.
•2,492,118 customers used the Library system last year.
•The Library system counts 1,147,278 items in its holdings.

Helzberg Auditorium

The Library's most versatile meeting space, the Helzberg Auditorium is located on the 5th floor of the library. Helzberg is also aggressively styled with contemporary and clean lines for an energetic atmosphere, and features performance quality acoustics using cork flooring and specially designed ceiling elements, built-in AV system, and floor-to-ceiling windows on multiple sides that provide natural lighting.

Gladys Feld Helzberg

Gladys Feld Helzberg was the wife of the late Barnett C. Helzberg, Sr, of Helzberg Diamonds. Helzberg jewelry store was founded in 1915 by the late Morris Helzberg, in Kansas City, Kan., and expanded to a regional market by Barnett C. Helzberg, Sr. Gladys was an active member of the Kansas City Chapter of the Association for Women in Communications and one of the founders of Veterans' Voices. The Gladys Feld Helzberg Scholarship Fund was established in 1960 for talented journalism students and is administered by the University of Kansas endowment fund. She was also the founder of the Greater Kansas City chapter of the Brandeis Women's Committee.

Trainee Elevator Pitch Session

The Trainee Elevator Pitch Session provides trainees the opportunity to deliver an elevator pitch in a 1-slide, 2-minute presentation on Thursday, October 18, from 4:15-4:50 pm in the Wahl Hall West Auditorium (KUMC Campus).

The purpose of this exercise is to develop a concise and clear explanation of your research that even your grandmother may understand. Efficiently conveying your science to the public as well as to the scientific community is an important skill that will have life-long benefits if you can do it well. The purpose of an elevator pitch is to promote yourself, your skills, or the importance of your research, with the end goal of getting oneself introduced to a targeted person, creating a possibility for future communications, building a professional collaboration, or leading to a job interview.

Trainee Elevator Pitch Presenters *(in order of presentation)*

1	Nehemiah	Alvarez	PhD	Postdoctoral Fellow	University of Kansas Medical Center
2	Pavla	Brachova	PhD	Postdoctoral Fellow	University of Kansas Medical Center
3	Bailey	Bye	BS	Research Assistant	University of Kansas Medical Center
4	Ananya	Ghosh	MS	Graduate Student	University of Kansas Medical Center
5	Ayesha	Hasan	MD	Maternal Fetal Medicine Fellow	University of Kansas Medical Center
6	Marija	Kuna	PhD	Postdoctoral Fellow	University of Kansas Medical Center
7	Ikram	Mohamed	BS	Student Intern	Harris-Stowe State University
8	Philma Glora	Muthuraj	MS	Graduate Student	University of Nebraska-Lincoln
9	Masanaga	Muto	PhD	Postdoctoral Fellow	University of Kansas Medical Center
10	Rikki	Nelson	BS	Graduate Student	University of Kansas Medical Center
11	Stephen	Pierce	BS	Research Assistant	University of Kansas Medical Center
12	Regan	Scott	MS	Research Assistant	University of Kansas Medical center
13	Kaela	Varberg	PhD	Postdoctoral Fellow	University of Kansas Medical Center
14	Ayushi	Vashisht	MS	Pre-doctoral student	University of Kansas Medical Center
15	Xiaoyu	Zhang	PhD	Postdoctoral Fellow	University of Kansas Medical Center

Speaker Information

Keynote Lecturer

Sandra T. Davidge, PhD

Executive Director, Women and Children's Health Research Institute
Canada Research Chair in Maternal and Perinatal Cardiovascular Health
Professor, Departments of Obstetrics and Gynecology and Physiology
University of Alberta

"Impact of Pregnancy Complications on Maternal and Offpring Cardiovascular Health"

Dr. Sandy Davidge received her PhD from the University of Vermont in 1993 and continued postdoctoral fellowship training at the Magee Womens Research Institute in Pittsburgh. Dr. Davidge then moved to Edmonton, Alberta Canada in 1996 where she is currently the Executive Director of the Women and Children's Health Research Institute and Professor in the Departments of Obstetrics & Gynecology and Physiology at the University of Alberta. She is a Tier 1 Canada Research Chair in Maternal and Perinatal Cardiovascular Health and a Fellow in the Canadian Academy of Health Science. Dr. Davidge serves on many national and international grant panels and is on the editorial board for the Biology of Sex Differences and American Journal of Physiology. Dr. Davidge's research program encompasses studying cardiovascular function as it relates to 1) complications in pregnancy (preeclampsia and maternal aging) and 2) developmental origins of adult cardiovascular disease. Dr. Davidge has published over 220 original peer-reviewed manuscripts and 27 review articles in these areas and is currently funded by the CIHR Foundation Grant Program.

The 2018 Keynote Lecture is supported in part by a generous contribution from the Society for the Study of Reproduction. For more information regarding SSR, please stop by our registration table for a brochure, or visit them online at SSR.org.

Session I

Paul S. Cooke, PhD
Professor and Chair
Department of Physiological Sciences
University of Florida

"Mechanism of Action of Membrane Estrogen Receptor 1: Role of the Histone Methyltransferase EZH2"

Paul S. Cooke received a Ph.D. in Physiology in 1983 from the University of California-Berkeley. Following an NIH Postdoctoral Fellowship with Jerry Cunha at the University of California-San Francisco, in 1987 he joined the Department of Veterinary Biosciences at the University of Illinois, where he rose to the rank of full professor and served as the Billie A. Field Endowed Chair in Reproductive Biology from 2004-2011. In 2011, Dr. Cooke moved to the University of Florida, where he presently serves as the chair of the Department of Physiological Sciences and as a University of Florida Research Foundation (UFRF) Professor.

Ramakrishna Kommagani, PhD
Assistant Professor
Department of Obstetrics and Gynecology
Washington University School of Medicine, St. Louis

"The Gut Microbiota: A Central Player in Endometriosis"

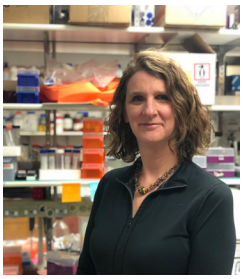
Dr. Ramakrishna Kommagani received B.S. and M.S. in Microbiology from Osmania University, India and Ph.D. in Biomedical Sciences from Wright State University, Ohio. Subsequently, Dr. Kommagani conducted postdoctoral training in the laboratory of Dr. Bert O'Malley at Baylor College of Medicine, where he investigated the cellular and molecular mechanisms of Steroid Receptor Coregulator (SRC-2) function in normal endometrial functions. Dr. Kommagani was then a Research Instructor in the Department of Molecular and Cellular Biology at Baylor College of Medicine. His current research focuses on the relevance of the genetics, epigenetics and metagenomics, and their respective roles in the uterine function and dysfunction. Presently, Dr. Kommagani is an Assistant Professor in the Department of Obstetrics & Gynecology and a faculty member in the Center for Reproductive Health Sciences. In 2015, Dr. Kommagani received the Early Investigators Award from the Endocrine Society. He has published more than 20 peer-reviewed manuscripts in high impact journals including Cell Metabolism, Cell Research and PLoS Genetics. He is also a recipient of the NIH/NICHD K99/R00 grant to establish his independent research program on two endocrine-related clinical issues that adversely affect a woman's reproductive health: early implantation failure and endometriosis.

Session II

Rebecca A. Simmons, MD
Hallam Hurt Professor in Neonatology
Department of Pediatrics
University of Pennsylvania School of Medicine

"Eating for Two: Effects of Maternal and Paternal Diet on the Offspring"

Dr. Simmons completed her M.D. at the University of Arizona in Tucson and then went on to a Residency in Pediatrics at the University of Arizona Health Sciences Center followed by a Neonatal-Perinatal Medicine Fellowship at UCSF. Dr. Simmons is now the Hallam Hurt Endowed Chair and Professor of Pediatrics at the Perelman School of Medicine and an Attending Physician at the Children's Hospital of Philadelphia. Her research focuses on the causal mechanistic links between the intrauterine milieu and type II diabetes and obesity in the adult with a focus on epigenetics and mitochondria function. Dr. Simmons is a PI of the March of Dimes Preterm Birth Research Center at the University of Pennsylvania. She is also the Co-Director of the Center for Excellence in Environment and Toxicology Research at the University of Pennsylvania.



Joan S. Jorgensen, DVM, PhD
Associate Professor
Department of Comparitive Biosciences
University of Wisconsin

"Cooperation Between Irx3 and Irx5 Promote Primordial Follicle Maturation and Survival"

Joan S. Jorgensen got her DVM from the University of Wisconsin-Madison in 1993 and then became specialized in equine medicine with ACVIM Board certification in 1997. She went on to Case Western Reserve University to do her PhD and a short Post doc with Dr. John Nilson focusing on sex steroid regulation of gonadotropin subunits. Her first faculty position was at the University of Illinois from 2002-2008 where she transitioned to studying gonad differentiation. In 2008, she moved back to her alma mater, the University of Wisconsin-Madison, where she is currently an Associate Professor.

Session III

Satoshi H. Namekawa, PhD
AssociateProfessor
Department of Pediatrics
Cincinnati Children's Hospital Medical Center

"Epigenetics in Spermatogenesis from Stem Cells to Sperm"

Dr. Namekawa received his PhD from Tokyo University of Science in 2005. He completed postdoctoral training in the laboratory of Dr. Jeannie T. Lee at Massachusetts General Hospital and Harvard Medical School in 2009, and attained his faculty appointment at Cincinnati Children's Hospital Medical Center in 2009. He received the Basil O'Connor Award from March of Dimes Foundation in 2011, the New Investigator Award from the Society for the Study of Reproduction in 2015, and the Research Achievement Award from Cincinnati Children's Hospital Medical Center in 2016.

Todd S. Macfarlan, PhD
Investigator
Eunice Kennedy Shriver National Institute of Child Health and Human Development (NIH)

"The Impact of a Retroviral/Zinc finger Gene 'Arms Race' on Mammalian Evolution"

Todd earned his PhD in Cell and Molecular Biology from the University of Pennsylvania in 2000 working in the lab of Debu Chakravarti, studying the histone binding and transcriptional repressive activities of THAP domain proteins. After his PhD, Todd joined the laboratory of Samuel Pfaff at the Salk Institute for Biological Studies, where he explored the function of the histone demethylase LSD1 during mouse development, unexpectedly uncovering a role of LSD1 in the regulation of Endogenous Retroviruses, and second, a role for Endogenous Retroviruses as maker genes for early stages of development. Todd was then recruited to the NIH in July of 2012 as part of the Earl Stadtman Investigator search in Chromosome Biology and Epigenetics. Within the Division of Developmental Biology at the NICHD, Todd now heads the Unit on Mammalian Epigenome Reprogramming, spending most of his time exploring the impact of Endogenous Retroviruses and their KRAB-zinc finger protein controllers on embryonic development and on the evolution of new traits in mammals.

Abstract Titles

1) **TRAINEE ORAL PRESENTATION AND POSTER: Tissue Factor Pathway Inhibitor Regulation of Endovascular Trophoblast Cell Development and Uterine Spiral Artery Remodeling at the Placentation Site.** **Masanaga Muto**, Damayanti Chakraborty, Kaela M. Varberg, Khursheed Iqbal, Regan L. Scott, and Michael J. Soares.

2) **Rapid Changes in Cellular Metabolism Induced by Luteinizing Hormone in the Corpus Luteum.** **Emilia Przygrodzka**, Pan Zhang, Hou Xiaoying, and John S. Davis.

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5) **Atypical protein kinase C iota is essential to establish maternal-fetal exchange surface during mammalian embryonic development.** **Bhaswati Bhattacharya** and Soumen Paul.

6) **Signaling of the Pro-Inflammatory Cytokine TNFa through NFkB-p65 Increases Gdf9 and Decreases Figla mRNAs in Oocytes of Primary Follicles**. **Kelsey R. Timme**, Heidi B. Miller, and Jennifer R. Wood.

7) **Transposable element expression in placental development.** **Nehemiah S. Alvarez**, Kesiuke Kozai, Damayanti Chakraborty, Khursheed Iqbal, and Michael J. Soares.

8) **Establishing endometrial epithelial organoids to investigate uterine gland function in humans and mice.** **Harriet C. Fitzgerald**, Pramod Dhakal, Linda M. Rowland, Danny J. Schust, and Thomas E. Spencer.

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27) **Altered Blood Plasma and Follicular Fluid Lipid Profiles Predict Alterations in Cell Signaling, Metabolism, and Immune Function in Cows with Androgen Excess. Alexandria P. Snider**, Renata Spuri Gomes, Sarah M. Romereim, Adam F. Summers, Mohamed A. Abedal-Majed, Sarah C. Tenley, Scott G. Kurz, Jeff Bergman, Robert A. Cushman, John S. Davis, Jennifer R. Wood, and Andrea S. Cupp.

28) **Development of novel mouse models using CRISPR genome editing approaches. Katelin Gibson**, Illya Bronshteyn, Julia Draper, Melissa A. Larson, and **Jay L. Vivian.**

29) **A growth factor that influences placental health in mice. Ikram Mohamed.**

30) **The Role of Interferon Gamma Signaling on Hemochorial Placentation. Keisuke Kozai,** Regan L. Scott, Khursheed Iqbal, Masanaga Muto, Michael J. Soares.

31) **Ovarian Cortex from High A4 Cows Secrete Excess Steroid Hormones Contributing to Arrested Follicle Development, Increased Oxidative Stress and Fibrosis Which can be Rescued by Angiogenic VEGFA165. SA Springman**, MA Abedal-Majed, ML Hart, V Largen, MPS Magamage, SG Kurz, KM Sargent, J Bergman, RM McFee, RA Cushman, JS Davis, JR Wood, and AS Cupp.

32) **Barriers to Fertility Preservation in Adolescents Exposed to Fertility Threatening Therapy.** **Emily Pfeifer**, Elizabeth Kresie, and Courtney Marsh.

33) **Normalizing the Immune System of the Rat for Analysis of Immune Cell Function at the Maternal-Fetal Interface.** **Regan L. Scott** and Michael J. Soares.

34) **Alterations in fetal neurogenesis and offspring cognitive functions in a murine model of hypoxia-induced placental insufficiency.** **Pei-Shan Wang**, Chu-Yen Chen, and Fu-Sheng Chou.

35) **Attainment and Maintenance of Pubertal Cyclicity May Predict High A4 cows with Reduced Fertility.** **Sarah Nafziger**, Mohamed A. Abedal-Majed, Sarah Tenley, Adam Summers, Mariah Hart, Jeff Bergman, Scott Kurz, Jennifer Wood, Robert Cushman, and Andrea S. Cupp.

36) **IL17f and the Maternal-Fetal Interface; A genetic rat model.** **Stephen H. Pierce**, Khursheed Iqbal, Masanaga Muto, Keisuke Kozai, and Michael J. Soares.

37) **Exploring the Role of Catechol-O-methyltransferase (COMT) in pregnancy outcome.** **Khursheed Iqbal**, **Stephen Pierce**, Pramod Dhakal, and Michael J. Soares.

38) **TRAINEE ORAL PRESENTATION ONLY - Biological Role of Prostaglandin Synthase 2 (PTGS2) on Early Conceptus Development in Pigs.** **C.A. Pfeiffer**, A.E. Meyer, L.D. Spate, J.A. Benne, R.F. Cecil, T.E. Spencer, R.S. Prather, and R.D. Geisert.

39) **TRAINEE ORAL PRESENTATION ONLY - Dynamic Regulation of the Mitochondrial Effector Dynamin Like 1 (DNM1L) and Steroidogenesis in the Bovine Corpus Luteum.** **Michele R. Plewes**, Heather Talbott, Xiaoying Hou, Pan Zhang, and John S. Davis.

40) **TRAINEE ORAL PRESENTATION ONLY - Lean maternal gestational diabetes mellitus impacts the ovarian proteome basally and in response to a stressor in later life.** **Kendra L. Clark**, Omonseigho Talton, Shanthi Ganesan, Laura C. Schulz, and Aileen F. Keating.

Full Abstracts

1) **TRAINEE ORAL PRESENTATION AND POSTER: Tissue Factor Pathway Inhibitor Regulation of Endovascular Trophoblast Cell Development and Uterine Spiral Artery Remodeling at the Placentation Site.** **Masanaga Muto**, Damayanti Chakraborty, Kaela M. Varberg, Khursheed Iqbal, Regan L. Scott, and Michael J. Soares. Department of Pathology and Laboratory Medicine, University of Kansas Medical Center, Kansas City, Kansas.

Hemochorial placentation is characterized by the development of trophoblast cells specialized to interact with uterine and fetal vascular beds. These specialized trophoblast cells arise from a trophoblast stem (TS) cell population that possesses the capacity to differentiate into multiple trophoblast cell lineages. Among the differentiated trophoblast lineages are cells that acquire an endothelial cell-like phenotype, termed “endovascular trophoblast cells”. To investigate regulatory mechanisms that control the development of the endovascular trophoblast cell lineage, we utilized rat TS cells for RNA sequence analysis. The differentiation phenotype was characterized by transcript signatures consistent with acquisition of known differentiated trophoblast cell lineages and a striking endothelial cell-like phenotype. Among the upregulated transcripts were anti-coagulation factors, including tissue factor pathway inhibitor (*Tfpi*). Disruption of TFPI expression in rat TS cells interfered with development of the endovascular trophoblast cell phenotype. Furthermore, TFPI was shown to be expressed in endovascular trophoblast cells of the rat placentation site. To examine an in vivo role for trophoblast cell *Tfpi*, we initially utilized ex vivo rat trophoblast-specific lentiviral delivery of control shRNAs (LV-control shRNAs) or *Tfpi* shRNAs (LV-*Tfpi* shRNA) followed by embryo transfer to pseudopregnant recipient female rats. Fetal and placental weights of LV-*Tfpi* shRNA transduced embryos were significantly decreased at gestation days 15.5 and 18.5 compared to treatment with LV-control shRNAs. In vivo TFPI knockdown profoundly restricted the depth of intrauterine trophoblast invasion and was associated with a prominent increase in uterine spiral arteriole fibrin/fibrinogen deposition. A complementary rat model generated by *Crispr/Cas9* genome editing of the *Tfpi* locus was used to generate a knockout rat model. The *Tfpi* mutation resulted in prenatal lethality. Its impact of the mutation on placentation is still under investigation. To examine conserved molecular mechanisms of TFPI action on trophoblast development, shRNA-mediated TFPI knockdowns were performed using a human TS cell culture model. LV-*TFPI* shRNA transduced human TS cells failed to differentiate into the extravillous trophoblast cell differentiation. Overall, these results implicate *Tfpi* as a potential regulator of invasive endovascular trophoblast cell development, uterine spiral artery remodeling, and hemostasis at the maternal-fetal interface. (Supported by Lalor Foundation Postdoctoral Fellowships; NIH HD020676, HD079363)

2) **Rapid Changes in Cellular Metabolism Induced by Luteinizing Hormone in the Corpus Luteum.** **Emilia Przygrodzka**[1], Pan Zhang[1], Hou Xiaoying[1], John S. Davis[1,2], [1]Olson Center for Women’s Health, Department of Obstetrics and Gynecology, University of Nebraska Medical Center; and [2]Veterans Affairs Medical Center, Omaha, NE.

The corpus luteum (CL) is an endocrine gland that produces progesterone (P_4), a steroid hormone responsible for establishment and maintenance of pregnancy. Luteinizing hormone (LH) is crucial for the formation, function and maintenance of the CL. However, the cellular responses to LH that mediate luteal steroidogenesis remain to be fully determined. In the present study, the metabolic responses to LH treatment were examined in bovine small luteal cells (SLC). The SLC were isolated from bovine CL and treated with LH (10 ng/ml) for 10, 30, 60 and 240 minutes. Cells and *post*-incubation media were harvested to determine metabolomics changes using GC/MS and LC/MS/MS platforms.

Metabolomics changes were verified by using Seahorse analysis. Metabolomics data and Seahorse results were analyzed using Welch's two-sample t-test and one-way ANOVA test, respectively. Analysis revealed 276 and 117 metabolites in cell extracts and media, respectively. The most up- and down-regulated metabolites were lipids (55.81%) and carbohydrates (38.88%) in cell extracts, and lipids (33.33%) and amino acids (31.25%) in culture media. Concentrations of P_4 and cAMP rapidly increased ($p<0.05$) in cells and media *post*-LH treatment. The content of isocaproate, a product of CYP11A1, and lanosterol, a cholesterol precursor, were increased ($p<0.05$) in cells and media. Glucose and fructose were significantly decreased ($p<0.05$) in cells and media after LH treatment. Simultaneously, lactate was increased ($p<0.05$) cells and media, while pyruvate was depleted ($p<0.05$) in media. Since, metabolomics results suggest a stimulatory effect of LH on glycolysis pathway, Seahorse method allowing live analysis of mitochondria function was performed. LH stimulated ($p<0.05$) ATP production and basal oxygen consumption rate, an indicator of oxidative phosphorylation. LH also increased ($p<0.05$) the extracellular acidification rate, an glycolysis indicator. The results indicate that LH stimulates glycolysis in SLC providing both appropriate ATP production and substrates for P_4 synthesis. Supported by NIFA USDA 2017-67015-26450, VA and NIH R01HD092263.

3) **Menstrual endometrial biopsy cyclinA2 expression correlates with in vitro fertilization outcome.** **Katelyn Schumacher,** Courtney A. Marsh, Kristin Holoch, Michael Lydic, Amanda Graham, Warren B. Nothnick. University of Kansas Medical Center.

Objective: Although there are multiple modalities to test etiology of infertility, there are few biologic markers to predict success with assisted reproductive technology (ART). Cyclin A2 (CCNA2) is emerging as a multi-functional protein capable of regulation of tissue regeneration as well as functioning as an RNA-binding protein. Absence of CCNA2 in the germ line is associated with embryonic lethality. Although considerable tissue regeneration occurs during the early stages of the menstrual cycle, the role of CCNA2 in the endometrium is poorly understood. In this study, we examine the function of CCNA2 in the endometrium and its association with pregnancy. **Design**: A prospective design was utilized which involved a cohort on women, aged 18-45, seen in a university setting reproductive endocrine clinic undergoing ART to conceive. **Materials and Methods**: Women undergoing in vitro fertilization were subjected to a scratch biopsy, which was performed in normal sterile fashion with an endometrial pipelle on menstrual cycle day 3. Endometrium was prepared and subjected to immunohistochemical (IHC) localization for cyclin A2 (CCNA2) and qRT-PCR assessment of mRNA. Primary outcome of interest was clinical pregnancy, which was defined as fetal cardiac activity seen on ultrasound from pregnancy resulting in same cycle as endometrial biopsy. Fisher's exact test was performed with $p<0.05$ used for determining statistical significance between the groups. CCNA2 IHC outcome values were expressed as H-SCOREs (intensity of staining X percent of cells staining at that intensity X 100%) for each cell type and data were separately analyzed using unpaired t-tests. **Results**: CCNA2 protein localized to stromal and glandular epithelium with stromal expression being more predominant. CCNA2 localization in both cell types was exclusively nuclear. Stromal and glandular epithelia positive nuclei were significantly greater in those women which achieved pregnancy compared to those that did not ($P<0.0001$; H-SCORE STROMA = 57 + 10 vs. 3 + 0.6; H-SCORE EPITHELIUM = 6 + 3 vs. 3 + 0.6). Despite significant differences in protein expression, CCNA2 mRNA expression levels were similar between groups. Based upon these data, we defined a positive Stromal H-SCORE of 25 or higher as positive outcome for CCNA2 staining. We constructed a 2 x 2 contingency table in which pregnancy outcome was defined as either positive or negative, and CCNA2 H-SCORE was defined as either positive (>25 stroma) or negative (<25 stroma). Fisher's exact test revealed statistical significance between groups ($P = 0.0045$; sensitivity 95% CI = 0.664 – 1.00; specificity 95% CI = 0.292 – 1.00). There was no association between pregnancy outcome or CCNA H-SCOREs when controlling for patient age, cause of infertility, endometrial thickness or type of hormonal stimulation. **Conclusions:** We interpret these data to suggest that endometrial CCNA2 expression is altered during the menstrual stage of the menstrual cycle. These alterations may impair proper development and/or responsiveness to hormonal signaling essential for preparation of a suitable endometrial environment for successful pregnancy. As such, CCNA2 expression in the menstrual endometrium may be associated with ART success. A larger study population is needed to assess the validity of these findings and increase specificity and sensitivity.

4) **Effects of Developmental Exposure to Bisphenol A or Bisphenol S on Metabolism and Voluntary Physical Activity.** Jiude Mao[1,2], Michelle J. Farrington[1,2], Rebecca J. Welly[3], Victoria J. Vieira-Potter[3], **Cheryl S. Rosenfeld**[1,2,4] [1]Bond Life Sciences Center, [2]Biomedical Sciences, [3]Nutrition & Exercise Physiology, [4]Thompson Center for Autism and Neurobehavioral Disorders, University of Missouri, Columbia, MO 65211.

Environmental chemicals may be contributing to the dramatic rise in obesity. As a widely prevalent endocrine disrupting chemical (EDC), phenolic compounds, such as bisphenol A (BPA) have received considerable attention as a potential "obesogen". Extensive studies have linked developmental exposure to BPA with later obesity and metabolic disorders. More recently, the BPA substitute, BPS, has also been implicated with metabolic disease. Both bisphenols have been shown to operate primarily through estrogen (E_2) receptor α (ESR1), which is highly expressed in brain, especially during fetal development. These EDCs might act as an agonists or antagonists of ESR1. In previous studies, we showed that adult female California mice (*Peromyscus californicus*) developmentally exposed to BPA exhibit suppressed voluntary physical activity (PA) and impaired fat metabolism. Only a few other studies to date have examined whether BPA and other EDCs affect PA, even though physical inactivity is a major contributor to the chronic positive energy balance that causes obesity. We hypothesize that during development, maternal BPA or BPS exposure suppresses fetal brain ESR1 signaling resulting in reduced dopamine signaling in key brain regions (especially the nucleus accumbens- NAc) needed to initiate PA. Based on recent evidence that maternal exercise has fetal programming capacity, such that offspring of exercising dams display more PA and are protected against later metabolic dysfunction, we further sought to determine if maternal exercise has the capacity to combat the harmful behavioral and metabolic effects of BPA and BPS. Using C57BL6 mice, we validated our previous finding that exposure of dams to 200 mg BPA or BPS/kg body weight two weeks prior to breeding and throughout gestation and lactation reduced energy expenditure and voluntary PA in offspring. Importantly, provision of running wheels to dams reversed some of the adverse EDC-induced effects on F_1 offspring. Current work suggests that developmental exposure to bisphenols suppresses later PA, potentially by altering ESR1-dopamine signaling in the NAc, but maternal exercise helps mitigate some of these detrimental offspring effects. These studies for the first time explore the possibility that encouraging mothers to exercise might help combat adverse chemical exposure risks to their unborn offspring.

5) **Atypical protein kinase C iota is essential to establish maternal-fetal exchange surface during mammalian embryonic development.** **Bhaswati Bhattacharya** and Soumen Paul. Department of Pathology and Laboratory Medicine, Institute of Reproductive Health and Perinatal Research, University of Kansas Medical Center, Kansas City, KS.

Defective placentation leads to early pregnancy loss, which is a serious health concern.
A major cause of defective placentation is defect in establishment of the maternal-fetal exchange surface due to impaired development of the syncytiotrophoblast (SynT) lineage. In humans and rodents, which are characterized with hemochorial placentation, SynTs are in direct contact with the maternal blood and constitute the main exchange surface. During placentation, SynTs are developed via differentiation of trophoblast stem and progenitor cells (TSPCs) of a placenta primordium and specific transcription factors are implicated in SynT development. However, signaling mechanisms that are involved in TSPC to SynT transition are incompletely understood. Here, we show that Atypical Protein Kinase C iota (PKCi), a conserved protein in mammals, is essential for differentiation of TSPCs to SynTs. Loss of PKCi in a developing mouse embryo leads to abrogation of labyrinth formation leading to embryonic death at ~E9.0. PKCi mediated priming of trophoblast progenitors to SynT development is also a conserved event during human placentation. PKCi is selectively expressed in the first-trimester cytotrophoblast progenitors in human placenta. Depletion of PKCi impairs differentiation of human trophoblast stem cells towards SynTs *in vitro* as well as after transplantation in immunocompromised mice. Our mechanistic analyses revealed that PKCi signaling is important to induce key transcription factors including GCM1, GATA2 and DLX3 in TSPCs within mouse placenta primordia and human TSCs. Our study uncovers a conserved molecular mechanism, in which PKCi signaling regulates establishment of the maternal-fetal exchange surface by promoting TSPC to SynT transition.

6) **Signaling of the Pro-Inflammatory Cytokine TNFa through NFkB-p65 Increases Gdf9 and Decreases Figla mRNAs in Oocytes of Primary Follicles.** **Kelsey R. Timme**, Heidi B. Miller, and Jennifer R. Wood. Department of Animal Science, University of Nebraska-Lincoln, Lincoln, NE.

Female obesity is associated with ovarian inflammation, oxidative stress, and reduced oocyte quality. Our previous studies demonstrated that C57BL/6 mice fed a high fat diet (HFD) had increased ovarian expression of Tnfa mRNAs, and increased phosphorylation of signal transducer and activator of transcription 3 (STAT3) and NFkB p65. Several transcription factors and maternal effect genes mRNAs were increased in ovulated oocytes and/or whole ovaries depleted of antral follicles. We hypothesized that acute treatment of primary follicles with TNFa would activate NFkB signaling and alter Dppa3, Pou5f1, Nobox, Figla, and Gdf9 transcript abundance within the growing oocytes. To test this hypothesis, ovaries were collected from 12 day old pre-pubertal CD1 mice and primary follicles were isolated. Immunofluorescence studies confirmed expression of total NFkB p65 (p65) in the oocyte of primary follicles. Ten primary follicles were cultured in media containing 0, 1, 10, or 100 ng/ml TNFα for twenty minutes. Western blot analysis demonstrated a dose response effect of TNFα on phosphorylation of p65 with the greatest effect seen in follicles exposed to 10 ng/ml TNFα. Next, 20 primary follicles were cultured in 10 ng/ml TNFa for 0, 2, and 8 hours, and RNA isolated, reverse transcribed, and droplet digital PCR performed using primers against *Dppa3*, *Pou5f1*, *Gdf9*, *Figla*, *Nobox* and the housekeeping gene calnexin (*Canx*). *Gdf9/Canx* was increased two-fold in follicles treated for 8 hours (3.97 +/- 0.35) compared to 0 hour (2.01 +/- 0.48) controls (p-value = 0.027). Conversely, there was a numerical decrease in *Figla/Canx* mRNA abundance between 0 (0.39 +/- 0.18), 2 (0.26 +/- 0.08), and 8 (0.16 +/- 0.09) hours post-TNFα treatment. These preliminary data indicate that acute treatment with TNFα differentially regulates oocyte mRNAs. In future studies, follicles will be encapsulated in alginate and treated for 1-7 with 0 or 1ng/ml of TNFα in order to mimic chronic inflammation. Supported by UN Foundation Food for Health funds and the Nebraska Agricultural Experiment Station with funding from the Hatch Multistate Research capacity funding program (Accession Number 1013511) from the USDA National Institute of Food and Agriculture.

7) **Transposable element expression during placental development.** **Nehemiah S. Alvarez**[1,2], Kesiuke Kozai[1,2], Damayanti Chakraborty[1,2], Khursheed Iqbal[1,2], Kaela M. Varberg[1,2], Pavla Brachova[1,3], Hiroaki Okae[6], Takahiro Arima[6], Gerald G. Schumann[7], Kathleen H. Burns[8,9,10], and Michael J. Soares[1,2,4,5,11] [1]Institute for Reproduction and Perinatal Research, [2]Departments of Pathology and Laboratory Medicine, [3]Molecular and Integrative Physiology, [4]Pediatrics, and [5]Obstetrics and Gynecology, University of Kansas Medical Center, Kansas City, KS, [6]Department of Informative Genetics, Environment and Genome Research Center, Tohoku University, Japan, [7]Paul-Ehrlich-Institut, Division of Medical Biotechnology, Langen, Germany, [7]Department of Pathology, [8]McKusick–Nathans Institute of Genetic Medicine, [9]Sidney Kimmel Comprehensive Cancer Center, [10]High Throughput Biology Center, Johns Hopkins University School of Medicine, Baltimore, MD, [11]Center for Perinatal Research, Children's Research Institute, Children's Mercy, Kansas City, MO.

Trophoblast cells (TC) of the early embryo directly interact with the uterus and differentiate into specialized cell types that make up the placenta. Deficiencies in the differentiation of TC are a major contributing factor to early pregnancy loss, but the mechanisms remain poorly understood. One possible cause is the reduced ability of TC to respond to environmental signals such as oxygen tension or nutrient status. Our previous studies demonstrate that TC respond to hypoxia through epigenetic and transcriptional reprogramming. We hypothesize that hypoxia activates epigenetic and transcriptional programs that are necessary for adaptation and survival of TC. Here, we utilized the rat as a model of hemochorial placenta development. We performed RNA-seq on rat placenta and observed high expression of transposable elements (TE). Furthermore, rat trophoblast stem cells (rTSC) and human (hTSC), showed differential expression patterns of TE. Consistent with TE expression, ChIP-seq of rTSC revealed a genome-wide decrease of H3K9me marks across TE during differentiation conditions. Our observations indicate that TE expression is a common feature of rat placenta development. Therefore, we predicted that hypoxia exposure might alter the TE expression profile. We exposed pregnant rats to hypoxia and performed RNA-seq on placental tissue. Analysis revealed upregulation

of several TE. A similar phenomenon was observed in vitro in rTSC exposed to hypoxia. ChIP-seq analysis of rTSC exposed to hypoxia revealed reduction in H3K9me on TE in the rat genome. We also observed that in hTSC exposed to hypoxia, LINE-1 ORF1p binds more RNA, without a concomitant increase in protein expression. Our observations reveal that under stress conditions, a transcriptional program is activated in the placenta that has the capacity to alter the genomic and transcriptome landscape. We propose that rTSC and hTSC undergo genome-wide epigenetic alterations in low oxygen that activate transcriptional networks necessary for adaptations. (Supported by Lalor Foundation, American Heart Association, and NIH Postdoctoral Fellowships; NIH grants: HD020676, HD079363)

8) **Establishing endometrial epithelial organoids to investigate uterine gland function in humans and mice.** **Harriet C. Fitzgerald**1, Pramod Dhakal1, Linda M. Rowland1, Danny J. Schust2, Thomas E. Spencer1,2 1Division of Animal Sciences, University of Missouri, Columbia, MO 2Department of Obstetrics, Gynecology and Women's Health, University of Missouri, Columbia, MO

The endometrium of both humans and mice is incredibly important in providing the site of implantation as well as facilitating the growth and development of the blastocyst. Indeed, uterine glands and their secretions are essential for pregnancy establishment, blastocyst implantation, stromal cell decidualization and conceptus survival. As such, any perturbations in uterine gland function may also contribute to infertility in women. Conventional 2D cell culture systems lack the 3D microenvironment essential for mechanical and biochemical cues for cells, and cell-cell communication. Epithelial organoids cultured in 3D provide a promising avenue to further elucidate the role of uterine glands in pregnancy establishment in humans and mice. Endometrial epithelial organoids (EEO) were grown in culture using modified protocols (Turco MY et al., *Nature Cell Biology* 2017; Boretto M et al., *Development* 2017). Epithelial cells were isolated from adult mouse uteri or biopsies of human endometrium using enzymatic dissociation, resuspended in Matrigel, placed in a 48-well dish, and continuously cultured under a defined WNT-activating stem cell media. Round epithelial organoids were established within 3 to 4 days and after 10 days were differentiated with steroid hormones. Mouse EEO were differentiated with estradiol-17β (E2; 1nM) for 2 days and progesterone (P4; 50 ng/mL) for 2 days. Human EEO were treated with estradiol-17β (E2; 10nM) for 2 days, followed with either E2 and medroxyprogesterone acetate (MPA; 1μM) or E2, MPA and cAMP (1 μM) for a further 6 days. Mouse EEO immunostained positive for FOXA2, ESR1, and CDH1, but not PGR, which are signatures of differentiated glands. Mouse EEO responded to E2 with upregulation of *Cxcl15* and P4 with upregulation of *Ihh, Prss28*, and *Prss29* and downregulation of *Cxcl15*. The expression of *Ihh* was upregulated with E2 and E2+MPA treatment in human EEO. *Spp1* and *Paep* were significantly ($P<0.05$) upregulated in human EEO with E2+MPA+cAMP treatment. These results indicate that both the human and mouse EEO are hormone-responsive and will differentiate under specific culture conditions. These in vitro models will enable critical investigations into the impact of uterine glands on stromal cell decidualization and pregnancy establishment in humans and mice. This research was supported by NIH 1R01 HD096266.

9) **ESR2-regulated *Kiss1* expression in the ovary.** **V. Praveen Chakravarthi**, Vincentaben Khristi, Subhra Ghosh, Eddie Dai, Sireesha Yerrathota, Katherine F. Roby, Michael W. Wolfe, and M.A. Karim Rumi. Institute for Reproduction and Perinatal Research, University of Kansas Medical Center, Kansas City, KS.

Hypothalamic expression of *Kiss1* plays an essential role in the onset of puberty, gonadal development, and ovulation. Estrogens regulate the expression of *Kiss1* in the hypothalamus through ESR1. *Kiss1* is also expressed in the ovary, where its expression correlates with the onset of puberty and progression of the estrous cycle. We recently observed that gonadotropin-induced *Kiss1* expression was absent in *Esr2*-null rat ovaries even though *Esr1* was present. Wildtype granulosa cells abundantly expressed *Kiss1* and oocytes expressed the *Kiss1* receptor. We characterized ESR2-regulation of *Kiss1* expression in granulosa cells by identifying granulosa cell-specific transcript variants and potential regulatory regions. The *Kiss1* promoter, an upstream enhancer and a downstream enhancer, all possessed conserved EREs and showed active histone marks in gonadotropin-stimulated

granulosa cells. The transcriptionally active *Kiss1* promoter, as well as the enhancers, also revealed enrichment for ESR2 binding. Furthermore, activity of a *Kiss1* promoter construct was induced following overexpression of ESR2 and was blocked upon mutation of an ERE within the promoter. Finally, PMSG and hCG administration induced phosphorylation of ESR2 and upregulated the AP-1 proteins FOSL2 and JUNB in granulosa cells. These gonadotropin-induced changes paralleled *Kiss1* expression in granulosa cells. Taken together, we conclude that gonadotropin-stimulated *Kiss1* expression in granulosa cells is dependent upon both the activation of ESR2 and the upregulation of AP-1. This research was supported by an NIH grant (P20 GM103418) awarded to KINBRE and an NIH grant (UL1TR002366) awarded to Lied Basic Science Program of the KUMCRI.

10) **TRAINEE ORAL PRESENTATION AND POSTER: Zika Virus Infection Induces Endoplasmic Reticulum Stress in Placental Trophoblast cells.** **Philma Glora Muthuraj**, Ezhumalai Muthukrishnan, Aryamav Pattanik, Prakash Kumar Sahoo, and Sathish Kumar Natarajan. Department of Nutrition and Health Sciences, University of Nebraska-Lincoln, NE

Zika Virus (ZIKV) infection in pregnant women is highly associated with Congenital Zika Syndrome and the development of microcephaly, intra uterine growth retardation and ocular damage in the fetus. Recent advances suggest that ZIKV can be vertically transmitted to the fetal organs including the fetal brain via the placenta. Placental infection during the first and second trimester plays a crucial role in ZIKV transmission from maternal circulation to the fetus resulting in Congenital Zika Syndrome. Further, ZIKV infection induces placental trophoblast cell apoptosis. However, the mechanism of trophoblast apoptosis caused due to the ZIKV infection is unclear. Here **we hypothesize** that endoplasmic reticulum (ER) stress is the mechanism behind ZIKV-induced placental trophoblast apoptosis. **Methods:** HTR-8, a human normal immortalized trophoblast cells and human malignant-derived trophoblast (JEG-3 and JAR) cell lines were infected with 0.1-1.0 MOI ZIKV. X-box binding protein 1 (XPB1) splicing assay and relative C/EBP homologous protein (CHOP) mRNA expression was quantified using qRT-PCR as markers of ER stress after 3- 24 h of ZIKV infection. Apoptosis was assessed by characteristic nuclear morphology staining with DAPI and caspase 3/7 activity assay. **Results**: We observed a significant increase in the mRNA levels of CHOP after 12-16 h of ZIKV infection in placental trophoblast cells. We also observed a dramatic increase in the spliced form of XBP1 in placental trophoblast cells infected with ZIKV after 16 h indicating ER stress. As prolonged ER stress can cause apoptosis, we observed a dramatic increase in placental trophoblast apoptosis after 48 h of ZIKV infection as evidenced by biochemical characteristic nuclear morphology and caspase 3/7 activation. **In conclusion**, ER stress could be the potential molecular mechanism underlying ZIKV-induced placental trophoblast apoptosis. The critical role of ER stress activation in placental trophoblast cells with ZIKV infection is now under investigation.

11) **Low Total Motile Sperm in Transgender Women Seeking Hormone Therapy: A Case-Control Study.** Courtney Marsh, **Megan McCracken**, Meredith Gray, Ajay Nangia, Judy Gay, Katherine F. Roby. University of Kansas Medical Center, Kansas City, KS.

Objective: This pilot study was undertaken to compare semen quality, hormonal status, and social factors in transgender women seeking fertility preservation with those of cis-men. Long range goals are to establish standard practice measures to ensure optimum semen quality for cryopreservation and fertility preservation in transgender women. **Design:** This is an IRB-approved fully consented case-control study carried out at an academic medical center. **Materials and Methods:** Semen parameters in transgender women (cases; n=11) at the time of fertility preservation were measured and compared to those of cis-men recently fathering a child (controls; n=16). Exclusion criteria included prior use of hormones. All participants completed a questionnaire which included the Depression Anxiety Stress Scales 21 Survey (DASS-21) via a secure online portal. Follicle stimulating hormone, estradiol and testosterone and risk factors that may alter semen parameters were measured and compared. Complete semen analysis was carried out in a clinical andrology laboratory according to WHO guidelines. Hormones were analyzed by LCMSMS at Quest Diagniostics. Data were analyzed by Mann-Whitney or Student t-test. **Results:** Sperm concentration was significanctly lower in transgender women compared to controls (28.9±7.8 vs 71.4±20.2 million; p=0.023). In addition, total motile sperm in transgender women was significantly lower than controls (43.2±14.7 vs 110.1±22.6

million; p<0.05). Other semen parameters were not different between groups. FSH, estradiol and testosterone concentrations were not different between groups. The DASS-21 survey indicated transgender women were more likely to have symptoms of depression, anxiety and stress (p<0.01) compared to controls. Additonal survey results indicated greater use of tucking and tight undergarments by transgender women (p<0.05), however both groups reported a similar number of ejaculations per week. **Conclusions:** Sperm concentration and total motile sperm in transgender women prior to hormone treatment were lower compared to cis-men that recently fathered a child. \ Although sperm counts were low, cryopreservation of sperm prior to the initiation of hormone therapy is a viable option for fertility preservation. The etiology of the differences in semen parameters is not known, but use of tight undergarments may play a role in reducing sperm production and enhanced education related to behaviors prior to cryopreservation may improve future fertility potential. On going studies seek to further substantiate the present pilot findings and to investigate the underlying mechanisms leading to oligospermia in order to design interventions ensuring transgender women the opportunity for optimum fertility preservation. Support: KUMC Research Institute, Clinical Pilot Grant Program.

12) Integration of in vitro and in vivo models to identify conserved mechanisms regulating development of the invasive trophoblast lineage at the maternal-fetal interface. **Kaela M. Varberg**1, Regan L. Scott1, Masanaga Muto1, Khursheed Iqbal1, Keisuke Kozai1, Michael J. Soares1,2. 1Institute for Reproduction and Perinatal Research, Departments of Pathology & Laboratory Medicine, Pediatrics, and Obstetrics and Gynecology, University of Kansas Medical Center, Kansas City, KS; 2Center for Perinatal Research, Children's Research Institute, Children's Mercy, Kansas City, MO.

Oxygen and nutrient demands of a developing fetus increase as gestation progresses. Thus, the vessels, or spiral arteries, that facilitate transfer of maternal blood to the conceptus must undergo extensive remodeling to ensure sufficient nutrient delivery and successful pregnancy. Although numerous cells comprise the maternal interface, the invasive trophoblast cell lineage is required for remodeling of uterine spiral arteries and placentation. Thus, our aim is to identify critical and conserved gene regulatory networks of trophoblast lineage development. Achaete-scute family bHLH transcription factor 2 (ASCL2) is essential to extraembryonic development in the mouse, as ASCL2-deficient placentation sites exhibit differences in placental organization, including compromised development of the junctional zone, the site of invasive trophoblast cell progenitors. Thus, we hypothesized that ASCL2 is essential for invasive trophoblast lineage development. To test our hypothesis, extravillous trophoblast (EVT) cell differentiation was examined using a human trophoblast stem cell culture model. Human trophoblast stem cells can be effectively differentiated into EVT and syncytiotrophoblast cell lineages. Differentiation of human trophoblast stem cells into EVT was characterized by morphologic transformation from round to elongated cells, upregulation of transcripts characteristic of EVT (i.e. *ASCL2*), and increased expression of major histocompatibility complex, class I, G (HLAG) protein. Short hairpin RNA-mediated knock down of ASCL2 impaired EVT cell differentiation, as indicated by altered cell morphology and decreased expression of EVT-specific transcripts, including HLAG and matrix metallopeptidase 2 (MMP2). In addition to the in vitro analysis, an in vivo role for ASCL2 in the regulation of trophoblast invasion is being investigated in the rat. Similar to humans, the rat possesses hemochorial placentation with deep trophoblast cell invasion and trophoblast-mediated spiral artery remodeling. Using the CRISPR/Cas9 system, an *Ascl2* mutant rat has been generated for investigation of the role of ASCL2 in hemochorial placentation. With these in vitro and in vivo experimental tools we can begin to evaluate regulatory roles for ASCL2 in development of the invasive trophoblast lineage and trophoblast-guided uterine spiral artery remodeling. Overall, elucidating regulatory mechanisms uteroplacental vascular remodeling during pregnancy will aid preventative efforts to detect pregnancy disorders at earlier onset and, ultimately, develop effective interventions. (Supported by Lalor Foundation Fellowships to KMV and MM, an American Heart Association Fellowship to KK, and NIH grants HD020676 and HD079363)

13) **TRAINEE ORAL PRESENTATION AND POSTER: ADAR1 A-to-I RNA editing alters mRNA stability in oocytes.** **Pavla Brachova**1*, Nehemiah S. Alvarez2, 3,*, Xiaoman Hong1, Kailey A. Vincent4, Keith E. Latham4, Lane K. Christenson1ϕ 1 Department of Molecular and Integrative Physiology, University of Kansas Medical Center, Kansas City, KS 66160, 2 Department of Pathology and Laboratory Medicine, University of Kansas Medical Center, Kansas City, KS 66160, 3 De Novo Genomics, Kansas City, KS, 4 Department of Animal Science and Reproductive and Developmental Sciences Program, Michigan State University, East Lansing, MI

Fully grown mammalian oocytes and eggs are transcriptionally quiescent, and thus have a unique RNA milieu in which cellular processes depend on post-transcriptional regulation. RNA editing of adenosines into inosines (A-to-I) by adenosine deaminases acting on RNA (ADARs) is a common post-transcriptional gene regulatory mechanism, yet it has not been systematically studied in oocytes. We performed a genome-wide RNA editing analysis in pools of transcriptionally active growing oocytes from postnatal day 12 (PND12) mice (n=3), fully grown germinal vesicle (GV) oocytes (n=3), and transcriptionally quiescent metaphase II (MII) eggs (n=7). We identified an abundance of A-to-I editing of mRNA transcripts in GV oocytes (3,207 ± 117 transcripts per sample; Mean ± SEM) and MII eggs (3,003 ± 290), with significantly fewer levels in PND12 immature oocytes (733 ± 49 edited transcripts/sample) ($p<0.05$, one-way ANOVA). This was consistent with increased ADAR1 transcripts and protein in GV oocytes and MII eggs, compared with PND12 oocytes. Compared to somatic tissues, oocytes exhibited a distinct pattern of RNA editing, with a high proportion of RNA edits occurring in coding regions. These edits resulted in nucleotide substitutions that were enriched at the third nucleotide of the codon (wobble position) and altered codon usage. Codon usage can affect mRNA stability and translation efficiency, and RNA editing of the six most frequently edited codons was associated with unstable transcripts in GV oocytes and MII eggs. ADAR1 RNA editing may affect overall mRNA stability through editing of codons. To examine the functional role of ADAR1 in mouse oocytes, we crossed ADARFL/FL mice with ZP3-Cre mice to generate oocytes deficient in ADAR1-mediated RNA editing. After priming mice with PMSG and hCG, ADARFL/FLZP3-Cre female mice were able to ovulate at normal levels, however embryos generated after timed breeding to WT C57B/6 males had delayed entry into 2-cell and 8-cell stages. In summary, we provided evidence in support of a previously unreported phenomenon of selective ADAR1 editing of the codon wobble position, and mice with deficient ADAR1-RNA editing in oocytes produce a high percentage of degenerate embryos. Editing of the wobble position has the potential to fine tune post-transcriptional gene regulation through altering codon usage, and this may be essential for early embryo development.

14) **3-hydroxy fatty acids Induce Placental Trophoblast Necroptosis during Acute Fatty Liver of Pregnancy.** Prakash Kumar Sahoo, **Ezhumalai Muthukrishnan**, Philma Glora Muthuraj, and Sathish Kumar Natarajan. Department of Nutrition and Health Sciences, University of Nebraska-Lincoln, NE

Mitochondrial beta-oxidation is one of the major energy-producing mechanisms in the human placenta, which supports growth and development of both the placenta and the fetus; therefore, dysfunctions in this pathway has severe consequences on both maternal and fetal health. Fetus with homozygous in the enzyme Long-chain 3-hydroxy acyl-CoA dehydrogenase (**LCHAD**) is highly associated with the development of Acute Fatty Liver of Pregnancy (AFLP). AFLP is a maternal liver injury marked by microvesicular steatosis and acute liver failure that develops in the last trimester of pregnancy. The mutation in the enzyme LCHAD results in the accumulation of 3-hydroxy fatty acids and subsequently infiltrates to the liver from the placenta through maternal circulation. In this study, we aim to understand the molecular mechanisms underlying 3-hydroxy fatty acid-induced lipotoxicity in placental trophoblast cells **Methods:** Human choriocarcinoma-derived trophoblast cells (JEG-3 and JAR) were treated with various concentrations (100-200 μM) of 3-hydroxy myristic acid (3-HMA) for 16hr. Cell death was assessed by characteristic nuclear morphology changes and Caspase 3/7 activity. Mitochondrial bioenergetics were assessed using Seahorse XF24 Extracellular Flux Analyzer. **Results:** We observed that placental trophoblast cells treated with increasing concentration of 3-HMA showed enhanced biochemical characteristic nuclear morphological changes of cell death; however, there was no caspase 3/7 activation. These results suggest that 3-HMA induces caspase-independent cell death. Further, 3-HMA-induced cell death was prevented with the inhibition of receptor interacting protein

kinase 1 (RIPK1), using necrostatin suggesting necroptosis as a mechanism of cell death. We also observed that treatment of 3-HMA to placental trophoblast cells showed mitochondrial dysfunction altering its bioenergetics as evidenced by a dramatic decrease in mitochondrial spare respiratory capacity compared to controls**. In conclusion**, 3-hydroxy fatty acids induce mitochondrial dysfunction and placental trophoblast necroptosis. Further studies are underway to characterize the signaling mechanism of 3-HMA-induced placental trophoblast necroptosis.

15) **Weight Loss, Physical Activity, and Conception Rates in Women with Polycystic Ovarian Syndrome vs. Other Infertility Diagnoses.** **Anna M. Gorczyca**, Courtney A. Marsh, Joseph E. Donnelly. Center for Physical Activity and Weight Management, Department of Internal Medicine, University of Kansas Medical Center 2 Center for Advanced Reproductive Medicine, Department of Obstetrics and Gynecology, University of Kansas Medical Center.

The objective of this study was to compare weight loss, physical activity, and rates of conception in obese infertile women diagnosed with Polycystic ovarian syndrome (PCOS) vs. women with other infertility diagnoses following completion of a weight management program. Obese infertile women, referred by a reproductive endocrinologist, completed the University of Kansas Weight Management Program (KWMP). This program included reduced energy intake, (portion controlled entrees, low calorie shakes, fruits & vegetables, & non-caloric beverages), increased moderate-to-vigorous physical activity (MVPA) targeting 300 min•wk. and healthy lifestyle strategies. Participants were asked to monitor weekly MVPA (self-report) and pedometer step counts. Height and weight were assessed weekly by trained staff in the clinic. The cumulative average of MVPA and steps over the last 3-wks. of participation were used in the analysis. Pregnancy outcomes were obtained from a review of medical records. PCOS was diagnosed using the Rotterdam criteria. The Kruskal-Wallis nonparametric test was used to compare differences in percent weight loss, physical activity (MVPA min•wk.-1, steps•wk.-1), and time in the KWMP between women diagnosed with PCOS vs. other infertility diagnoses. Chi-squared test was used to compare conception rates between women with PCOS vs. other infertility diagnoses. There were no differences in age or baseline BMI between women with PCOS compared to women with other infertility diagnoses. Women with a PCOS diagnosis as their cause of infertility were younger (28.3 yrs. vs. 35.2 yrs.; P = 0.01), in the KWMP program longer (26 ± 5 wks. vs. 12 ± 7; P = 0.01), and had higher step counts per week (73,209 ± 8,927 steps/wk. vs. 53,261 ± 8,919; P = 0.009) than women with other infertility diagnoses. One-hundred percent of women with PCOS conceived after participating in the KWMP compared to 50% of women with other infertility diagnoses (P= 0.28). It is important to focus future research on anovulatory women with PCOS vs. women with other infertility diagnoses as there may be a larger benefit in this population such as restoration of ovulation and spontaneous conception.

16) **Differential regulation of ZsGreen1 abundance by the human cytomegalovirus immediate early promoter in a wide array of porcine tissues.** **Amy T. Desaulniers**[1], Rebecca A. Cederberg[2], Elizabeth P. Carreiro[2] and Brett R. White[2] [1]University of Central Missouri, School of Natural Sciences, 319 W.C. Morris, Warrensburg, MO 64093 [2]University of Nebraska- Lincoln, Department of Animal Science, 3940 Fair Street, Lincoln, NE 68583

The advent of genetically engineered pig production has revealed a wide array of opportunities to enhance both biomedical and agricultural industries. One powerful method to develop these models is transgenesis; however, selection of a suitable promoter to drive transgene expression is critical. The cytomegalovirus (CMV) promoter is the most commonly used viral promoter as it robustly drives transgene expression in a ubiquitous nature. However, recent reports suggest that the level of CMV promoter activity is tissue-dependent in the pig. Therefore, the objective of this study was to quantify the activity of the CMV promoter in a wide range of porcine tissues. Swine harboring a CMV-ZsGreen1 transgene with a single integration site were utilized for this study. Thirty five tissue samples were collected from neonatal hemizygous (n = 3) and homozygous (n = 3) transgenic piglets and analyzed for ZsGreen1 abundance via immunoblot. ZsGreen1 was detected in all tissues examined; however, quantification revealed that ZsGreen1 protein levels were tissue-specific. Within organs of the digestive system, for example, ZsGreen1 was most abundant in the salivary gland, moderately produced in the

esophagus and levels were lowest in the stomach ($P < 0.05$). Interestingly, abundance of ZsGreen1 also differed within organ. For instance, levels were highest in the right ventricle compared with other chambers of the heart ($P < 0.05$). There was no effect of transgene dose as ZsGreen1 expression patterns were similar between homozygous and hemizygous piglets ($P > 0.05$). Ultimately, these results elucidate the tissue-specific activity of the CMV promoter in the neonatal pig. Moreover, this model can serve as a useful tool for research applications requiring reporter gene activity in mammalian organs.

17) **Loss of REST in Uterine Leiomyoma leads to an Altered Progesterone Response.** **Ashley Cloud**1, Michelle McWilliams1, Faezeh Koohestani1, Sumedha Gunewardena1, Vargheese Chennathukuzhi1 1Department of Molecular and Integrative Physiology, University of Kansas Medical Center, Kansas City, KS.

Uterine Leiomyoma (UL) are benign tumors that arise in the smooth muscle tissue of the uterus, known as the myometrium. UL is present in over 75% of women, often causing heavy bleeding, severe pain, and reproductive dysfunction. Despite their prevalence, there is no long-term pharmaceutical treatment for UL, due to the lack of understanding about the molecular pathogenesis of the disease. Extensive evidence has also indicated an aberrant response to steroid hormones, estrogen and progesterone, plays a critical role in the pathogenesis of UL. Importantly, REST (repressor element silencing transcription factor) is a tumor suppressor whose loss in UL leads to aberrant expression of its target genes. We found a large number of REST target genes are also targets of progesterone receptor (PGR). Our CHIPseq data shows conserved REST binding sites (RE1 sites) within 100bp of PGR binding sites (PREs). To investigate the role of REST in UL, we generated a uterus specific conditional knockout mouse model of REST. When REST is lost in our cKO mouse we see a UL phenotype and an altered response to progesterone in the uterus. This altered response to progesterone was confirmed with our RNAseq data. The phenotype consists of hyperproliferation in the uterus throughout the estrus cycle despite normal E2 and P4 levels. This is unusual as the role of progesterone is to suppress the proliferative effects of estrogen during the menstrual cycle. Taken together, our data indicates a novel link between an altered progesterone response and loss of REST in UL.

18) **Microarray Analysis Predicts Differential Expression of Steroidogenesis and Steroid Metabolism Genes in Theca Cells from Cows with High Intrafollicular Androstenedione.** **Kerri A. Bochantin**, Adam F. Summers, William E. Pohlmeier, Kevin M. Sargent, Scott G. Kurz, Sarah M. Romereim, Oluremi Daudu, Renee M. McFee, John S. Davis, Andrea S. Cupp, and Jennifer R. Wood. University of Nebraska, Lincoln.

Populations of cows in the UNL physiology are classified based on androstendione concentration in follicular fluid of the dominant follicle; High A4 (>40 ng/ml) or control (<20 ng/ml). High A4 cows have irregular estrous cycles and reduced calving rates. Furthermore, in theca cells from High A4 cows CYP11A1, CYP17A1 and LHCGR mRNAs are increased. The hypothesis of the current study is that theca cells from High A4 cows have a unique gene expression profile, which contributes to increased androgen synthesis. To test this hypothesis, the estrous cycles of High A4 and Control cows were synchronized with an injection of GnRH and a controlled internal drug release device (CIDR). After 7 days, the CIDR was removed, an injection of prostaglandin F2 alpha was given, and ovariectomies performed 36 hours later. Theca cells were microdissected from the dominant estrogen-active follicle and RNA extracted. High quality RNA from High A4 (n = 3) and control (n = 4) cows were labeled and hybridized to Affymetrix Bovine GeneChip Gene 1.0 ST Arrays at the University of Nebraska Microarray Core facility. Following hybridization, normalized data was analyzed using the NIA Array Analysis tool. Hierarchical clustering and principal component analysis showed clustering of cows based on A4 classification. Analysis of Variance (ANOVA, $P < 0.05$) with False Discovery Rate (FDR < 0.05) correction identified 1184 differentially expressed transcripts; 1104 transcripts were overexpressed and 80 transcripts were underexpressed in theca cells from High A4 compared to Control cows. These transcripts represented xx-annotated genes (xx upregulated and xx downregulated). Importantly, CYP17A1 was increased 6-fold in theca cells from High A4 compared to control cows. Ingenuity Pathway Analysis (IPA) identified 2 networks of genes associated with steroid synthesis. The first network included CYP17A1, SULT1E1 (estrogen metabolic process), BMP5 (TGF beta family member),

and DGK (diacylglycerol kinase – PKC signaling). The second network suggested that beta-estradiol synthesis is associated with increased HSD17B6 (converts DHT to the estrogen 3 beta-Adiol which preferentially binds to Estrogen Receptor-beta) and CYP2C9 (drug metabolizing enzyme). Functional studies will determine how signaling pathways contribute to the increase A4 phenotype in theca cells from High A4 cows.

19) **Pluripotent stem cell models in the KUMC Transgenic Facility.** **Julia Draper,** Katelin Gibson, Illya Bronshteyn, Jay L. Vivian, and Melissa Larson. Transgenic and Gene Targeting Institutional Facility, University of Kansas Medical Center, Kansas City, KS.

Pluripotent stem cells are important tools for biomedical researchers to study gene function and develop models of human disease. Gene targeting in mouse embryonic stem cells is a critical tool for advanced manipulation of the mouse genome. Patient specific human induced pluripotent stem cells provide unique tools for capturing the genetic information of a patient into a cell line with the capacity to differentiate into virtually any cell type. The techniques employed for the generation of pluripotent stem cell models require technical expertise. The KUMC Transgenic and Gene-Targeting Institutional Facility is a core facility that supports researchers interested in both mouse and human pluripotent stem cell models. The Facility uses cutting edge methods, state-of-the-art instrumentation, and novel reagents for this work. The Facility's stem cell core performs gene targeting in stem cells, cell culture and preparation for injection for generating chimeric mice, and karyotyping. The Facility also has expertise in differentiation of human pluripotent stem cells, and in reprogramming primary cells to generate new induced pluripotent stem cell (iPSC) lines. Our recent efforts include successful site-directed transgene integration and mutagenesis into human and mouse pluripotent stem cells using genome editing tools such as CRISPR/Cas9. In this poster we will present recent projects supported by the TGIF using pluripotent stem cell models.

20) **Disruption of ESR1 alters the expression of genes regulating hepatic carbohydrate and lipid metabolism.** **Vincentaben Khristi,** Anamika Ratri, Subhra Ghosh, Shaon Borosha, Tianhua Lei, Eddie Dai, V. Praveen Chakravarthi, Michael W. Wolfe, and M.A. Karim Rumi. Institute for Reproduction and Perinatal Research, University of Kansas Medical Center, Kansas City, KS.

The liver helps maintain energy homeostasis by synthesizing and storing glucose and lipids. Gonadal steroids, particularly estrogens, play an important role in regulating metabolism. The liver expresses high levels of estrogen receptor alpha (ESR1) in both males and females, which mediates the hepatic response to estrogens. Loss of ESR1 causes increased weight gain and obesity in female rats, while causing males to become smaller in size. Obesity in *Esr1*-null females was associated with metabolic dysfunction. Although *Esr1*-null male rats have a reduced body weight, they also exhibited an impaired glucose tolerance and increased adiposity. We investigated whether this metabolic disorder in *Esr1*-null male rats was linked with the loss of transcriptional regulation by ESR1 in the liver. RNA-sequencing was performed on liver RNAs purified from wildtype and *Esr1*-null male rats to identify the genes regulated by ESR1. Based on an absolute fold change of 2 with a p-value ≤ 0.05, a total of 618 differentially expressed genes were identified in the *Esr1*-null male liver. Pathway analyses demonstrated that the differentially expressed genes included transcriptional regulators, transporters, and regulators of lipid biosynthesis, mitochondrial function, and hormone metabolism. Many of these genes showing an altered expression are related to pathways of carbohydrate and lipid metabolism in the liver. Our findings indicate that ESR1 is a critical regulator of hepatic carbohydrate and lipid metabolism in both sexes despite the sexual dimorphism in weight gain. This research was supported in part by an NIH grant (HD072100) and a pilot grant from KUMC-KIDDRC.

21) **Loss of Adenosine Deaminase Acting on RNA (ADAR1) in Granulosa Cells Causes Infertility.** **Rikki N. Nelson,** Xiaoman Hong, Pavla Brachova, Lane K. Christenson. Department of Molecular and Integrative Physiology, University of Kansas Medical Center, Kansas City, KS.

Acuity in post-transcriptional gene regulation contributes to the cell's ability to maintain or respond to its physiological environment by altering gene expression without transcriptional reprogramming. RNA sequencing has highlighted the abundance of non-encoded polymorphisms in RNA and the potential for RNA editing to contribute to post-transcriptional regulation. Both coding and noncoding regions of

mRNA can be edited resulting in altered codons, altered splice sites, changes in transcript stability, and changes in translation efficiency. Adenosine deaminases acting on RNA (ADAR) catalyze adenosine to inosine (A-to-I) editing, and comprise one family of RNA editing enzymes. There are two catalytically active adenosine deaminases, ADAR1 (*Adar*), and ADAR2 (*Adarb1*). The third adenosine deaminase, ADAR3 (*Adarb2*) lacks catalytic activity. The periovulatory period provides a landscape for evaluating the role of post-transcriptional regulation as the somatic cells are undergoing differentiation and integrating signals from the maturing oocyte. Analysis of published granulosa cell RNA-seq datasets indicates that *Adar* is the highest expressed adenosine deaminase (10.66±0.02 fragments per kilobase of transcript per million mapped reads) compared to *Adarb1* (2.11±0.17) and *Adarb2* (0.05±0.02). An organism-wide *Adar* deletion is embryonic lethal in mice, so a granulosa cell specific *Adar* depleted model was created to examine the role of ADAR1 in ovarian function. ADARFL/FL/Aromatase-Cre (n=5) and wild-type control littermate (n=6) female mice were bred to wild-type males for fertility evaluation over a 7-month period. To assess follicular development and ovulation, $ADAR^{FL/FL}$/Arom-Cre (n=8) and control (n=11) females were administered 5IU of PMSG, 5IU of hCG 46 hours after PMSG, and eggs were collected from oviducts 16 hours following hCG. In the mating trial, control females had 8.0±0.4 pups/litter while $ADAR^{FL/FL}$/Arom-Cre females were infertile. Hormonal stimulation resulted in the recovery of 3.0±2.0 eggs in the $ADAR^{FL/FL}$/Arom-Cre females, while control mice had 38.5±4.2 ovulated eggs. Ovarian histology following PMSG+hCG stimulation revealed that antral follicles developed, but lacked evidence of luteinization. Ongoing studies are evaluating the temporal expression of *Adar* in granulosa cells and assessing the effect of *Adar* deletion on expression of genes regarding follicular development, ovulation, and luteinization. This provides the foundation for identifying the mechanism by which *Adar* impacts ovarian function.

22) Testosterone supplementation in women with diminished ovarian reserve. **Erin Ahart**, Courtney Marsh, Matthew Goering. The University of Kansas Medical Center.

Introduction: Women with DOR have extremely low pregnancy rates after IVF cycles, and there are currently few treatment options available. Testosterone supplementation may improve ovarian response to stimulation via enhanced folliculogenesis. **Methods**: This retrospective cohort study analyzed 83 IVF cycles based on inclusion criteria of age < 42 and diagnosis of DOR (basal FSH > 10, AMH < 1, antral follicle count < 6, or history of poor response [< 4 follicles]). Cycles in the control group were carried out using the standard IVF protocol while cycles in the treatment group involved the addition of transdermal testosterone prior to ovarian stimulation. Four primary outcomes were evaluated: total number of oocytes retrieved, number of mature oocytes retrieved, number of embryos generated, and pregnancy potential of the embryos. **Results**: Pretreatment with transdermal testosterone had no impact on the total number of eggs retrieved after ovarian stimulation. Testosterone had a negative impact of the number of mature oocytes retrieved, but had no impact on the number of embryos generated from those oocytes. Pregnancy rates between the treatment and control groups were no different per embryo transfer, but were lower per cycle initiation with testosterone therapy. **Conclusions**: Within this study population, retrospective analysis of testosterone therapy revealed no improvement in IVF outcomes. A randomized controlled trial is recommended to further investigate this association.

23) Prefoldin-5 is a novel regulator of c-Myc expression in endometriotic epithelial cells whose expression correlates with that of RPLP1 and cell proliferation. **Zahraa Alali**, Fatimah Aljubran, Amanda Graham, Warren B. Nothnick. Molecular and Integrative Physiology, Center for Reproductive Sciences, University of Kansas Medical Center, Kansas City, KS, USA

Endometriosis is a common disease in women of reproductive age in which endometrial tissue establishes and survives in ectopic locations, yet its pathogenesis is poorly understood. MYC regulates numerous targets associated with endometriotic cell survival including RPLP1. Recently, we discovered an increase in endometriotic tissue and epithelial cell expression of pre-foldin-5 (PFDN5) which correlates with cellular proliferation. PFDN5 is a tumor suppressor, which inhibits the transcriptional activity of MYC, thus blocking its action. If PFDN5 functions in a similar manner in endometriotic tissue and cells is unknown. The objective of this study was to examine if endometriotic

epithelial cell expression of PFDN5 regulates MYC expression and in turn cell proliferation. To test our hypothesis, endometriotic epithelial (12Z) cells were transfected with a scrambled siRNA (control-transfected) or siRNA to PFDN5 (siRNA SMARTPool; 25 nM final concentration; N=3 experiments). Cells were harvested at 24 and 48h post-transfection and mRNA and protein expression were examined by qRT-PCR and Western blot analysis, respectively. PFDN5 knockdown was associated with increased RPLP1 (2.1-fold increase) and MYC expression (1.7-fold increase) at 24h, which returned to near baseline levels by 48h. Alterations to cellular proliferation were further confirmed by assessing cyclin E (CCNE) expression in 12Z cells. PFDN5 knockdown was associated with increased CCNE1 transcript (2.7-fold increase compared to control-transfected cells). In conclusion, PFDN5 is expressed in endometriotic epithelial cells and its expression is correlated with cell proliferation. We conclude that this regulatory pathway involves PFDN5 regulation of MYC which modulates expression of known MYC targets such as RPLP1 and CCNE1 and in turn cell proliferation. Enhancing our understanding on the role of PFDN5 in the pathophysiology of endometriosis may lead to novel approaches to curtail endometriotic lesion survival and development of novel therapeutic approaches for treating this debilitating disease.

24) **Antenatal exposure to maternal hypertensive disorders may affect postnatal growth in extremely-low-birth-weight appropriate-for-gestational-age infants.** **Fu-Sheng Chou**, Hung-Wen Yeh, Mmeyeneabasi D. Essien, Vishal Pandey. Department of Pediatrics, University of Kansas Medical Center, Kansas City, KS.

Postnatal growth failure (PGF) is common in extremely-low-birth-weight (ELBW) infants, particularly those who are born small-for-gestational-age (birth weight z-score < -1.28). It is not known whether the adverse intrauterine environment alters postnatal growth trajectory in appropriate-for-gestational-age (AGA) ELBW infants. In this retrospective study, we aimed to investigate whether antenatal exposure to maternal hypertensive disorders (mHTN) affects postnatal weight z-score trajectory. We identified 73 AGA ELBW infants without necrotizing enterocolitis or intestinal perforation. Body weight data at six timepoints (T_1: birth, T_2: lowest weight on the growth chart, T_3: full enteral nutrition establishment, T_4: 36 weeks' corrected gestational age, T_5: around the original due date, and T_6: 1-2 month corrected age) were collected from medical charts and were converted into z-scores using 2013 gender-specific Fenton growth charts. We then analyzed age- and gender-corrected weight z-scores using mixed-effects ANOVA models. We found that weight z-scores varied across time, and were significantly associated with mHTN status, but not with gender. Using Akaike Information Criteria, an mHTN-status-by-time interaction model was selected, suggesting an influence of mHTN on weight z-score trajectory. Specifically, weight z-scores at T_1 were significantly higher and decreased more rapidly from T_1 to T_3 in the non-mHTN group than in the mHTN group, reaching non-significance between the two groups at T_3. Interestingly, weight z-scores remained stable from T_3 onwards in the non-mHTN group but continued to decrease further until T_4 in the mHTN group, resulting in significantly lower z-scores at subsequent timepoints in the latter group. Comparing the two groups, there were no significant differences in average intake of protein and calories during the first week of life, in the rate of culture-positive sepsis, and in post-menstrual days at hospital discharge. Notably, infants in the non-mHTN group were born at significantly lower gestational age and took longer to establish full enteral nutrition, had more days of antibiotics administration during NICU hospitalization, and were more likely to develop bronchopulmonary dysplasia than infants in the mHTN group. Taken together, our data suggest a role of mHTN exposure in determining postnatal weight trajectory and an overall impact of fetal (re) programming on postnatal growth.

25) **Effects of Uterine Luminal Secretions on Conceptus Growth in Sheep.** **Eleanore V. O'Neil**, Gregory W. Burns, Kelsey E. Brooks and Thomas E. Spencer. Division of Animal Sciences, University of Missouri-Columbia

In sheep, the blastocyst develops into an ovoid conceptus and elongates into a filamentous conceptus by day 14. During elongation, the trophectoderm produces interferon-tau (IFNT) to signal pregnancy recognition and modulate uterine receptivity. In vitro studies with embryos and in vivo studies with the uterine gland knockout (UGKO) ewe model support the idea that uterine secretions are essential for

blastocyst/conceptus survival and elongation. Study One determined effects of uterine luminal fluid (ULF) on blastocyst growth. The uterine lumen of wildtype (WT) day 14 cyclic (C) and pregnant (P) ewes was flushed with PBS and the ULF was clarified by centrifugation. Osmotic pumps were secured to the uterine horn of day 8 bred WT ewes, and the catheter inserted into the uterine lumen. Osmotic pumps contained: (1) C ULF; (2) P ULF; or (3) recombinant ovine IFNT (IFNT) (n=5 ewes). Ewes were collected on day 12. Conceptuses from uteri infused with P ULF were longer (3.5 mm+0.5 mm) ($P<0.05$) than those infused with C ULF (1.5+0.5 mm) or IFNT (1.9+0.5 mm). Study Two determined if C ULF repletion could rescue conceptus growth in UGKO ewes. ULF was obtained from day 14 C WT ewes as in Study One. UGKO ewes were bred and implanted with an osmotic pump on day 10 with PBS (n=3) or C ULF (n=5). All ewes were collected on day 14, including bred WT ewes (n=5). A conceptus was recovered from two PBS-infused UGKO ewes (1 and 21 cm in length) and three C ULF-infused UGKO ewes (1.3, 3.1, and 4.1 cm) (WT ewe conceptuses range from 6.2-25.0 cm). Western blot analysis determined that IFNT was greater ($P<0.01$) in the ULF of WT than UGKO ewes. Collectively, these results support the ideas that: (1) adoptive transfer of ULF is not detrimental to conceptus survival; (2) factors other than IFNT in the ULF of day 14 P ewes stimulate blastocyst growth; and (3) infusion of ULF from WT ewes into UGKO ewes does not affect conceptus growth. This project was supported by grant 2016-67015-24741 from the USDA National Institute of Food and Agriculture.

26) Embryonic Hematopoiesis and Angiogenesis: Placenta Holds the Clue. **Pratik Home**[1], Ram Parikshan Kumar[2], Avishek Ganguly[1], Bhaswati Bhattacharya[1], Ananya Ghosh[1], Soumen Paul[1 1] Department of Pathology and Laboratory Medicine, Institute for Reproduction and Perinatal Research, University of Kansas Medical Center, Kansas City, KS USA. [2] Department of Developmental Neurobiology, St. Jude Children's Research Hospital, Memphis, TN, USA.

The mid-gestation mouse placenta acts as one of the major organs for hematopoietic stem cell (HSC) generation where placental labyrinth vasculature acts as a site for HSC expansion and provides a temporary niche for definitive HSC pool. However, the signaling mechanisms that regulate the hematopoietic and angiogenic development in the placenta are poorly understood. Different studies have implicated the role of GATA family of transcription factors in the development of HSCs in other organs. Recently we demonstrated that simultaneous knockout of both *Gata2* and *Gata3* in trophoblast lineage severely affected placental development and leads to very early embryonic lethality. Interestingly, the double knockout also resulted in severe loss of hematopoietic population in both the embryonic and extraembryonic tissues. Moreover, our ChIP-seq and RNA-seq analyses in mouse trophoblast cells showed that several pathways associated with the hematopoiesis and vasculogenesis were targets for both GATA transcription factors. In this study, we aim to define how GATA-dependent paracrine signaling from the parietal trophoblast giant cell (TGC) layer dictate hematopoiesis as well as angiogenesis in the mouse placenta. Our study revealed that the TGC-specific dual knockout of *Gata2* and *Gata3* resulted in the loss of placental and embryonic hematopoiesis accompanied by angiogenic defects in the placenta. The conditional double knock-out also led to intrauterine growth retardation of the embryos. Based on these findings we propose that the combinatorial role of GATA2 and GATA3 plays a critical part in the placental hematopoiesis and angiogenesis.

27) Altered Blood Plasma and Follicular Fluid Lipid Profiles Predict Alterations in Cell Signaling, Metabolism, and Immune Function in Cows with Androgen Excess. **Alexandria P. Snider**1, Renata Spuri Gomes1, Sarah M. Romereim1, Adam F. Summers2, Mohamed A. Abedal-Majed3, Sarah C. Tenley1, Scott G. Kurz1, Jeff Bergman1, Robert A. Cushman4, John S. Davis5, Jennifer R. Wood1, and Andrea S. Cupp1 1University of Nebraska-Lincoln, Lincoln, Nebraska; 2New Mexico State University, Las Cruces, New Mexico; 3University of Jordan, Amman, Jordan; 4USDA-ARS U.S. Meat Animal Research Center, Clay Center, Nebraska; 5University of Nebraska Medical Center, Omaha, Nebraska.

UNL physiology herd has cows with excess androstenedione (A4; High A4 > 40 ng/ml; control < 20 ng/ml) in follicular fluid of dominant follicles, reduced Sex Hormone Binding Globulin, and arrested follicular development leading to anovulation and reduced fertility. Our hypothesis was that altered lipid profiles in High A4 cows would identify metabolic and signal transduction processes contributing to altered follicular development resulting in anovulation. Blood plasma samples were collected at day 7 and 15 of a non-stimulated cycle and at ovariectomy after FSH stimulation (20ng/ml/12 hours). Lipid compounds (863) were identified in the follicular fluid and plasma samples via HPLC mass spectrometry with 115 lipid compounds actually annotated. The top 4 lipid compounds per sample were chosen in High A4 compared to control cows using the Random Forest Algorithm for each sample. At day 7 of the non-stimulated cycle lysophosphatidylethanolamine 22:4 (LysoPE(22:4)), which induces the MAPK signal transduction pathway, and C760 was significantly reduced in blood plasma in High A4 cows ($P<0.05$). On day 15 of the non-stimulated cycle, blood plasma had greater concentrations of C272, lysophosphatidylcholine (LPC) 22:4 (LPC(22:4)) and lysophosphatidylcholine 22:5 (LPC(22:5)) in High A4 cows $P<0.05$. The LPCs, interact with G protein-coupled receptors, and are involved in carbohydrate and lipid metabolism suggestive of increased metabolic rate in High A4 cows. The follicular fluid collected at ovariectomy in the FSH-stimulated cycle was different across all 4 lipids, with C825, C600 and 1-(1Z-octadecenyl)-2-oleoyl-sn-glycero-3-phosphocholine (Plg-SOPC) being increased and Sphingomyelin (SM(d18:0/16:1(9Z))) decreased in High A4 cows ($P<0.05$). Plg-SOPC, is produced in response to oxidative stress. Sphingomyelin helps form lipid rafts regulating signal transduction. Taken together, these data indicate that altered lipids in the blood plasma of High A4 cows may increase MAPK and G-protein receptor signaling to increase metabolic rate. Lipids in follicular fluid of High A4 cows increase oxidative stress and inhibit G-protein receptor signaling compared to controls. Thus, variations in lipid profiles of High A4 and control cows suggest potential differences in metabolic, immune and cell signaling in the High A4 cows which may contribute to their follicular arrest, anovulation and infertility. This research was funded through USDA grant 2013-67015-20965. USDA is an equal opportunity employer.

28) Development of novel mouse models using CRISPR genome editing approaches. **Katelin Gibson**, Illya Bronshteyn, Julia Draper, Melissa A. Larson, and **Jay L. Vivian**. Transgenic and Gene Targeting Institutional Facility. University of Kansas Medical Center, Kansas City, KS.

Genetic manipulation of the mouse has become a standard and indispensable tool for investigating gene function in vivo and for the development of animal models of human disease. Although the use of genetically modified mice is widespread in the biomedical research community, including KUMC, the techniques employed for the generation of these models require specialized equipment and technical expertise. The KUMC Transgenic and Gene Targeting Institutional Facility is an institutional support facility providing a centralized service for the production of transgenic and gene-targeted mice, and the related services of sperm and embryo cryopreservation, in vitro fertilization, and rederivation. By centralizing operations into the Transgenic and Gene-Targeting Facility, the gene-modified mouse is available as a research tool to all investigators of research universities in Kansas and the surrounding Kansas City research community. The Facility uses cutting edge methods, state-of-the-art instrumentation, and novel reagents for this work. Our services include microinjection services via pronuclear injection and blastocyst injection of embryonic stem cells.

The Facility is also closely involved in the development of new transgenic technologies to enhance the rapid development of novel models. We have have place significant effort in developing and optimizing methods for using CRISPR/Cas9 genome editing in vivo. Our efforts have developed a pipeline for the design, synthesis, and validation of CRISPR genome editing reagents, and their successful use in generating novel genetically modified mouse models. We will present elements of this experimental design platform in this poster, and include examples of the various genetically altered strains that have recently been developed.

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29) A growth factor that influences placental health in mice. **Ikram Mohamed**. The University of Missouri – Columbia.

The placenta is the organ responsible for the exchange of nutrients from the mother to the fetus to support growth. The placenta consists of the junctional zone that transports maternal blood to the labyrinth zone in which exchange of nutrients and oxygen occur between blood spaces. Previously, we have shown that a maternal factor called myostatin changes fetal growth without actually contacting the fetus, suggesting that removing this factor alters the development of the placenta to make it more efficient at supporting fetal growth. My goal is to determine whether this inhibition affects the development of the placenta to make it more efficient. Placentas were collected from two mice treated with an inhibiting antibody to block myostatin in the maternal blood, and two mice treated with a control antibody, from days 2.5-17.5 of pregnancy. I photographed and measured the cross-sectional areas of the junctional and labyrinth zones by using a tiling microscope and ImageJ software. In pregnant mice treated with the inhibiting antibody, there was a larger variance in the areas of the junctional and labyrinth zones than in the controls. There was no significant difference in junctional and labyrinth zone areas based on the antibody treatment. There was some evidence of increased labyrinth zone area in the inhibiting antibody-treated mice compared to controls, but it was not statistically significant. The ratio of the junctional to the labyrinth zone was not affected by the antibody treatment. In the future, we plan to measure maternal and fetal blood spaces in the labyrinth zone. We hope to use this approach to insure the placenta is efficient, to allow both mother and child to have the healthiest pregnancy possible.

30) The role of interferon gamma signaling on hemochorial placentation. **Keisuke Kozai**[1], Regan L. Scott[1], Khursheed Iqbal[1], Masanaga Muto[1], Michael J. Soares[1,2] [1]Institute for Reproduction and Perinatal Research, Departments of Pathology & Laboratory Medicine, Pediatrics, and Obstetrics and Gynecology, University of Kansas Medical Center, Kansas City, KS; [2]Center for Perinatal Research, Children's Research Institute, Children's Mercy, Kansas City, MO.

During early pregnancy, natural killer (NK) cells accumulate within the decidua where they comprise approximately 70% of all leukocytes in the uterus. We have previously reported that NK cell deficiency resulted in profound effects on hemochorial placentation, including morphogenesis of the placenta, accelerated trophoblast invasion, and enhanced trophoblast cell-guided uterine spiral artery remodeling. However, the underlying mechanism of the effects of NK cells is poorly understood. Among the extracellular signals produced by NK cells, interferon gamma (IFNG) is reported to affect invasive trophoblast cell behavior and uterine spiral artery remodeling. To explore the role of IFNG signaling on hemochorial placentation, we generated and characterized *Ifng* and IFNG receptor 1 (*Ifngr1*) mutant rat models using the CRISPR/Cas9 system. Founders with each of the mutations were backcrossed to wild type rats and the genotypes of offspring were analyzed. *Ifng* and *Ifngr1* mutations were successfully transmitted through the germline. To validate the *Ifng* mutant rat model, we used an IFNG-specific ELISA to measure IFNG protein in medium conditioned by splenocytes cultured with vehicle or concanavalin A (ConA, 5 μg/ml for 72 h). Supernatants from the splenocytes from wild type rats showed robust accumulation of IFNG (79,514.76 ± 7,717.51 pg/ml), whereas ConA treated splenocytes from *Ifng* null rats did not produce detectable IFNG (<15.6 pg/ml). Hemochorial placentation was assessed in wild type, *Ifng* null, and *Ifngr1* null conceptuses. Both morphologic (cytokeratin immunocytochemistry) and biochemical (expression of *Prl5a1* and *Prl7b1*) indices of invasive trophoblast demonstrated evidence for accelerated intrauterine trophoblast invasion in the *Ifng* and *Ifngr1* mutants. In summary, these findings suggest that IFNG signaling may contribute to at least some of the restraining effects of NK cells on intrauterine trophoblast invasion. Additional experimentation is underway to further characterize a role for IFNG in hemochorial placentation. (Supported by an American Heart Association Fellowship to KK, a Lalor Foundation Fellowship to MM, and NIH grants HD020676 and HD079363)

31) Ovarian Cortex from High A4 Cows Secrete Excess Steroid Hormones Contributing to Arrested Follicle Development, Increased Oxidative Stress and Fibrosis Which can be Rescued by Angiogenic VEGFA165 **SA Springman**1, MA Abedal-Majed2, ML Hart1, V Largen1, MPS Magamage3, SG Kurz1, KM Sargent1, J Bergman1, RM McFee1, RA Cushman4, JS Davis5, JR Wood1 and AS Cupp1 1Department of Animal Science, University of Nebraska-Lincoln, Lincoln, Nebraska; 2Department of Animal Production, University of Jordan, Amman, Jordan; Department of Livestock Production, 3Sabaragamuwa University of Sri Lanka; 4USDA-ARS U.S. Meat Animal Research Center, Clay Center, Nebraska; 5Department of Obstetrics and Gynecology, University of Nebraska Medical Center, Omaha, Nebraska

We identified a population of cows within the UNL physiology herd characterized by excess androstenedione (A4; High A4) in follicular fluid, anovulation, 17% reduction in calving rate and 43-fold higher A4 secretion from ovarian cortex cultures. Genetically un-related heifers at the U.S. Meat Animal Research Center also secreted greater A4 into media from ovarian cortex cultures; suggesting, the High A4 phenotype is present in other herds. We hypothesized that ovarian folliculogenesis is disrupted in High A4 cows due to excess A4 synthesis by the ovarian microenvironment; and vascular endothelial growth factor A (VEGFA) isoform treatment would rescue folliculogenesis by decreasing A4 production. Ovarian cortical pieces were collected at ovariectomy from High A4 (n = 5) and Control (n = 5) cows and treated with PBS or VEGFA165 (50 ng/ml) for 7 days. Media was collected daily for steroid analysis. Ovarian cortex from High A4 cows treated with PBS secreted greater (P = 0.004) concentrations of A4 and other steroid hormones compared to controls. Treatment with VEGFA165 dramatically (P = 0.004) reduced A4 and other steroid hormones secreted by the ovarian cortex of High A4 cows. Numbers of primordial follicles were greater ($P \leq 0.01$) with fewer primary, secondary and antral follicles in uncultured High A4 ovarian cortex compared to Control. Treatment with VEGFA165 stimulated greater ($P \leq 0.02$) follicular progression to secondary and antral stages in ovarian cortex from Control cows than High A4 cows. Ovarian cortex treated with PBS from High A4 cows had increased staining for markers of oxidative stress and fibrosis. Treatment with VEGFA165 reduced staining for oxidative stress and tended (P = 0.056) to reduce staining for fibrosis in High A4 ovarian cortex compared to controls. Taken together, ovarian cortex from High A4 cows secrete greater concentrations of steroid hormones, which may contribute to increased oxidative stress and fibrosis, leading to follicular arrest. VEGFA165 isoform treatment can rescue folliculogenesis and reduce ovarian cortex steroid secretion. Thus, VEGFA165 may be a potential therapeutic to restore the ovarian microenvironment and enhance follicular maturation. This research was funded through USDA grant 2013-67015-20965. USDA is an equal opportunity provider and employer.

32) Barriers to Fertility Preservation in Adolescents Exposed to Fertility Threatening Therapy. **Emily Pfeifer**, Elizabeth Kresie, MD and Courtney Marsh. University of Kansas Medical Center, Kansas City, KS; Children's Mercy Hospital, Kansas City, MO

Background: Due to advances in childhood cancer therapy, there is an expanding population of survivors with fertility issues secondary to cancer therapy. Literature has shown an adult cancer population feels fertility is a major quality of life issue and several patient barriers may be responsible for the underutilization of fertility preservation (FP). **Purpose:** There are identifiable barriers to the utilization of fertility preservation in adolescents exposed to fertility threatening therapy. If these barriers are addressed, providers can effectively communicate to patients that they have fertility preservation options post-therapy and more patients may feel comfortable using fertility preservation. **Methods:** This study involves a questionnaire survey distributed to patients (or their caregivers) between 0-29 years of age who have received a formal diagnosis and/or treatment which threatens fertility, including patients currently undergoing treatment and survivors. A total of 50 study subjects will be enrolled without power calculation since this is a survey. Part 1 of the questionnaire survey is a demographic form, which seeks to identify formal cancer diagnosis, time-to-treatment, and insurance status at the time of diagnosis. Part 2 of the questionnaire survey aims to identify patient/caregiver awareness, attitudes, and perceptions of fertility preservation. **Results:** Preliminary results obtained from a small sample size (N=9) revealed participants were a mean age of 8 years-old at diagnosis. All were insured and began treatment for their malignancy a month following diagnosis. Only 2 patients (22%) were very

or extremely aware of medications and procedures to preserve fertility, while only 1 (11%) disagreed that preserving a child's/teenager's fertility is important. Three patients (33%) were significantly concerned that FP may delay cancer treatment. **Conclusions:** Identifying the barriers to fertility preservation will allow providers to directly address these issues during patient counseling. If these barriers are addressed, more patients may feel comfortable using fertility preservation.

33) **Normalizing the immune system of the rat for analysis of immune cell function at the maternal-fetal interface.** **Regan L. Scott**[1] and Michael J. Soares[1,2] [1]Institute for Reproduction and Perinatal Research, Departments of Pathology & Laboratory Medicine, Pediatrics, and Obstetrics and Gynecology, University of Kansas Medical Center, Kansas City, KS; [2]Center for Perinatal Research, Children's Research Institute, Children's Mercy, Kansas City, MO.

Rodent model systems are frequently used to study a wide variety of human diseases. Their genomes are extensively mapped, and the ability to quickly generate genetically manipulated models allows an in-depth examination of disease physiology otherwise inaccessible in the human. Specifically, rats are a suitable model to study pregnancy disorders because they possess a hemochorial placenta with deep trophoblast invasion and spiral artery remodeling. We know that immune cells play an essential role in placental development, and disruption of immune cell interactions within the uterus can compromise the establishment of pregnancy. However, recent studies have shed light on the limitations of experiments performed in specific pathogen free (SPF) laboratory rodents because these animals exhibit limited immune system development that does not resemble the complexity of the adult human immune system. Accurate recapitulation of a complex immune system in an animal model is critical for drawing biologically relevant conclusions of the role of immune cells in pregnancy. To address this limitation, we have developed a co-housing strategy to generate laboratory rats with mature immune systems. Laboratory rats are co-housed with rats previously maintained in an environment of robust pathogen exposure ("dirty rats"). The rats are maintained in Biological Level 3 Safety facility. One month of co-housing SPF laboratory rats with "dirty rats" resulted in the introduction of several new pathogens to our laboratory colony. Pathogen transmission from "dirty rats" to SPF rats was validated through PCR of rodent infectious agent panels. Spleen weights and transcript profiles of peripheral blood mononuclear cells (PBMCs) from our co-housed laboratory rats showed significant adaptations in their immune systems. Specifically, spleen weights increased and PBMCs exhibited up-regulation of transcripts associated with several pathways including the innate immune response, interferon signaling, tumor necrosis factor signaling, allograft rejection, cytokine signaling, antigen presentation, prolactin signaling, and toll like receptor signaling. Overall, these data suggest that the co-housed SPF rodent immune systems have adapted as a result of pathogen exposure. We hypothesize that this immune adapted rat model will provide a more accurate representation of the complex interplay of immune cells at the maternal fetal interface. (Supported by NIH grants HD020676, HD079363, R01ES029280)

34) **Alterations in fetal neurogenesis and offspring cognitive functions in a murine model of hypoxia-induced placental insufficiency.** **Pei-Shan Wang**, Chu-Yen Chen, Fu-Sheng Chou. Department of Pediatrics, University of Kansas Medical Center, Kansas City, KS.
Placental insufficiency is a common cause of chronic fetal hypoxia and fetal growth restriction (FGR). Individuals with growth restriction prenatally are at significantly increased risk for neurodevelopmental abnormalities. Clinical imaging showed decreased total brain and cortical grey matter volume in FGR infants, suggesting altered cerebral cortex development. Fetal cortical neurogenesis is a time-sensitive process in which fetal neural stem cells (NSCs) follow a distinct pattern of layer-specific neuron generation to populate the cerebral cortex as the gestation progresses. It has been shown in an *in vitro* system that profound hypoxia induces cell cycle arrest in NSCs. However, the *in vivo* effect of hypoxia in fetal NSCs remains unclear. We hypothesize that chronic fetal hypoxia disrupts temporal development of cerebral cortices by affecting NSC cell cycle progression and neurogenic cell division. We aimed to test the hypothesis by using a murine maternal hypoxia-induced placental insufficiency model. In this model, timed-pregnant mice were exposed to hypoxia during the active stage of fetal neurogenesis, followed by fetal brain harvest for cryosectioning and immunostaining. In the hypoxia-exposed fetal brains, we found a significant reduction in cerebral cortical thickness accompanied by

decreases in intermediate progenitors and in layer-specific neurons. These findings suggest delayed neurogenesis. Interestingly, we also observed a defect in self-renewal in a subset of NSCs, leading to premature neuronal differentiation. Following relief from maternal hypoxia exposure, the remaining fetal NSCs re-established their neurogenic ability and resumed production of layer-specific neurons. Surprisingly, the newly generated neurons matched their control counterparts in layer-specific marker expression, suggesting preservation of the fetal NSC temporal identity despite hypoxia exposure. As expected, the number of neurons generated in the FGR group remained lower compared to that in the control group. Finally, the FGR offspring mice exhibited poorer cognitive functions by Y-maze and pre-pulse inhibition tests than the control offspring mice. Taken together, fetal hypoxia exposure is associated with a defect in neurogenesis, and has a long-term impact on offspring cognitive development. Our findings also pointed to a possible scenario where the temporal identity of the fetal NSCs is uncoupled from the process of neurogenesis.

35) **Attainment and Maintenance of Pubertal Cyclicity May Predict High A4 cows with Reduced Fertility.** **Sarah Nafziger**1, Mohamed A. Abedal-Majed1, Sarah Tenley1, Adam Summers2, Mariah Hart1, Jeff Bergman1, Scott Kurz1, Jennifer Wood1, Robert Cushman3, Andrea S. Cupp1 1 Department of Animal Science, University of Nebraska-Lincoln, Lincoln, Nebraska 2 Department of Animal Science, New Mexico State University, Las Cruces, New Mexico 3 USDA, ARS, U.S. Meat Animal Research Center, Clay Center, Nebraska 68933

The UNL physiology herd has a population of cows that secrete excess androstenedione (A4; High A4) in follicular fluid and ovarian cortex, have irregular cycles, and often are anovulatory with reduced calving rates. High A4 cows reached puberty 45 days earlier than control cows (P=0.17). To determine if manner of pubertal attainment predicted the High A4 phenotype, blood plasma samples were collected from weaning to breeding (October-May) each year from 2012-2017 (n=611). Progesterone (P4) greater than 1ng/ml was used to define puberty date with continued cyclicity. A custom SAS analysis was developed, and four distinct puberty groups were detected using puberty date as time of first P4≥1ng/ml and continued cyclicity prior to breeding: **1)** Early- 317.0±3.6 days of age (DOA) with continued cyclicity (n=143); **2)** Typical- 378.4±2.1 DOA with continued cyclicity (n=279); **3)** Start-Stop- 265.3±4.1 DOA with interrupted cyclicity (n=91); and **4)** Non-Cycling- no P4≥1ng/ml (n=98). There were no differences in birth weight, but Early and Typical heifers had greater average weaning weights and yearling weights compared to Start-Stop and Non-Cycling heifers (P<0.0001). There were no differences in prebreeding antral follicle counts between groups. Early puberty heifers had the highest average prebreeding reproductive tract scores, followed by Typical, Start-Stop, and Non-Cycling heifers (P<0.0001). At breeding, heifers were give 2 injections of prostaglandin F2α 14-days apart, and all heifers that showed estrus were artificially inseminated. Typical (78.9%) and Early (79.5%) puberty heifers displayed the greatest percentage estrus in response to prostaglandin (P<0.001), and a greater percentage of Start-Stop heifers (50.3%) displayed estrus and were artificially inseminated compared to Non-Cycling heifers (12.6%) (P<0.001). All heifers were exposed to bulls, and overall pregnancy rate did not differ between groups. However, a greater percentage of Typical (57.9%), Early (51.0%), and Start-Stop (45.2%) heifers calved in the first 21 days of the calving season compared to Non-Cycling (20.9%) heifers (P<0.001). Ovarian cortex from a subset of heifers in each puberty group was cultured, and both Start-Stop and Non-Cycling heifers secreted 47-fold greater A4 in ovarian cortex culture media than Typical or Early heifers (P=0.001). The greater concentrations of A4 produced by ovarian cortex of Start-Stop and Non-Cycling heifers along with irregular or no cyclicity prior to breeding indicates that these females may become High A4 cows. USDA is an equal opportunity provider and employer. This research was funded through USDA grant 2013-67015-20965.

36) **IL17f and the Maternal-Fetal Interface; A genetic rat model.** **Stephen H. Pierce**, Khursheed Iqbal, Masanaga Muto, Keisuke Kozai, and Michael J. Soares. Institute for Reproduction and Perinatal Research, Departments of Pathology and Laboratory Medicine, Pediatrics, and Obstetrics and Gynecology, University of Kansas Medical Center, Kansas City, Kansas; Center for Perinatal Research, Children's Research Institute, Children's Mercy, Kansas City, MO.

Interleukin 17F (IL17F) is the newest member of the IL17 family of cytokines. It shares significant homology with IL17A. IL17F is expressed as a homodimer, or as a heterodimer along IL17A. IL17 receptors A and C possess affinity for IL17F and transduce cellular signals upon engagement with IL17F. Preliminary data and genome-wide transcriptome analyses indicate that the placenta and more specifically trophoblast cells are a source of IL17F. *Il17f* transcripts are readily detected in the developing rat placenta. Most interestingly, IL17 signaling has been directly implicated in maternal immune activation. However, a role for IL17F in the biology of pregnancy is unknown. This study describes the generation of an *Il17f* mutant rat strain using CRISPR/Cas9 genome editing with the goals of investigating potential roles for IL17F in the modulation of pregnancy, placentation, and/or fetal development. Guide RNAs were designed to target two exons within the *Il17f* locus of functional significance (Exons 3 and 4). Cas9 proteins along with *Il17f* targeted guide RNAs were electroporated into rat zygotes and transplanted into the oviducts of appropriately-timed pseudopregnant female rats. Out-of-frame mutations in the offspring of the recipient mothers were confirmed via PCR screening and DNA sequencing. These founder *Il17f* mutant rats were mated with wild-type rats in order to confirm germline transmission and to generate heterozygous pups. *Il17f* heterozygous males were mated with female heterozygous litter mates in order to generate *Il17f* null pups. *Il17f* null offspring are viable and present with normal physical features. This *Il17f* mutant rat model will be used to investigate putative roles for IL17F in the regulation of normal pregnancies and pregnancies challenged by maternal immune activation. (Supported by Lalor Foundation and American Heart Association Postdoctoral Fellowships; NIH HD020676, HD079363)

37) Exploring the Role of Catechol-O-methyltransferase (COMT) in pregnancy outcome. **K Iqbal**[1], **Stephen Pierce**[1], Pramod Dhakal[1] and M J Soares[1,2] [1]Institute for Reproductive Health and Perinatal Research, Departments of Pathology and Laboratory Medicine and Anatomy and Cell Biology, and Pediatrics, University of Kansas Medical Center, Kansas; [2]Fetal Health Research, Children's Research Institute, Children's Mercy, Kansas City, MO

Catechol-O-methyltransferase (COMT) is an enzyme involved in the catabolism of catecholamines and other molecules possessing a catechol structure, such as estrogens. COMT modifies 2-hydroxyestradiol to 2-methoxyestradiol (2ME), a compound with biological functions implicated in regulatory processes associated with angiogenesis, HIF activity, trophoblast, and preeclampsia. Comt knockout mice show pregnancy complications and pregnant mice exhibit a preeclampsia-like phenotype resulting from an absence of 2-methoxyoestradiol (2-ME). Additionally, COMT pregnant knockout mice show failures in adaptations to hypoxia however no effects on placental and fetal growth was observed. The purpose of this study was to utilize a rat genetic model of COMT deficiency to investigate the involvement of COMT in placentation and pregnancy outcome. To accomplish this task, we utilized CRISPR/Cas9-mediated genome editing of the COMT gene. We designed gRNAs targeting the exons coding for S-adenosylmethionine-dependent methyltransferases (SAM-MTase) forming the active site of COMT enzyme. Following genotypic characterization of offspring, we identified a founder containing a 374 bp exonic deletion where most part of the SAM-MTase protein coding exon was deleted. The deletion resulted in a frameshift and premature stop codon as well. The mutation was transmitted to progeny, and caused a loss of the COMT protein as determined by Western blot. Similar to COMT null mice, COMT null male and female rats were viable and fertile. COMT deficiency did not significantly impact pregnancy outcomes, including litter size, sex ratio and mendelian ratio. There were no significant difference in fetal and placental weights at gestation day 18.5. There was no effect of exposure to prenatal hypoxia (10.5% ± 0.3% O2) from gestation day 6.5 to 18.5 on placental and fetal weight. All together, our data indicate that COMT gene activity is not essential for early development or pregnancy outcome. (Supported by NIH grants; ES029280 and ES028957-01A1)

38) TRAINEE ORAL PRESENTATION ONLY: **Biological Role of Prostaglandin Synthase 2 (PTGS2) on Early Conceptus Development in Pigs.** **C.A. Pfeiffer**, A.E. Meyer, L.D. Spate, J.A. Benne, R.F. Cecil, T.E. Spencer, R.S. Prather, and R.D. Geisert*: Division of Animal Sciences, University of Missouri, Columbia, MO, USA.

Pig conceptuses produce and secrete estrogens (E2), interleukin 1 beta 2 (IL1B2), and prostaglandins (PG) during the period of rapid trophoblast elongation and establishment of pregnancy. Previous studies established that IL1B2 is essential for rapid conceptus elongation (Whyte et al., *Proc Natl Acad Sci USA* 2018), whereas E2 is not essential for conceptus elongation or early maintenance of the corpora lutea (CL). Prostaglandin synthase 2 (*PTGS2*) expression increases during early pig conceptus development along with production of prostaglandins (PGs). Blastocysts express *PTGS2* but not *PTGS1* during early development. To evaluate the role of conceptus PTGS2-derived PGs in early pregnancy, CRISPR/Cas9 gene editing was used to create a deletion in exon 1 of the *PTGS2* gene. Both *PTGS2+/+* and *PTGS2-/-* embryos were generated using edited fibroblast cells and somatic cell nuclear transfer. Culture media from *PTGS2+/+* and *PTGS2-/-* blastocysts was collected at day 7. Total PG was substantially lower ($P = 0.0062$) in the culture media of *PTGS2-/-* compared to *PTGS2+/+* blastocysts. Next, *PTGS2+/+* and *PTGS2-/-* blastocysts were transferred into the uterus of surrogate gilts, and the reproductive tract was collected on either day 14 or 17 of pregnancy. Elongating and filamentous type conceptuses were recovered from the uterine lumen by flushing. The conceptuses were cultured for 3 hours to determine overall PG production. Total PG was lower ($P = 0.0166$) in media of *PTGS2-/-* conceptuses compared to *PTGS2+/+* conceptuses. However, total content of PGE2 and PGF2α in the flushings of the uterine lumen containing either *PTGS2-/-* or *PTGS2+/+* conceptuses were not different (P>0.10). Next, *PTGS2-/-* blastocysts were transferred into surrogate gilts to assess pregnancy establishment beyond 17 days. The uterus from surrogate gilts was harvested on day 34. Pregnancy was maintained and numerous viable *PTGS2-/-* embryos were present in the uterine horns of the surrogate gilts. These findings indicate that PTGS2-derived PGs from the elongating conceptus are not essential in pregnancy establishment in the pig. Research supported by USDA NIFA grant 2017-12211054.

39) TRAINEE ORAL PRESENTATION ONLY: Dynamic Regulation of the Mitochondrial Effector Dynamin Like 1 (DNM1L) and Steroidogenesis in the Bovine Corpus Luteum. **Michele R. Plewes**1,Heather Talbott1, Xiaoying Hou1, Pan Zhang1, and John S. Davis1,2 1Olson Center for Women's Health/Obstetrics and Gynecology Department, University of Nebraska Medical Center, 989450 Nebraska Medical Center, Omaha, NE 68198-9450, USA 2Veterans Affairs Medical Center, 4101 Woolworth Ave, Omaha, NE 68105, USA

The corpus luteum (CL) is an endocrine gland that synthesizes and secretes progesterone. Luteinizing hormone (LH) activates protein kinase A (PKA) signaling in luteal cells, stimulating progesterone biosynthesis. In the ruminates, prostaglandin (PG) F2α acts on the CL, initiating downstream signaling events leading to regression of the gland. Mitochondria maintain a highly regulated equilibrium between fusion/fission, to sustain biological function. Dynamin-like-1(DNM1L), is a key mediator of mitochondrial fission. Phosphorylation events at two different sites near the DNM1L GTPase effector domain regulate mitochondrial fission. Phosphorylation on Ser616 activates GTPase activity, promoting mitochondrial fission, while phosphorylation on Ser637 inhibits the GTPase activity, promoting mitochondrial stability and elongation. The mechanism by which DNM1L is regulated in the ovary is largely unknown. We hypothesize that LH and PGF2α differentially regulate the phosphorylation of DNM1L(Ser616 or Ser637) in bovine luteal cells. Bovine ovaries were obtained from a local abattoir, CL were dispersed, and small (SLC) and large (LLC) luteal cells were enriched via centrifugal elutriation. Transcriptome profiling revealed that the CL expresses transcripts for dynamin-family members, including DNM1L. In SLC, LH stimulated phosphorylation of DNM1L(Ser637) and inhibited of phosphorylation of DNM1L(Ser 616) in SLC. Overexpression of a PKA inhibitor blocked the effects of LH on DNM1L phosphorylation. Additionally, LH decreased the association of DNM1L with the mitochondria. Studies using small molecule inhibitors and siRNA knockdown of DNM1L showed that DNM1L is required for optimal LH-induced progesterone biosynthesis. In contrast, PGF2α increased phosphorylation of DNM1L(Ser616), but had no effect on phospho-DNM1L(Ser637) in LLC. Moreover, PGF2α increased the association of

DNM1L with the mitochondria. These results indicate that DNM1L is differentially regulated by LH and PGF2α signaling pathways and that DNM1L is required for optimal luteal progesterone synthesis. Taken together, the findings suggest LH may stabilize luteal mitochondria and promote steroidogenesis in bovine luteal cells via modulating the phosphorylation and activity of the GTPase DNM1L; and luteolytic hormones like PGF2α may stimulate mitochondrial fission by increasing the activity of DNM1L.

40) TRAINEE ORAL PRESENTATION ONLY: Lean maternal gestational diabetes mellitus impacts the ovarian proteome basally and in response to a stressor in later life. **Kendra L. Clark**[1], Omonseigho Talton[2], Shanthi Ganesan[1], Laura C. Schulz[2], Aileen F. Keating[1] [1]Department of Animal Science, Iowa State University [2]Department of Obstetrics, Gynecology, and Women's Health, University of Missouri

Gestational diabetes mellitus (GDM) is an obstetric disorder affecting approximately 10% of pregnancies. GDM is normally resolved at delivery, but may associate with lasting health effects for mother and progeny, with both having a higher risk of acquiring diabetes later in life. The 4HFHS (High Fat High Sucrose) mouse model emulates GDM in lean women, who comprise ~50% of GDM cases, which is characterized by insulin resistance in the first trimester, and glucose intolerance in the second-third trimester. Dams are fed a HFHS diet one week prior to mating and throughout gestation, which inhibits beta cell expansion, leading to inadequate insulin response to glucose in mid-late pregnancy. We have discovered that the ovarian response to DNA damage and environmental chemical insult is altered by metabolic changes that occur during obesity. Since the offspring of HFHS dams have increased adiposity, we hypothesized that maternal metabolic alterations during lean GDM would compromise ovarian function in offspring both basally and in response to a dietary stress later in life. Pups received either a control or HFHS diet from 23-31 weeks of age. Briefly, $D_{L}P_{C}$ were lean dams and control diet pups; $D_{L}P_{H}$ were lean dams and HFHS pups; $D_{H}P_{C}$ were HFHS dams and control diet pups and $D_{H}P_{H}$ were HFHS dams and HFHS pups. Ovarian protein was isolated, LC-MS performed and bioinformatic analysis completed. Proteins were considered to differ between treatments if the fold-change was above 1 and the *P*-value was < 0.1. A HFHS challenge in the absence of maternal GDM ($D_{L}P_{C}$ vs. $D_{L}P_{H}$) increased 3 and decreased 30 ovarian proteins. Maternal GDM in the absence of a dietary stress ($D_{L}P_{C}$ vs. $D_{H}P_{C}$) increased abundance of 4 proteins and decreased abundance of 85 proteins in the offspring ovary. Finally, 4 proteins increased and 87 proteins decreased in offspring ovaries due to dietary challenge and exposure to maternal GDM *in utero* ($D_{L}P_{C}$ vs. $D_{H}P_{H}$). Interestingly, canopy FGF signaling regulator 2 (CNPY2), DAZ associated protein 1 (DAZAP1), and serine/arginine-rich splicing factor 2 (SRSF2) were altered across multiple groups. Relative to offspring who did not experience GDM *in utero* or a dietary stress in later life ($D_{L}P_{C}$), CNPY2 decreased ($P \leq 0.05$) by 2.18-fold in offspring exposed to both GDM and HFHS diet ($D_{H}P_{H}$) and in offspring either from GDM pregnancies ($D_{H}P_{C}$; 1.72-fold) or fed a HFHS diet ($D_{L}P_{H}$; 1.65-fold). DAZAP1 also decreased ($P < 0.05$) by 5.13-fold in the $D_{L}P_{C}$ vs. $D_{H}P_{H}$ offspring and by 2.43-fold in the $D_{L}P_{C}$ vs. $D_{H}P_{C}$. In contrast, SRSF2 displayed a 1.42-fold increase ($P < 0.05$) in the $D_{L}P_{C}$ vs. $D_{H}P_{H}$ and increases of 1.91-fold and 1.70-fold in $D_{L}P_{C}$ vs. $D_{H}P_{C}$ and $D_{L}P_{C}$ vs. $D_{L}P_{H}$, respectively. Altered abundance of ovarian proteins in offspring who experienced maternal GDM underscore the potential long-term effects of metabolic changes on ovarian function. Together, these findings suggest a possible impact on fertility and oocyte quality in relation to GDM exposure *in utero* as well as in response to a western diet in later life.

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