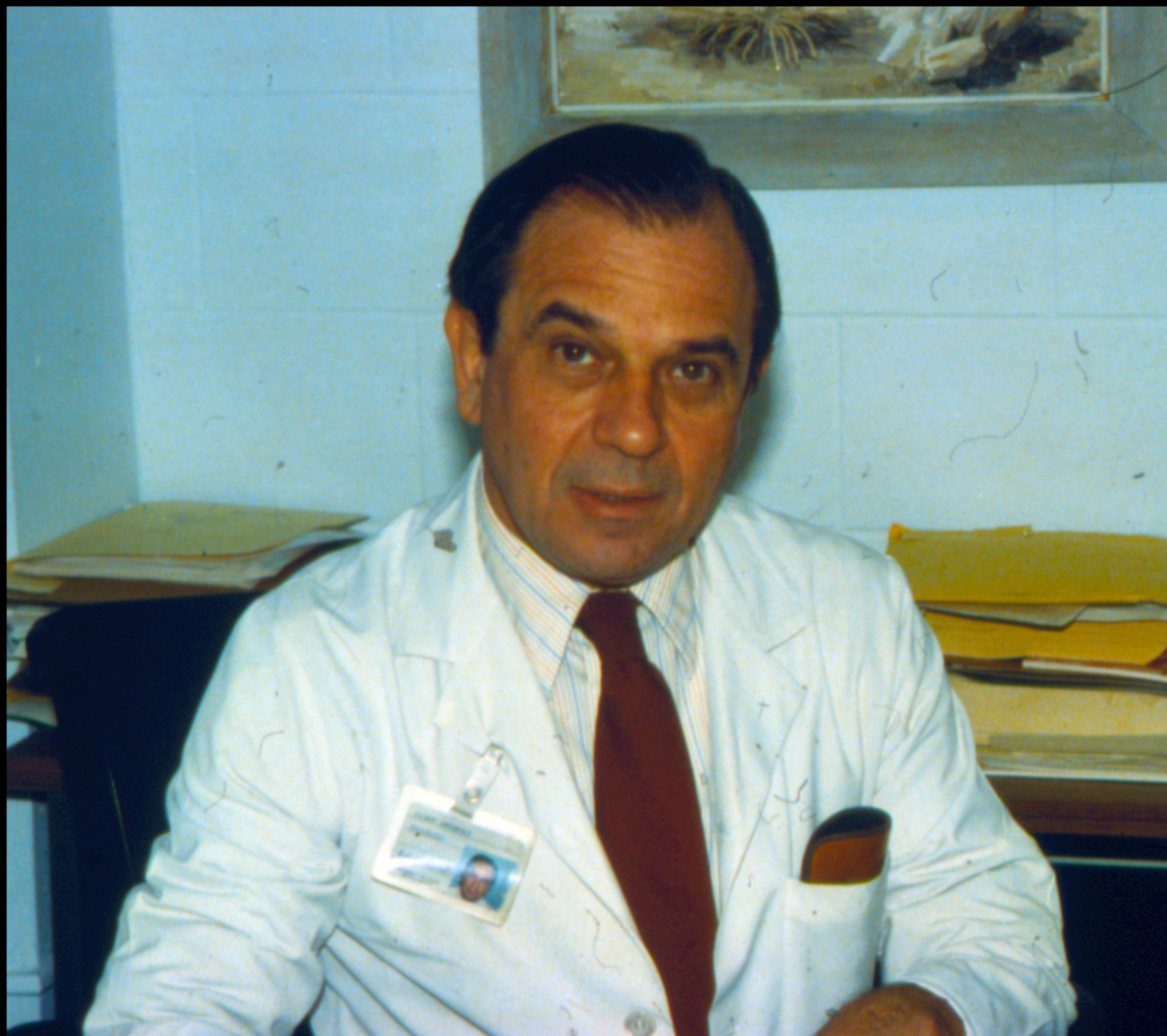


The 14th Annual Gilbert S. Greenwald Symposium on Reproduction and Regenerative Medicine

October 19 - 20, 2017

KU MEDICAL
CENTER
The University of Kansas



Biography - Gilbert S. Greenwald



The Institute for Reproductive Health and Regenerative Medicine 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.

TABLE OF CONTENTS

Gilbert S. Greenwald Biography	1
Sponsors & Volunteers	2
Organizing Committee	3
History	4-5
Program Schedule	6-7
KUMC Campus Map	8
Kansas City Map (Library)	9
Venue Information	10
Speaker Biographies	11-14
Abstract Titles	15-19
Full Abstracts	20-41
Registrant List	42-43
Notes	44

Sponsors & Volunteers



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

Sponsors

Pola Greenwald
Beth Greenwald Jordan
Department of Anatomy and Cell Biology, KUMC
Department of Pharmacology, Toxicology and Therapeutics, KUMC
University of Kansas Cancer Center
Kansas Intellectual and Developmental Disabilities Research Center
School of Medicine Bohan Endowed Speaker Program
Institute for Reproductive Health and Regenerative Medicine
Donald C. Johnson Scholar Fund
NIH R13 HD083029 (Katherine Roby, PI)

Volunteers

Bhaswati Bhattacharya, MS, Graduate Student
Kaela Varberg, PhD, Postdoctoral Fellow
Jackson Nteeba, PhD, Postdoctoral Fellow
Keisuke Kozai, PhD, Postdoctoral Fellow
Masanaga Muto, PhD, Postdoctoral Fellow
Huizhen Wang, Research Associate
Khursheed Iqbal, PhD, Research Assistant Professor
Elizabeth Thoenen, MS, Graduate Student
Regan Scott, MS, Research Assistant
Stephen Pierce, BS, Research Assistant
Ashley Cloud, BS, Graduate Student
Zahraa Alali, MS, Graduate Student
Pavla Brachova, PhD, Postdoctoral Fellow
Nehemiah Alvarez, PhD, Postdoctoral Fellow

Organizing Committee



MEMBERS:

Katherine F. Roby, PhD (Chair)
Research Associate Professor of Anatomy and Cell Biology

Soumen Paul, PhD
Associate Professor of Pathology and Laboratory Medicine

Lane K. Christenson, PhD
Associate Professor of Molecular and Integrative Physiology

Warren B. Nothnick, PhD, HCLD
Professor of Molecular and Integrative Physiology

Clifford W. Mason, PhD
Assistant Professor of Obstetrics and Gynecology

TRAINEE REPRESENTATIVES

Jackson Nteeba, PhD,
Postdoctoral Fellow, Pathology and Laboratory Medicine

Pavla Brachova, PhD
Postdoctoral Fellow, Molecular and Integrative Physiology

Bhaswati Bhattacharya, MS
Graduate Student, Pathology and Laboratory Medicine

EVENT SUPPORT STAFF:

Institute for Reproductive Health and Regenerative Medicine

Priscilla Nechrebecki, BS, Coordinator

Stacy McClure, 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 Francisco

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 Francisco
Osborn Address

Romana A. Nowak, PhD
University of Illinois

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, Oregon National Primate Research Institute

Sarah Kimmis, PhD, McGill University

Donald F. Conrad, PhD, Washington University

Deborah M. Sloboda, PhD, McMaster University

Kathleen M. Caron, PhD, University of North Carolina

Program Schedule



THURSDAY, October 19th

University of Kansas Medical Center

3901 Rainbow Blvd., Kansas City, KS 66160

4:00 p.m.

Welcome from **Greenwald Symposium Trainee Elevator Pitch Organizer Pavla Brachova, PhD**, 1006 Wahl West (Auditorium)

4:00 - 4:45 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 **Interim Executive Vice Chancellor, and Dean of the KU School of Medicine Robert D. Simari, MD**

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 by **Soumen Paul, PhD, Associate Professor**

5:10 - 6:15 p.m.

Keynote Lecture: Kent Thornburg, PhD, Oregon Health and Science University

"Adult-Onset Chronic Disease: Blame the Placenta"

6:30 - 8:30 p.m.

Reception and Poster Session, 5th FI Health Education Building (HEB), Ad Astra Room (Poster Session Begins at 7 p.m.)

FRIDAY, October 20th

BRING IN YOUR PARKING TICKET

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

(Parking garage located on NW corner of 10th & Baltimore, just West of library)

8:00 - 8:30 a.m.

Breakfast

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.)

Hugh Clarke, PhD, McGill University

(Pavla Brachova, PhD, introducing)

"Germline-Somatic Communication in the Ovary: a New Model and Implications for Fertility"

9:05 - 9:35 a.m.

(Q&A 9:30-9:35 a.m.)

Diana Laird, PhD, University of California - San Francisco

(Kaela Varberg, PhD, introducing)

"Epigenetic Dysregulation of Fetal Germ Cells by Environmental Exposures"

9:35 - 9:50 a.m.

(Q&A 9:47-9:50 a.m.)

Kelsey Timme, BS, University of Nebraska-Lincoln

(Michael Wolfe, PhD, introducing)

"Ovarian Inflammation and Oxidative Stress Associated with Diet Induced Obesity (DIO) Impacts RNA-Binding Protein Expression and mRNA Stability in the Murine Oocyte"

Program Schedule



9:50 - 10:05 a.m.
(Q&A 10:02-10:05 a.m.)

Omonseigho Talton, BS, University of Missouri

(Michael Wolfe, PhD, introducing)

“Maternal Glucose Intolerance Increases Offspring Adipose Mass and Insulin Signaling in Mice”

10:05 - 10:30 a.m.

Morning Break

Session II

10:30 - 11:00 a.m.
(Q&A 10:55-11 a.m.)

Liang Ma, PhD, Washington University - St. Louis

(Zahraa Alali, MS, introducing)

“Protein Ubiquitylation in Murine Spermatogenesis”

11:00 - 11:30 a.m.
(Q&A 11:25-11:30 a.m.)

James Pru, PhD, Washington State University

(Ashley Cloud, BS, introducing)

“PGRMC1 and PGRMC2 Functions in Female Fertility Disease”

11:30 - 11:45 a.m.
(Q&A 11:42-11:45 a.m.)

Zahraa Alali, MS, University of Kansas Medical Center

(Vargheese Chennathukuzhi, PhD, introducing)

“Identification of RPLP1 as a Novel Target of miR-451a Whose Expression is Elevated in Endometriotic Lesion Tissue and Correlates with Endometriotic Lesion Tissue and Cell Proliferation”

11:45 - 12:00 p.m.
(Q&A 11:57 a.m.-12 p.m.)

Andrew Kelleher, BS, University of Missouri

(Warren Nothnick, PhD, HCLD introducing)

“Forkhead box a2 (FOXA2) and Endometrial Glands are Essential for Uterine Function and Fertility”

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.)

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

(Bhaswati Bhattacharya, MS, introducing)

“Towards a Mechanism of Epigenetic Inheritance”

2:15 - 2:45 p.m.
(Q&A 2:40-2:45 p.m.)

Mellissa Mann, PhD, Magee-Womens Research Institute

(Jackson Nteeba, PhD, introducing)

“Impact of Assisted Reproductive Technologies on Genomic Imprinting”

2:45 - 3:00 p.m.
(Q&A 2:57-3:00 p.m.)

Yahan Li, BS, University of Missouri

(Clifford Mason, PhD, introducing)

“Assessment of Misregulated microRNAs and Their Target mRNAs in an Assisted Reproduction-induced Congenital Overgrowth Syndrome in Bovine”

3:00 - 3:15 p.m.
(Q&A 3:12-3:15 p.m.)

Jackson Nteeba, PhD, University of Kansas Medical Center

(Jay Vivian, PhD, introducing)

“Disruption of Pancreatic Prolactin Receptor Signaling Impairs Maternal Glucose Homeostasis”

3:15 - 3:30 p.m.

Closing comments - meeting adjourned

KUMC Campus Map



14th Annual Gilbert S. Greenwald Symposium on Reproduction and Regenerative Medicine

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

Parking Instructions:

Eaton Street can be accessed from either Rainbow Blvd. or 39th Ave. Once on Eaton St., access to the P5 Garage entrance is located on the West side.

1006 Wahl West (Auditorium):

From the P5 garage, follow the sidewalk that runs between the Hemenway building (HLSIC) and Dykes Library. Enter the Health Education Building via the exterior stairs. Once inside the HEB, you will be on the 1st Floor - walk across the sky-walk 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 past the Orr-Major elevators returning to the bridge to cross 39th Ave. Take the HEB elevators up to the 5th floor. Exit the elevator to your right and follow the North hallway (and signs) to the registration table, located inside the Ad Astra Room.

After the event, exit the North doors on either the ground and/or 1st floors to access the sidewalk that runs between the Hemenway building and Dykes Library to return back to the P5 Garage.

Agenda:

4:00-4:45 p.m.

Trainee Elevator Pitches, 1006 Wahl West

5:00-6:15 p.m.

Keynote Lecture, 1006 Wahl West

6:30-8:30 p.m.

Reception & Poster Session,
Ad Astra Room, 5th floor

- Event parking
- Event locations
- Walking route to event locations
- ↑↓ Elevator
- ♿ Accessible parking spaces

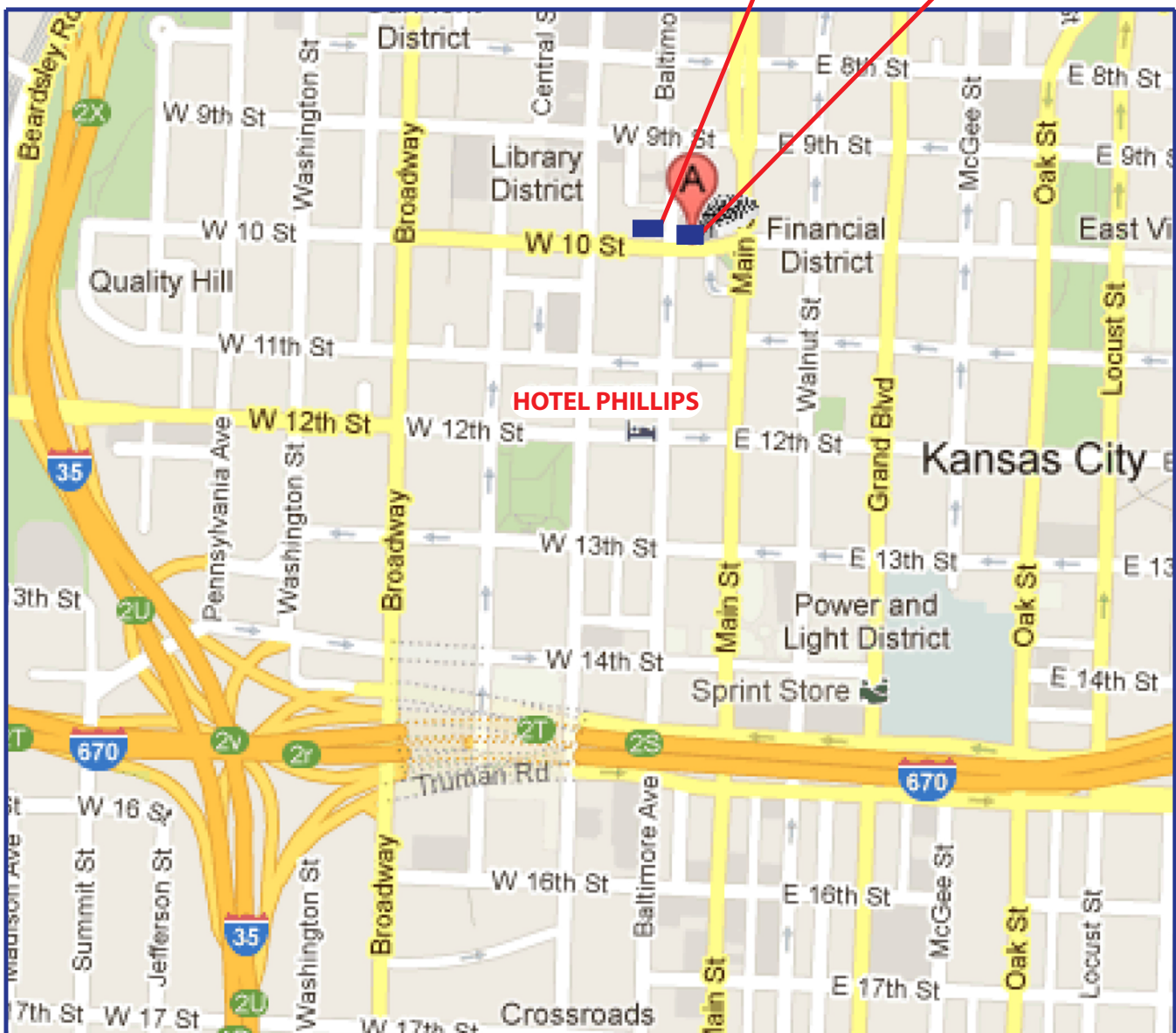
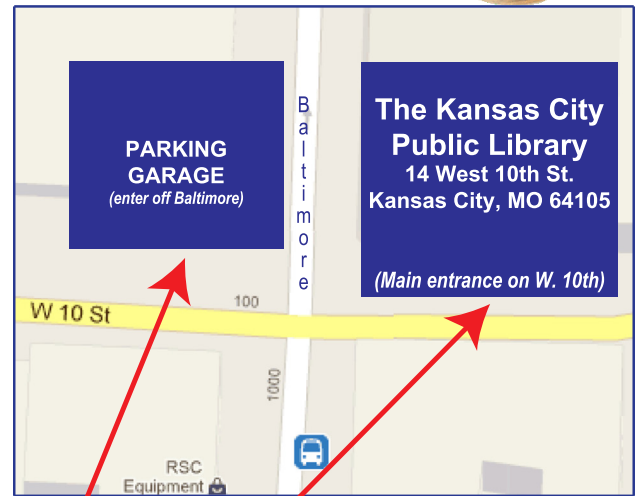
KU MEDICAL CENTER
The University of Kansas



Kansas City Map



The Kansas City Public Library - Central is located on the Northeast corner of W. 10th and Baltimore in downtown Kansas City, MO. The parking garage is West of the library, on the Northwest corner of W. 10th and Baltimore. **BE SURE TO BRING YOUR PARKING TICKET IN WITH YOU 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.

Speaker Information



Keynote Lecture



Kent Thornburg, PhD

M. Lowell Edwards Chair, Professor of Medicine
Director, Center for Developmental Health, Knight
Cardiovascular Institute

Director, Bob and Charlee Moore Institute for Nutrition and
Wellness

Oregon Health and Science University

“Adult-Onset Chronic Disease: Blame the Placenta”

Kent L. Thornburg, PhD, is the M. Lowell Edwards Chair of Cardiovascular Research, Professor of Medicine in the Knight Cardiovascular Institute at the Oregon Health & Science University. He holds joint professorships in the Departments of Physiology & Pharmacology, Medical Informatics and Clinical Epidemiology and Obstetrics & Gynecology. He directs the Center for Developmental Health in the Knight Cardiovascular Institute and the OHSU Bob and Charlee Moore Institute for Nutrition & Wellness. He studies how women adapt to pregnancy and the roles of maternal diet and body composition in regulating fetal growth and lifelong health. He collaborates with scientists in England, New Zealand, Switzerland, Finland, Australia and India. He oversees clinical studies in rural Oregon and Alaska. Kent Thornburg serves regularly on advisory panels at the National Institutes of Health, the American Heart Association and the Children's Heart Foundation and serves on the medical advisory board of the Preeclampsia Foundation. He is director of research training for the Knight Cardiovascular Institute and holds grants from the NIH. He recently co-chaired the task force to determine the 10 year vision of the developmental origins of health and disease for the National Institute of Child Health and Human Development. He is currently co-chairing the planning committee on genetic and epigenetic effects on mothers and children for the NIH Environmental influences on Child Health Outcomes (ECHO) Program.

Session I



Hugh Clarke, PhD

Professor
Dept. of Obstetrics and Gynecology
McGill University
Montreal, Canada

“Germline-Somatic Communication in the Ovary: a New Model and Implications for Fertility”

Dr. Clarke is a Professor in the Department of Obstetrics and Gynecology at McGill University where he holds the Richard Cruess Chair in Reproductive Biology. He is co-Associate Leader of the Child Health and Human Development programme at the Research Institute of the McGill University Health Centre and Director of the Research Division of Obstetrics and Gynecology. Research in Dr. Clarke's laboratory focuses on the development of the mammalian female germ cell – notably, understanding how communication between the oocyte and its follicular environment becomes established and is regulated, and developing conditions that support oocyte growth and differentiation in vitro – and is supported by the Canadian Institutes of Health Research, National Institutes of Health (USA), and the Natural Sciences and Engineering Research Council (Canada). He has served on multiple grant review panels in Canada and the USA. In July 2017, Dr. Clarke became co-Editor-in-Chief of Biology of Reproduction.



Diana Laird, PhD

Associate Professor
Dept. of Reproductive Sciences
University of California - San Francisco

“Epigenetic Dysregulation of Fetal Germ Cells by Environmental Exposures”

Dr. Diana Laird is an Associate Professor in the UCSF Department of Obstetrics, Gynecology and Reproductive Sciences and the Eli and Edythe Broad Center for Regeneration Medicine and Stem Cell Research. Her research focuses on the developmental mechanisms that determine the fitness of our germ cells to pass information to the next generation. Work in her lab has focused on the regulation of primordial germ cell migration and expansion in the mouse embryo by intrinsic and niche mechanisms, including the Wnt and Kit signaling pathways. This interest was inspired by her graduate work on germline stem cell competition in ascidians. Her group has also developed methodology for 3D quantitative imaging of developing ovaries as well as implanting embryos. These endeavors aim toward understanding the causes of infertility and birth defects, as well as the potential for environmental exposures to alter our germ cells and impact the health of future generations. Dr. Laird earned an undergraduate degree in physics at Harvard University and a PhD in Immunology/Stem Cells at Stanford. She is the recipient of the NIH Director's New Innovator Award. She lives in San Francisco with her husband and two children.

Session II



Liang Ma, PhD

Associate Professor
Dept. of Developmental Biology
Washington University - St. Louis

“Protein Ubiquitylation in Murine Spermatogenesis”

Dr. Ma is an Associate Professor in the Department of Medicine, Division of Dermatology at Washington University. He received his B.A. degree in 1989 from University of California, Berkeley in biochemistry and his Ph.D. degree in 1995 from University of Southern California in biochemistry and molecular biology where his thesis mentor was Dr. Robert Maxson. His postdoctoral training was with Dr. Richard Maas at Brigham and Women's Hospital and Harvard Medical School where he discovered Abdominal B Hox genes as targets of diethylstilbestrol in the developing uterus. Dr. Ma's first academic position was in the Department of Cell and Molecular Biology at Tulane University. In 2004, he was recruited to Washington University Division of Dermatology where he was promoted to Associate Professor with tenure in 2011. Dr. Ma uses transgenic and knockout mouse models to elucidate genetic pathways controlling organogenesis and determine how exogenous factors alter key developmental processes. He has published more than 50 papers and is widely recognized for his contributions to signal transductions during organogenesis. He currently serves as a standing member of the Cellular, Molecular and Integrative Reproduction (CMIR) study section in addition to participating in numerous reviewing and advisory panels of NIH, NSF as well as other governmental and private foundations. He also serves on the editorial board of several journals including Biology of Reproduction. Dr. Ma has trained a number of graduate students and post-doctoral fellows. His research has been continually funded by NIH and NSF.



James K. Pru, PhD

Professor, Dept. of Animal Sciences
Associate Director, Center for Reproductive Biology
Washington State University

“PGRMC1 and PGRMC2 Functions in Female Fertility Disease”

Dr. Pru is a Professor in the Department of Animal Sciences and Associate Director of the Center for Reproductive Biology at Washington State University (WSU). He also holds an adjunct position in the School of Molecular Biosciences. Dr. Pru completed his graduate studies at the University of Wyoming in 2000 before conducting his postdoctoral training at Massachusetts General Hospital, Harvard Medical School. He spent six years transitioning from Instructor to Assistant Professor within the Harvard system and then relocated to his current position at WSU in Pullman, WA. Dr. Pru's research centers on three different, but related areas of endometrial biology. Using transgenic mouse models, Dr. Pru's research group and collaborators are interested in understanding the sophisticated molecular dialog that exists between the implanting embryo and receptive endometrium as pregnancy is established. As part of this process, mechanisms coordinating decidualization of the stromal cell compartment of the endometrium are of particular interest. As the endometrium is arguably the most highly regenerative tissue in mammals, a second research focus is to understand how the endometrium regenerates following menses and parturition. Fibrosis is a common element of repair/regeneration in most tissues; however, unlike these other tissues, endometrial regeneration occurs without fibrosis. Studies in the Pru lab are focused to understand pathways (e.g., stem cell-based and mesenchymal-to-epithelial transition) that allow for fibrosis-free regeneration of the endometrium. Finally, Dr. Pru has been evaluating non-classical progesterone signaling in the endometrium. Progesterone receptor membrane component (PGRMC) 1 and PGRMC2 are purported non-classical progesterone receptors that may mediate progesterone signaling in the endometrium. Dr. Pru is working toward understanding both progesterone-dependent and progesterone-independent functions of PGRMC1 and PGRMC2 in the contexts of female reproductive physiology and pathophysiology.

Session III



Eric Greer, PhD

Assistant Professor
Dept. of Pediatrics/Newborn Medicine
Harvard Medical School
Boston Children's Hospital

“Towards a Mechanism of Epigenetic Inheritance”

Eric Greer is an Assistant Professor at Harvard Medical School the Division of Newborn Medicine at Boston Children's Hospital. The Greer lab is interested in identifying how epigenetic information is transmitted from parents to their descendants and how this information can regulate complex phenotypes. An increasing number of complex phenotypes, such as physical appearance, energy metabolism, psychological state, and longevity, have recently been shown to be regulated, in part, by epigenetic information. Epigenetics describes how gene expression changes occur without changes to the DNA sequence. How this information, which is not directly coded in our DNA, is passed from generation to generation is still unknown. We have previously identified chromatin-modifying enzymes that regulate complex transgenerational phenotypes in *C. elegans*, including longevity and fertility. Mutation of a histone H3 lysine 4 (H3K4) trimethylation complex regulates worm lifespan in both the generation in which the mutation occurs and in subsequent generations lacking the mutation. More recent work focuses on understanding how deletion of the *C. elegans* H3K4me2 demethylase, *spr-5*, leads to inherited accumulation of the euchromatic H3K4me2 mark and a progressive decline in fertility in successive generations. To investigate the underlying molecular mechanism behind progressive sterility of *spr-5* mutant worms, we carried out an RNAi screen and identified both suppressors and enhancers of sterility. This screen led to a working model for how epigenetic changes in histone H3 methylation might be inherited to affect complex organismal traits. We also identified a novel form of DNA modifications in Metazoa, methylation of adenines (6mA), which may be responsible for stable transgenerational epigenetic inheritance.



Mellissa Mann, PhD

Associate Professor
Dept. of Obstetrics, Gynecology and Reproductive Sciences
Magee-Womens Research Institute

“Impact of Assisted Reproductive Technologies on Genomic Imprinting”

Dr. Mellissa Mann received her doctorate in Dr. Susannah Varmuza's laboratory at The University of Toronto. She then trained with Dr. Marisa Bartolomei at The University of Pennsylvania as a Howard Hughes Medical Institute Fellow and Lalor Foundation Postdoctoral Fellow. In 2005, Dr. Mann joined the Departments of Obstetrics & Gynecology, and Biochemistry at The University of Western Ontario, and the Children's Health Research Institute in 2005. In 2011, Dr. Mann was appointed to Associate Professor. In 2015, Dr. Mann joined the University of Pittsburgh and the Magee Women's Research Institute and foundation, where she is a Magee Auxiliary Research Scholar. Research. Dr. Mellissa Mann's laboratory focuses on molecular mechanisms that regulate genomic imprinting during gametogenesis and early embryo development. Errors in imprinting can cause disorders, such as Beckwith-Wiedemann Syndrome, Angelman Syndrome, and Silver-Russell Syndrome. Research in her lab focuses on four main projects using the mouse as a model system: Effects of assisted reproductive technologies on genomic imprint maintenance; Role of the *Kcnq1ot1* long noncoding in stem cells and early embryos; Imprinted domain regulation; and Identification of genomic imprinting control regions.

Abstract Titles



- 1. (TRAINEE ORAL PRESENTATION) Assessment of Misregulated microRNAs and Their Target mRNAs in an Assisted Reproduction-induced Congenital Overgrowth Syndrome in Bovine. Yahan Li**¹, Darren E. Hagen², Zhiyuan Chen¹, Tieming Ji³, and Rocío Melissa Rivera¹ ¹Division of Animal Sciences, ³Department of Statistics, University of Missouri, Columbia, MO 65211, ²Department of Animal Science, Oklahoma State University, Stillwater, OK 74078
- 2. (TRAINEE ORAL PRESENTATION) Disruption of Pancreatic Prolactin Receptor Signaling Impairs Maternal Glucose Homeostasis. Jackson Nteeba**¹, Kaiyu Kubota¹, Wenfang Wang², Hao Zhu², Guoli Dai³, and Michael J. Soares^{1,4} ¹IRHRM, Department of Pathology and ²Department of Clinical Laboratory Sciences, University of Kansas Medical Center, Kansas City, KS; ³Department of Biology, Indiana University-Purdue University, Indianapolis, IN; ⁴Fetal Health Research, Children's Research Institute, Children's Mercy, Kansas City, MO.
- 3. Saturated Free Fatty Acids Induce Trophoblast Lipoapoptosis. Sathish Kumar Natarajan**, Ezhumalai Muthukrishnan, Philma Glora Muthuraj, Prakash Kumar Sahoo, Taylor Bruett, Justin L. Mott. Department of Nutrition and Health Sciences, University of Nebraska-Lincoln, Lincoln, NE
- 4. Pluripotent Stem Cell Models in the KUMC Transgenic Facility. Julia Draper**, Jennifer Pace, Illya Bronshteyn, Jay L. Vivian, and Melissa Larson. Transgenic and Gene Targeting Institutional Facility, University of Kansas Medical Center, Kansas City, KS.
- 5. The Recombination Landscape of *Drosophila virilis* Under Hybrid Dysgenesis. Lucas Hemmer** and Justin Blumenstiel. Ecology and Evolutionary Biology, University of Kansas, Lawrence, KS
- 6. 'wtf Causes Infertility?': Investigating Poison-antidote Meiotic Drivers in Fission Yeast. Nicole Nuckolls**¹, María Angélica Bravo Nuñez, and Sarah Zanders¹ ¹Stowers Institute for Medical Research
- 7. Mutp53 Inhibits Stress Granule Formation in Osteosarcoma Cells. Elizabeth Thoenen**, Alejandro Parrales-Briones, Atul Ranjan, Satomi Yamamoto, Dan A. Dixon, and Tomoo Iwakuma. University of Kansas Medical Center.
- 8. Impact of Glyphosate on Ovarian Signaling Pathways Regulating Folliculogenesis and Steroidogenesis. Ganesan, S.**, Nteeba, J. and Keating, A.F. Department of Animal Science, Iowa State University, Ames, IA 50011
- 9. Effect of Sire Conception Rate on Pregnancy Establishment in Dairy Cattle. M. Sofia Ortega**, João G. N. Moraes, David J. Patterson, Michael F. Smith, and Thomas E. Spencer. Division of Animal Sciences, University of Missouri, Columbia, MO, 65211
- 10. Development of Novel Mouse Models Using Genome Editing Approaches. Melissa A. Larson**, Illya Bronshteyn, Jennifer Pace, Julia Draper, and Jay L. Vivian. Transgenic and Gene Targeting Institutional Facility. University of Kansas Medical Center, Kansas City, KS.

- 11. Endocrine Profiles during Attainment of Puberty may Predict Reproductive Longevity in Heifers.** Sarah Nafziger¹, Mohamed A. Abedal-Majed¹, Sarah Tenley¹, Adam Summers², Mariah Hart¹, Gavin Harsh¹, 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
- 12. Novel Markers of Early Human Trophoblast Differentiation.** Rowan M. Karvas, Toshihiko Ezashi, Danny Schust, R. Michael Roberts and Laura C. Schulz*, the University of Missouri- Columbia.
- 13. Signaling Reciprocity Between PKC Iota and Bone Morphogenetic Protein GDF6 Balances Self-renewal Versus Differentiation of TSC-like Progenitor in the Placenta Primordia.** Bhaswati Bhattacharya¹, Pratik Home¹, Soma Ray¹ and Soumen Paul¹ ¹Department of Pathology and Laboratory Medicine, Institute for Reproductive Health and Regenerative Medicine, University of Kansas Medical Center, Kansas City, Kansas.
- 14. The Testicular Explant System is a Suitable Translational Tool to Determine the Toxicity Threshold of Male Germ Cell Toxicants.** Prabakaran Esakky, Deborah A. Hansen, Andrea M. Drury, Paul Felder, Andrew Cusumano, Kelle H. Moley. Research, Department of Veterans Affairs Medical Center, St. Louis MO. Department of Obstetrics and Gynecology, Washington University School of Medicine in St. Louis, Missouri 63110.
- 15. Palmitoleate Protects Zika Virus-induced Placental Trophoblast Apoptosis.** Philma Glora Muthuraj, Ezhumalai Muthukrishnan, Prakash Kumar Sahoo, Asit Pattnaik and Sathish Kumar Natarajan. Department of Nutrition and Health Sciences, University of Nebraska-Lincoln, NE
- 16. Dioxin-Activated Aryl Hydrocarbon Receptor Signaling Promotes Adaptations in Hemochorial Placentation.** Khursheed Iqbal¹, Pramod Dhakal¹, Katherine F. Roby¹, Stephen Pierce¹ and Michael J. Soares^{1,2} ¹Institute for Reproductive Health and Regenerative Medicine, Departments of Pathology and Laboratory Medicine and Anatomy and Cell Biology, and Pediatrics, University of Kansas Medical Center, Kansas; ²Fetal Health Research, Children's Research Institute, Children's Mercy, Kansas City, MO
- 17. Effects of FOXA2 Conditional Overexpression on Female Reproduction in Mice.** Peng Wang¹, Kelsey E. Brooks¹, San-Pin Wu², Franco J. Demayo², and Thomas E. Spencer¹. ¹Division of Animal Sciences, University of Missouri, Columbia, MO; ²Reproductive & Developmental Biology Laboratory, National Institute of Environmental Health Sciences, Research Triangle, NC.
- 18. Ovarian Cortex from High A4 Cows Secretes Excess A4, and Exhibits Increased Oxidative Stress, and Arrested Follicle Development Which can be Partially Rescued by Angiogenic VEGFA Isoforms.** Mohamed A. Abedal-Majed¹, Mariah L. Hart¹, Valerie Largent¹, Manjula PS Magamage², Scott G. Kurz¹, Kevin M. Sargent¹, Jeffrey Bergman¹, Renee M. McFee³, Robert A Cushman⁴, John S Davis⁵, Jennifer R Wood¹ and Andrea S Cupp¹. ¹ Department of Animal Science, University of Nebraska-Lincoln, Lincoln, Nebraska ² Department of Livestock Production, Sabaragamuwa University of Sri Lanka RN 70140 ³School of Biomedical and Veterinary Science, University of Nebraska-Lincoln, Lincoln, NE ⁴USDA, ARS, U.S. Meat Animal Research Center, Clay Center, NE 68933 ⁵Department of Obstetrics and Gynecology, University of Nebraska Medical Center, Omaha, NE

19. Global Repression of Transposable Elements in the Overgrown Placentas Dwarf Hamster Hybrids. Jonathon Russel and Justin P. Blumenstiel. University of Kansas, Department of Ecology and Evolutionary Biology, Lawrence, KS

20. (TRAINEE ORAL PRESENTATION) Ovarian Inflammation and Oxidative Stress Associated with Diet Induced Obesity (DIO) Impacts RNA-Binding Protein Expression and mRNA Stability in the Murine Oocyte. Kelsey Timme, Fang Xie, Katie L. Bidne, John S. Davis, and Jennifer R Wood. Department of Animal Science, University of Nebraska-Lincoln, Lincoln, NE. OB/Gyn Department, University of Nebraska Medical Center, Omaha, NE

21. (TRAINEE ORAL PRESENTATION) Maternal Glucose Intolerance Increases Offspring Adipose Mass and Insulin Signaling in Mice. Omonseigho Talton, Keenan Bates, Kylie Hohensee and Laura Schulz. Division of Biological Sciences and Department of Ob, Gyn & Women's Health, University of Missouri, Columbia, MO.

22. Role of a Rare Variant of BHLHB9 in an Undiagnosed Pediatric Neurological Disorder. Jay L. Vivian¹, Michelle Winter¹, Jennifer Pace¹, Sarah Tague¹, Merlin G. Butler¹, Sarah Soden², Neil Miller², Kenneth E. McCarson¹, and Peter G. Smith¹ ¹Kansas Intellectual and Developmental Disabilities Research Center, University of Kansas Medical Center, Kansas City KS. ²Children's Mercy Center for Pediatric Genomic Medicine, Kansas City MO

23. Studying Early Onset Preeclampsia (EOPE) in a Model for Early Stage Human Placental Trophoblast. Megan Sheridan¹, Y Yang², A Lyons², Y Tian², DJ Schust³, LC Schulz³, T Ezashi², RM Roberts^{1,2} ¹Department of Biochemistry, ²Division of Animal Sciences, and ³Department of Obstetrics, Gynecology and Women's Health, University of Missouri-Columbia

24. Na,K-ATPase $\alpha 4$ and Not $\alpha 1$ is Essential for Sperm Function, but its Ouabain Binding Site is Not Required for Male Fertility. Gustavo Blanco, Jeff P. McDermott, Gladis Sánchez, and Liu Lijun. Dept. of Medicine, College of Medicine and Life Sciences, University of Toledo and Dept. of Molecular and Integrative Physiology, University of Kansas Medical Center. Kansas City, USA.

25. Investigating the Role of Type I Collagen in Mouse Uterine Function. Jenna DeCata, Arin K. Oestreich, Janae Judon, Charlotte L. Phillips, Laura C. Schulz. University of Missouri, Columbia, MO

26. Maternal Obesity Affects Fetal Growth with Maternal Obesity Associated Growth Restriction Attributed to Decreased 11 β -Hydroxysteroid Dehydrogenase Expression. Andrea R. McCain, Kristin A. Beede, Dustin T. Yates, Jennifer R. Wood.

27. Conceptus Elongation in Beef Heifers with Superior Uterine Capacity for Pregnancy. Joao G.N. Moraes¹, Thomas W. Geary², Peter J. Hansen³, Holly Neiberghs⁴, Susanta Behura¹, Thomas R. Hansen⁵, Thomas E. Spencer¹ ¹Division of Animal Sciences, University of Missouri, Columbia, Missouri ²USDA-ARS, Fort Keogh Livestock and Range Research Laboratory, Miles City, MT ³Department of Animal Sciences, University of Florida, Gainesville, FL ⁴Department of Animal Sciences and Center for Reproductive Biology, Washington State University, Pullman, WA ⁵Animal Reproduction and Biotechnology Laboratory, Colorado State University, Fort Collins, CO

28. Estrogen Receptor 2 Regulates the Granulosa Cell Genes Critical for Gonadotropin Induced Preovulatory Follicle Maturation and Ovulation. Vincentaben Khristi, Prabhakar Singh, Subhra Ghosh, Archit Pramanik, Shaon Borosha, Khyati Dalal, Katherine F. Roby, Michael W. Wolfe and M.A. Karim Rumi. Institute for Reproductive Health and Regenerative Medicine, Department of Pathology and Laboratory Medicine, Department of Anatomy and Cell Biology, Department of Molecular and Integrative Physiology, University of Kansas Medical Center, Kansas City, KS.

29. Autophagy: A Non-hormonal Contraceptive Target. Arin Oestreich, Ran Xu, Stephan, Gary Silverman, Stephen Pak, Kelle Moley. Washington University School of Medicine.

30. Progesterone Effects on Extracellular Vesicles in the Sheep Uterus. Gregory W. Burns¹, Kelsey E. Brooks^{1,2}, Eleanore V. O'Neil¹, Darren E. Hagen³, Susanta K. Behura¹, and Thomas E. Spencer¹
¹Division of Animal Sciences, 158 ASRC, 920 East Campus Drive, University of Missouri, Columbia, MO 65211 ²Current address: Division of Reproductive and Developmental Science, 3181 SW Sam Jackson Park Road, Oregon Health & Science University, Portland, OR 97239 ³Department of Animal Science, 101 Animal Science Building, Oklahoma State University, Stillwater, OK 74078

31. (TRAINEE ORAL PRESENTATION ONLY - NO POSTER) Identification of RPLP1 as a Novel Target of miR-451a Whose Expression Is Elevated in Endometriotic Lesion Tissue and Correlates with Endometriotic Lesion Tissue and Cell Proliferation. Zahraa Alali, Tommaso Falcone, Warren B Nothnick. Molecular and Integrative Physiology, University of Kansas Medical Center, Kansas City, KS, USA; Obstetrics, Gynecology and Women's Health Institute, Cleveland Clinic, Cleveland, OH, USA

32. Conceptus Derived Prostaglandin Synthase 2 (PTGS2) Regulates Embryonic Development in Sheep. Eleanore V. O'Neil, Joshua Benne, Gregory Burns, Kelsey Brooks and Thomas E. Spencer. Division of Animal Sciences, University of Missouri-Columbia

33. RNA Editing in Mammalian Oocytes. Pavla Brachova, Nehemiah S. Alvarez, Keith E. Latham, David F. Albertini, Lane K. Christenson. Molecular and Integrative Physiology, University of Kansas Medical Center, Kansas City, Kansas, USA; Pathology and Laboratory Medicine, University of Kansas Medical Center, Kansas City, Kansas, USA; Department of Animal Science, Michigan State University, East Lansing, Michigan, USA; Center for Human Reproduction, New York, New York, USA.

34. Aberrant Secretion of 10 Gonadal Steroids in Gonadotropin-releasing Hormone II Receptor Knockdown Boars. Amy T. Desaulniers¹, Rebecca A. Cederberg¹, Clay A. Lents² and Brett R. White¹
¹University of Nebraska-Lincoln, Lincoln, NE, ²USDA, ARS, USMARC, Clay Center, NE

35. Addition of Palmitate to Porcine Embryo Culture Improves the Number of Nuclei in the Resulting Blastocyst Stage Embryos. C. A. Pfeiffer^{1*}, B. K. Redel¹, L. D. Spate¹, R. S. Prather¹
¹Division of Animal Sciences, University of Missouri, Columbia, MO, U.S.A.

36. Epigenetic and transcriptional changes in rat trophoblast stem cells exposed to hypoxia. Nehemiah S. Alvarez, Kesiuke Kozai, Damayanti Chakraborty, and Michael J. Soares. Institute for Reproductive Health and Regenerative Medicine, Departments of Pathology and Laboratory Medicine and Pediatrics, University of Kansas Medical Center, Kansas City, KS; Fetal Health Research, Children's Research Institute, Children's Mercy, Kansas City, MO

37. wtf Causes Aneuploid Gametes. María Angélica Bravo Núñez¹, Nicole Nuckolls¹, Sarah Zanders^{1,2} ¹Stowers Institute for Medical Research, Kansas City; ²Department of Molecular and Integrative Physiology, University of Kansas Medical Center, Kansas City

38. Effect of Aromatase (CYP19A1) Deletion on Pre-implantation Embryo Development and Conceptus Elongation in Pigs. A.E. Meyer, R. D. Geisert, T.E. Spencer, R.S. Prather, K.E. Brooks, C. Murphy, L. Spate, J. Benne, S. Murphy, and R. Cecil. Division of Animal Sciences, University of Missouri, Columbia, MO, USA.

39. Tissue Factor Pathway Inhibitor Regulation of Endovascular Trophoblast Cell Development and Uterine Spiral Artery Remodeling at the Placentation Site. Masanaga Muto, Damayanti Chakraborty, Regan L Scott, and Michael J Soares. Institute for Reproductive Health and Regenerative Medicine, Departments of Pathology and Pediatrics, University of Kansas Medical Center, Kansas City, Kansas; Fetal Health Research, Children's Research Institute, Children's Mercy, Kansas City, Missouri.

40. (TRAINEE ORAL PRESENTATION) Forkhead box a2 (FOXA2) and Endometrial Glands are Essential for Uterine Function and Fertility. Andrew M. Kelleher, Susanta Behura, and Thomas E. Spencer. Division of Animal Sciences, 158 ASRC, 920 East Campus Drive, University of Missouri, Columbia 65211

41. IL33 and the Female Reproductive Tract: Analysis and Establishment of Genetic Rat Models. Keisuke Kozai, Khursheed Iqbal, Regan L. Scott, Pramod Dhakal, Damayanti Chakraborty and Michael J. Soares. Institute for Reproductive Health and Regenerative Medicine, Departments of Pathology and Laboratory Medicine and Pediatrics, University of Kansas Medical Center, Kansas City, KS. Fetal Health Research, Children's Research Institute, Children's Mercy, Kansas City, MO.

42. Placental Hematopoiesis in the GATA Light. Pratik Home, Bhaswati Bhattacharya, Soma Ray and Soumen Paul. ¹ Department of Pathology and Laboratory Medicine and Institute for Reproductive Health and Regenerative Medicine, University of Kansas Medical Center, Kansas City, KS USA.

43. Complex Modes of Transgenerational Gene Silencing by piRNA. Kelley Van Vaerenberghe¹, Danny E. Miller^{2,3}, Celeste Cummings¹, Marilyn Barragan¹, Alexandra Erwin¹ and Justin P. Blumenstiel¹ ¹University of Kansas, Department of Ecology and Evolutionary Biology, Lawrence, KS, 66049 ²Stowers Institute for Medical Research, Kansas City, MO ³University of Kansas Medical, Kansas City, KS

44. Transcriptomic Profiling of Trophoblast Cells Within the Hemochorial Placentation Site. Regan L. Scott¹, Masanaga Muto¹, Kaela M. Varberg¹, Damayanti Chakraborty¹, Jeremy Chien², and Michael J. Soares^{1,3}. ¹Institute for Reproductive Health and Regenerative Medicine, Departments of Pathology & Laboratory Medicine and Pediatrics, University of Kansas Medical Center, Kansas City, KS; ²Division of Molecular Medicine, Department of Internal Medicine, University of New Mexico School of Medicine, Albuquerque, NM; ³Fetal Health Research, Children's Research Institute, Children's Mercy, Kansas City, MO.

Full Abstracts



1. (TRAINEE ORAL PRESENTATION) Assessment of Misregulated microRNAs and Their Target mRNAs in an Assisted Reproduction-induced Congenital Overgrowth Syndrome in Bovine. Yahan Li¹, Darren E. Hagen², Zhiyuan Chen¹, Tieming Ji³, and Rocío Melissa Rivera¹ ¹Division of Animal Sciences, ³Department of Statistics, University of Missouri, Columbia, MO 65211, ²Department of Animal Science, Oklahoma State University, Stillwater, OK 74078

The use of assisted reproductive technologies (ART) can induce congenital overgrowth conditions in humans and ruminants, namely Beckwith-Wiedemann syndrome and large offspring syndrome (LOS), respectively. We have shown that these conditions share phenotypes and epigenotypes. Our recent results indicate global mRNA misregulation in LOS. microRNAs (miRNAs) function in post-transcriptional regulation of gene expression through translational repression or transcript degradation. We hypothesize that some miRNAs are misregulated in LOS and cause changes in protein abundance of their misregulated mRNA targets. Control and LOS conceptuses were produced by artificial insemination or ART, respectively. RNA from placenta, kidney, liver, and skeletal muscle of four control and four LOS conceptuses were subjected to small RNA sequencing. Approximately 4.5-6.5 million reads per library were sequenced for liver and ~8.2-12.6 million for other tissues. Trimmed reads were mapped to the bovine genome UMD3.1. In total, 647 known miRBase mature and 332 star miRNAs were detected in the four bovine tissues examined. Principal component analyses of detected miRNAs showed differences between control and LOS groups. Owing to the heterogeneous nature of the syndrome, expressed miRNAs for each LOS individual was compared to the average of the four controls for each tissue. Statistical analyses were conducted using edgeR package with false discovery rate controlled at 0.05. miRPath and TarBase were used to identify enriched biological pathways. We referred to human data due to the conservation of miRNA sequences between bovine and human and the abundant experimentally- examined miRNA-mRNA targeting relationships in human. The 103 miRNAs shown to be misregulated in LOS were enriched in pathways associated with cell proliferation and cancers (i.e. Hippo, ErbB, TGF-beta, Ras, and Wnt signaling pathways). Bovine mRNA targets of differentially expressed miRNAs were predicted using miRanda. Among the prediction results, bovine miRNA- mRNA targeting relationships conserved in human were kept for further investigation. At present, we are analyzing protein levels of YAP1 the Hippo signaling pathway effector, as its mRNA was identified as upregulated in the RNA-seq analysis. In addition, we are corroborating the levels of bta-miR-450b by qRT-PCR. This downregulated miRNA was predicted to target the 3' UTR of YAP1 in bovine.

2. (TRAINEE ORAL PRESENTATION) Disruption of Pancreatic Prolactin Receptor Signaling Impairs Maternal Glucose Homeostasis. Jackson Nteeba¹, Kaiyu Kubota¹, Wenfang Wang², Hao Zhu², Guoli Dai³, and Michael J. Soares^{1,4} ¹IRHRM, Department of Pathology and ²Department of Clinical Laboratory Sciences, University of Kansas Medical Center, Kansas City, KS; ³Department of Biology, Indiana University-Purdue University, Indianapolis, IN; ⁴Fetal Health Research, Children's Research Institute, Children's Mercy, Kansas City, MO.

Gestational diabetes afflicts 7% of all pregnancies in the USA, predisposing the mother and the developing infant to a high risk of a range of health disorders later in life. The cause of GDM is unknown. An unsatisfactory adaptation of maternal beta cells to pregnancy is a hallmark of the disease. It is hypothesized that maternal pancreatic adaptations are driven by prolactin and placental lactogen acting through the prolactin receptor (PRLR) at the beta cells. To test this hypothesis, we generated mice possessing Loxp sites flanking exon 5 of the Prlr gene (Prlrf/f) and crossed them with mice expressing Cre recombinase under the control of the Pdx1 gene promoter to produce mice with a pancreas-specific Prlr gene null mutation (Prlrd/d). Prlrf/f or Prlrd/d females were mated to wild-type males. Dams were euthanized on gestation day 15.5 to assess placental and fetal growth among genotypes. Body weight measurements and glucose tolerance tests following 6 h of fasting

were also performed. Loss of Prlr in the pancreas did not significantly affect body weight or blood glucose levels in nonpregnant females. Pregnant Prlrd/d mice had elevated fasting blood glucose and impaired glucose tolerance ($P < 0.001$). This inability to sustain normal blood glucose balance during pregnancy worsened with age. Prlrd/d dams returned to normal glycemic control 4 days postpartum. Pregnancy-induced beta cell mass expansion was compromised among Prlrd/d dams. ELISA revealed that Prlrd/d dams had 40% lower serum insulin compared to age-matched Prlrf/f dams ($P < 0.01$), indicating that the poor glucose homeostasis during pregnancy in Prlrd/d dams was due to decreased insulin production. Prlrd/d dams displayed increased fetal weights and significant deregulation of prolactin and inflammation-associated transcripts in the placenta. Together, these results indicate that the PRLR, acting within the pancreas, is involved in maintaining normal blood glucose homeostasis during pregnancy and therefore its dysfunction can compromise maternal glycemic control. (Support: JN, ADA Postdoctoral Fellowship 1-16-PMF-012; NIH HD020676)

3. Saturated Free Fatty Acids Induce Trophoblast Lipoapoptosis. Sathish Kumar Natarajan, Ezhumalai Muthukrishnan, Philma Glora Muthuraj, Prakash Kumar Sahoo, Taylor Bruett, Justin L. Mott. Department of Nutrition and Health Sciences, University of Nebraska-Lincoln, Lincoln, NE

Obesity during pregnancy increases the risk for maternal complications like gestational diabetes, preeclampsia, and maternal inflammation. Maternal obesity also increases the risk of childhood obesity, fetal intrauterine growth restriction (IUGR) and diabetes to the children. Earlier studies demonstrated placental trophoblast apoptosis occurs in patients with preeclampsia and IUGR due to hypoxia. Increased circulating free fatty acids (FFAs) in obesity due to adipose lipolysis induces lipoapoptosis to hepatocytes, cholangiocytes, and pancreatic- β -cells. During the third trimester of pregnancy, there is an increase in maternal lipolysis and release of FFAs into the circulation. It is currently unknown if increased FFAs during maternal obesity cause placental trophoblast lipoapoptosis. Palmitate, the predominant circulating FFA, has been shown to induce blastocyst lipoapoptosis and exposure of blastocysts before implantation to palmitate results in a smaller sized fetus. Here, we hypothesize the involvement of trophoblast lipoapoptosis in placental dysfunction during maternal obesity. **Methods:** Apoptosis was assessed by characteristic nuclear morphology staining with DAPI, and caspase 3/7 activity assay. Cleaved PARP and cleaved caspase 3 were examined by Immunoblot. **Results:** Treatment of trophoblast cell lines, JEG-3 and JAR cells with palmitate (PA) or stearate (SA)-induced trophoblast lipoapoptosis as evidenced by a significant increase in apoptotic nuclear morphology changes and caspase 3/7 activity. We observed that saturated FFAs caused a concentration-dependent increase in placental trophoblast lipoapoptosis. Further, we confirmed the saturated FFA-induced trophoblast lipoapoptosis using normal immortalized trophoblast cells, HTR-8. We also observed that palmitoleate, a mono-unsaturated omega-7 fatty acid mitigated placental cell lipoapoptosis caused due to PA exposure. In **conclusion**, we show that saturated FFAs induce trophoblast lipoapoptosis. The signaling mechanism of FFA-induced trophoblast lipoapoptosis are now under investigation.

4. Pluripotent Stem Cell Models in the KUMC Transgenic Facility. Julia Draper, Jennifer Pace, Ilyia 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 an important tool in biomedical research for both the study of gene function and the development of disease models. Mouse embryonic stem cells are a critical tool for advanced manipulation of the mouse genome. Human induced pluripotent stem cells are valuable models for capturing the genetic information of a patient, with the capacity to differentiate into virtually any cell type. The techniques employed for generating and manipulating pluripotent stem cell models require technical expertise. The KUMC Transgenic and Gene Targeting Institutional Facility (TGIF) supports research projects using 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. Our stem cell core performs cell culture, gene targeting, karyotyping, and differentiation protocols in preparation both for injection to generate chimeric mice and to establish human cell models. Our recent efforts include successful site-directed transgene integration and mutagenesis in 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. The TGIF services for pluripotent stem cell models are supported by institutional and NIH programmatic support, including the

KUMC School of Medicine, the COBRE Program Project in Molecular Regulation of Cell Development and Differentiation (NIH P30 GM122731), and the Kansas Intellectual and Developmental Disabilities Research Center (NIH U54 HD090216).

5. The Recombination Landscape of *Drosophila virilis* Under Hybrid Dysgenesis. Lucas Hemmer and Justin Blumenstiel. Ecology and Evolutionary Biology, University of Kansas, Lawrence, KS

DNA damage in the germline is a double-edged sword. Induced double-strand breaks establish the foundation for meiotic recombination and proper chromosome segregation but can also pose a significant challenge for genome stability. Within the germline, transposable elements are powerful agents of double-strand break formation. How different types of DNA damage are resolved within the germline is poorly understood. For example, little is known about the relationship between the frequency of double-stranded breaks, both endogenous and exogenous, and the decision to repair DNA through one of the many pathways, including crossing over and gene conversion. We aim to use the *Drosophila virilis* hybrid dysgenesis model to determine how recombination landscapes change under transposable element activation. In this system, a cross between two strains of *D. virilis* with divergent transposable element loads results in the hybrid dysgenesis phenotype, which includes the germline activation of diverse transposable elements, reduced fertility, and male recombination. However, only one direction of the cross results in hybrid dysgenesis. This allows us to examine recombination in genetically identical F1 females; those with baseline levels of programmed DNA damage and those with an increased level of DNA damage resulting from transposable element proliferation. We are using multiplexed shotgun genotyping to map crossover events to compare the recombination landscapes of hybrid dysgenic and non-hybrid dysgenic individuals.

6. ‘wtf Causes Infertility?’: Investigating Poison-antidote Meiotic Drivers in Fission Yeast. Nicole Nuckolls¹, María Angélica Bravo Nuñez, and SaraH Zanders¹ ¹Stowers Institute for Medical Research

Normally in meiosis, an allele is transmitted to 50% of the offspring of a heterozygous individual. Meiotic drive is when an allele can manipulate meiosis so that it is transmitted to more than the expected 50% of the offspring. Meiotic drive is a significant force that has molded genome structure, gene regulation, speciation, and more broadly, evolution. We identified *wtf4*, a gene in fission yeast *Schizosaccharomyces kambucha*, as a poison-antidote meiotic drive allele. *wtf4* has two functions as a drive element: it poisons gametes that do not inherit it, and rescues the gametes that do with a spore-specific antidote. It does so by utilizing dual, overlapping transcripts. The poison spreads throughout the ascus, while the antidote is spore-specific and appears to be retained at organelles within the spore. This project investigates the mechanism of poison-antidote meiotic drive and the differences between the two *Wtf4* proteins.

7. *Mutp53* Inhibits Stress Granule Formation in Osteosarcoma Cells. Elizabeth Thoenen, Alejandro Parrales-Briones, Atul Ranjan, Satomi Yamamoto, Dan A. Dixon, and Tomoo Iwakuma. University of Kansas Medical Center.

Stress granules are non-membranous cellular organelles comprised of RNA binding proteins and mRNA stalled in translation initiation. Stress granules play a role in development, neurodegenerative disease, and cancer progression. Specifically, in cancer cells exposed to hypoxia, low nutrition, and chemotherapeutic agents, stress granules enable cells to evade apoptosis and survive. While mutant KRAS has a known role in stress granule formation, no other oncogenes' roles have been described in this process. The tumor suppressor p53 is the most commonly mutated gene in cancers, with most mutations being missense mutations. Mutant p53 (*mutp53*) frequently displays oncogenic gain-of-function activities independent of wild-type p53 and allows cancer cells to survive under various stress conditions. In this study, we examined the role of oncogenic *mutp53* in stress granule formation and its associated cellular survival. Two common stress granule-inducers, thapsigargin and sodium arsenite, were used on KHOS/NP (p53R156H) cells with or without *mutp53* knockdown to measure changes in stress granule formation and colony formation. Contrary to our expectations, *mutp53* knockdown significantly increased formation of stress granules and colonies following thapsigargin and sodium arsenite treatment. These results suggest that *mutp53* suppresses stress granule formation and enhanced stress-induced cell death. Since p53R156H localizes to both the nucleus and the

cytoplasm while stress granules form in the cytoplasm, we next asked whether cellular localization of mutp53 plays a role in stress granule formation. We then prevented nuclear export of mutp53 in parental and mutp53 knockdown KHOS/NP cells with leptomycin B (LMB), followed by treatment with thapsigargin. In mutp53-knockdown KHOS/NP cells, stress granule formation was readily detected and unchanged with or without LMB treatment; however, in parental KHOS/NP cells, LMB treatment greatly increased stress granule formation. These results suggest that cytoplasmic mutp53, rather than nuclear mutp53, inhibits stress granule formation. Our study may implicate that mutp53 as an inhibitor of stress granule formation thereby enhancing cancer cell death under certain types of stress. Although detailed mechanisms behind mutp53-mediated inhibition of stress granule formation remain unclear, our findings may ultimately lead the application of stress-inducing agents in the treatment of mutp53-expressing cancers.

8. Impact of Glyphosate on Ovarian Signaling Pathways Regulating Folliculogenesis and Steroidogenesis. Ganesan, S., Nteeba, J. and Keating, A.F. Department of Animal Science, Iowa State University, Ames, IA 50011

Representing 50% of U.S. herbicide usage at approximately 155 million lbs (70.5 Kg) per annum, environmental glyphosate (GLY) abundance is extensive. In vitro GLY exposure reduces steroidogenic acute regulatory protein (STAR) and cytochrome P450 19A (CYP19A1) abundance - ovarian proteins that catalyze the first and last steps, respectively, of cholesterol conversion to 17 β - estradiol. This study investigated the hypothesis that GLY alters signaling pathways involved in steroidogenesis and folliculogenesis in vivo. Wild type non-agouti (a/a) mice were exposed to GLY (2 mg/kg/day) at PND42 five days per week over 20 weeks and were euthanized in the proestrus phase of their estrous cycle. GLY exposure did not impact ($P > 0.05$) body weight or weights of the ovary, uterus, kidney, or spleen. Hepatic weight, however, increased ($P < 0.05$) by GLY exposure. GLY exposure depleted ($P < 0.05$) primordial follicle number but no effect ($P > 0.05$) on primary, secondary, antral follicles or corpora lutea numbers was observed. The phosphatidylinositol-3 kinase (PIK3) pathway is critical for oocyte viability as well as of primordial follicle growth activation. GLY exposure did not impact ($P > 0.05$) mRNA encoding kit ligand (Kitl), KIT proto-oncogene receptor tyrosine kinase (Kit), insulin receptor (Insr) or insulin receptor substrate 2 (Irs2). Irs2 mRNA abundance was reduced ($P < 0.05$) by GLY exposure. Thymoma viral proto-oncogene 1 (AKT) is a central mediator of PIK3 signaling and while total AKT protein was unaffected ($P > 0.05$) by GLY exposure, phosphorylated AKT protein was increased ($P < 0.05$). The PIK3 pathway is also involved in regulating ovarian steroidogenesis, thus, we investigated impacts of GLY on steroidogenic signaling. Increased ($P < 0.05$) mRNA encoding Star, Cyp11a1, but reduced ($P < 0.05$) abundance of Cyp19a1 and Esr2 were observed in GLY exposed mice relative to control mice. STAR protein abundance was reduced, CYP11A1 unaffected, HSD3B increased and CYP19A1 decreased by GLY exposure ($P < 0.05$). These data support that GLY affects signaling components in the exposed mouse ovary that are essential for proper ovarian function, specifically those involved in regulation of folliculogenesis, viability of the female gamete and steroid hormone synthesis.

9. Effect of Sire Conception Rate on Pregnancy Establishment in Dairy Cattle. M. Sofia Ortega, João G. N. Moraes, David J. Patterson, Michael F. Smith, and Thomas E. Spencer. Division of Animal Sciences, University of Missouri, Columbia, MO, 65211

The average pregnancy rate is low in US dairy cattle and ranges from 15-65% in heifers and 14- 22% in cows with the majority of pregnancy losses occurring during the first two months after breeding (~44-66%). Establishment of pregnancy involves ovulation, fertilization, blastocyst formation and growth into an elongated conceptus, pregnancy recognition signaling, and development of the embryo and chorioallantoic placenta. Our central hypothesis is that the sire influences establishment of pregnancy. To begin testing that hypothesis, 10 Holstein bulls were selected based on their predicted transmitting ability (PTA) for sire conception rate (SCR) as high (PTA $> +3$, $n=5$) or low (PTA < -5 , $n=5$). SCR is an indicator of fertility of bulls used for artificial insemination (AI). First, nulliparous Holsteins ($n=208$) were synchronized and bred by fixed-time AI ($n\sim 20$ heifers per sire). Conception rate at day 32 tended to be higher ($P = 0.09$) for high than low SCR bulls (67% vs 55%, respectively). Next, in vivo produced (IVP) embryos from 3 high and 2 low SCR bulls were generated by inseminating superovulated Holstein heifers ($n=49$). Heifers inseminated with high-SCR bulls compared to those inseminated with low-SCR bulls produced more ($P < 0.01$) embryos of freezable quality (70 vs 42

%), a lower number ($P < 0.01$) of unfertilized oocytes (12 vs 37%), respectively. Subsequently, synchronized nulliparous Angus ($n=10$) received 5 IVP embryos (from a single SCR-classified sire and Holstein donor dam) on day 7 post-estrus. On day 16, recipients were slaughtered and conceptuses were recovered from the reproductive tract. Conceptus length was not different ($P = 0.42$) between groups and averaged 7.7 ± 1.5 cm (range: 0.9-21.8 cm) for high-SCR bulls and 6.1 ± 1.2 cm (range: 0.1-11.6 cm) for low-SCR bulls. Collectively, these studies support the hypothesis that sire has a direct influence on pregnancy establishment in cattle. However, conception rate differences observed on day 32 are not manifest during conceptus elongation but rather involve differences in sperm fertilizing ability, pre-implantation embryonic development, and/or development of the embryo and placenta after conceptus elongation and pregnancy recognition. Research supported by NIH R01 HD072898 and USDA AFRI 2013-68004-25256.

10. Development of Novel Mouse Models Using Genome Editing Approaches. Melissa A. Larson, Illya Bronshteyn, Jennifer Pace, Julia Draper, 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. The Facility makes extensive use of genome editing tools for in vivo mutagenesis and gene targeting in the mouse via site specific nucleases (zinc finger nucleases, TALENs, and CRISPR/Cas9 system). We also have active projects using site specific integrases (eg. PhiC31 integrase) for gene targeting of transgenes in vivo. In this poster we will present recent mouse models developed by the TGIF using genome editing approaches. The TGIF is supported by institutional and NIH programmatic support, including the KUMC School of Medicine, the COBRE Program Project in Molecular Regulation of Cell Development and Differentiation (NIH P30 GM122731), the University of Kansas Cancer Center (NIH P30 CA168524), and the Kansas Intellectual and Developmental Disabilities Research Center (NIH U54 HD090216).

11. Endocrine Profiles during Attainment of Puberty may Predict Reproductive Longevity in Heifers.

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We hypothesized that how heifers attained puberty would predict their reproductive longevity. Blood plasma was collected from 378 spring-born heifers from weaning to breeding (October-June) from 2012-2015. Four puberty classifications were determined by SAS using time, concentrations of progesterone (P4) $>1\text{ng/ml}$, and continued or discontinued cyclicity: 1) Early Puberty- 253.4 ± 10.8 days of age (DOA) with continued cyclicity; 2) Typical Puberty- 374.6 ± 3.6 DOA with continued cyclicity; 3) Start-Stop Puberty- 261 ± 3.9 DOA with discontinued cyclicity; and 4) Non-Cycling- no $P4 > 1\text{ng/ml}$ during the sampling period. A smaller percentage of Non-Cycling females responded to ProstaglandinF2, showed estrus, and were artificially inseminated; however, there were no differences in overall heifer pregnancy rates between puberty groups. In 2014 ($N=10$) and 2015 ($N=12$), a subset of heifers were more intensively evaluated from April-June with daily blood collection, ultrasound, and ovariectomy. Non-esterified fatty acid (NEFA) concentrations in follicular fluid during this period were greater in Early Puberty heifers ($0.35 \pm 0.02\text{mEq/L}$; $P < 0.05$) than in Start-Stop

($0.29 \pm 0.02 \text{ mEq/L}$), but not different from Typical heifers ($0.35 \pm 0.04 \text{ mEq/L}$). Serial blood collections were conducted (15 min intervals for 8 h) on 2 heifers from each group in the 2015-born heifers to determine LH and FSH mean concentrations, LH pulse amplitude, and frequency. Early Puberty heifers tended to have greater LH pulse amplitude than other groups ($1677.75 \pm 332.62 \text{ ng/ml}$ vs. $236.67 \pm 332.6 \text{ ng/ml}$; $P < 0.08$). Non-Cycling heifers had greater mean concentration of FSH than other groups (541.12 vs. 315.93 ng/ml ; $P < 0.05$). Primary cultures were conducted using ovarian cortex from heifers as well as cows previously classified at puberty in 2012-2014. Interestingly, ovarian cortex from Start-Stop and Non-Cycling heifers secreted higher androstenedione in culture media than Early or Typical heifers ($P < 0.01$). Cortex from cows classified as Start-Stop and Non-Cycling at puberty secreted higher androstenedione (18.3-fold higher; $P < 0.05$) in culture media compared to Typical cows. Taken together, the reduced NEFA (Start- Stop), increased FSH (Non-Cycling) and excess androstenedione secreted in ovarian cortex from heifers and cows previously identified as Start-Stop and Non-Cycling may predispose these females to reduced reproductive longevity in comparison to Early and Typical heifers. USDA is an equal opportunity provider and employer.

12. Novel Markers of Early Human Trophoblast Differentiation. Rowan M. Karvas, Toshihiko Ezashi, Danny Schust, R. Michael Roberts and Laura C. Schulz*, the University of Missouri- Columbia.

The developing human placenta is largely inaccessible to researchers from embryo implantation until shortly after clinical recognition of pregnancy. Yet it is during this period that the basic structure of the placenta is formed. Human embryonic stem cells (ESC) can be rapidly and synchronously differentiated into trophoblast by a combination of BMP4 and signaling inhibitors of FGF2 and TGFB/ACTIVIN, triggering differentiation of trophoblast (ESCd). However, transcriptome analysis of trophoblast isolated from ESCd reveals many transcripts expressed minimally in term placenta. Among these are GABRP, a chloride channel GABA receptor subunit, and WFDC2, regulators of invasion/migration, VTCN1, an immune regulator, and ACTC1, a cytoskeletal protein found in heart muscle. We hypothesized that first trimester placental villous trophoblast is functionally intermediate between ESC-derived and term trophoblast. Accordingly, we predicted that products of mRNAs found in ESCd but not term placenta would be expressed at a high level in early pregnancy and decline thereafter. Paraffin-embedded tissue sections were obtained from the first two trimesters of pregnancy (5w2d, 6w6d, 7w6d, 8w2d, 19w1d, 20w6d) and from three term placentas. Immunofluorescent staining for GABRP, WFDC2, VTCN1, and ACTC1 was confined to STB. Expression negatively correlated with gestational age and was absent at term. Work continues to identify additional antigens that distinguish early trophoblast. The function of some of these proteins in trophoblast remains to be elucidated, but they represent a first step towards uncovering the unique gene signature of an unexplored “black box” period in human placental development. Supported by NIH grants HD 067759 and HD 077108.

13. Signaling Reciprocity Between PKC Iota and Bone Morphogenetic Protein GDF6 Balances Self-renewal Versus Differentiation of TSC-like Progenitor in the Placenta Primordia. Bhaswati Bhattacharya¹, Pratik Home¹, Soma Ray¹ and Soumen Paul¹ ¹Department of Pathology and Laboratory Medicine, Institute for Reproductive Health and Regenerative Medicine, University of Kansas Medical Center, Kansas City, Kansas.

One of the most important causes for early pregnancy failure is defective placentation. However, the molecular mechanisms underlying proper placentation during early post-implantation development are poorly understood. We studied importance of a conserved Protein Kinase C family member, Atypical Protein Kinase C iota (PKCi), in the early post-implantation placenta development. PKCi is essential for survival of mouse embryos after implantation. Gene knockout studies in mice have shown that loss of Prkci gene, encoding PKCi, causes embryonic lethality prior to embryonic day (E) 9.5, a developmental stage equivalent to first trimester in humans. We have observed that PKCi is predominantly expressed in the trophoblast stem and progenitor cells (TSPCs) during early stages of mouse and human placentation. However, PKCi signaling in TSPCs and its importance in the context of early post-implantation placenta development has never been studied. In this study, we found that post-implantation placental development is impaired in Prkci^{-/-} mouse embryos, with a major defect in labyrinth zone formation. We have also found that Gdf6, also known as Bmp13, along with several other differentiation factors are significantly upregulated upon PKCi depletion using transcriptomic analysis in trophoblast stem cells. Furthermore, our study with PKCi-depleted mouse trophoblast stem cells

also reveal that PKCi is essential to establish the trophoblast stem state-specific gene expression program and to maintain the epithelial nature of these cells. Our study discovers novel trophoblast-specific function of PKCi in successful progression of pregnancy.

14. The Testicular Explant System is a Suitable Translational Tool to Determine the Toxicity Threshold of Male Germ Cell Toxicants. Prabakaran Esakky, Deborah A. Hansen, Andrea M. Drury, Paul Felder,

Andrew Cusumano, Kelle H. Moley. Research, Department of Veterans Affairs Medical Center, St. Louis MO. Department of Obstetrics and Gynecology, Washington University School of Medicine in St. Louis, Missouri 63110.

Paternal exposure to cigarette smoke is implicated in seminal and congenital anomalies, and childhood cancers. Cigarette smoke condensate is a germ cell mutagen and testicular toxicant. There is neither a risk-free level of exposure nor conclusive reports exist on reproductively tolerant limits of CS. Our recent studies using CSC revealed deleterious molecular changes in sire germ cells and phenotypic effects in their offspring. We hypothesize here that testicular explant can be used to determine the toxicity threshold at which CSC impairs spermatogenesis in the exposed males and developmental defects in their offspring. We established a mouse neonatal testicular explant model (P5.5 -11.5) and assessed various growth parameters by analyzing expression of cell specific markers. Our explant system maintained structural and functional integrity of in vivo testis and responded differentially upon exposure to various concentrations (40-160 $\mu\text{g/ml}$) of CSC. Detection of decreasing testosterone levels and increasing cotinine in the culture medium following CSC treatment indicated that the testicular explant is metabolically active. The in vivo toxicity threshold of CSC mimicked its ex vivo threshold in causing DNA damage, apoptosis, and oxidative stress. In addition, the neonatally exposed males at the predetermined toxicity threshold of CSC sired pups with smaller litter size and higher rate of resorption. Thus, the current report concludes that the toxicity threshold of CSC determined during the neonatal exposure at in vivo and ex vivo affects spermatogenesis and causes developmental defects in the offspring.

15. Palmitoleate Protects Zika Virus-induced Placental Trophoblast Apoptosis. Philma Glora

Muthuraj, Ezhumalai Muthukrishnan, Prakash Kumar Sahoo, Asit Pattnaik 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 in ZIKV infection suggest that the virus can be vertically transmitted to the fetal organs including brain via the placenta. Placental infection during the first and second trimester has also been suggested to play a crucial role in ZIKV transmission from maternal circulation to the fetus resulting in Congenital Zika Syndrome. Here we hypothesize that palmitoleate, an omega-7 monounsaturated fatty acid is a nutrient compound protects against ZIKV-induced placental trophoblast apoptosis. Methods: HTR-8, a human normal immortalized trophoblast cells and human malignant trophoblast (JEG-3 and JAR) cell lines were infected with ZIKV for 24-96h. Apoptosis was assessed by characteristic nuclear morphology staining with DAPI and caspase 3/7 activity assay. We used both MR766 and PRVABC59 obtained from CDC. Results: Using a cell culture model, we confirmed that 1 MOI of ZIKV infection induces placental trophoblast apoptosis as evidenced by a significant increase in percent apoptotic nuclear morphological changes and an increase in caspase 3/7 activity after 48 h of infection. Similar results of ZIKV-induced trophoblast apoptosis were observed after 72 or 96 h of infection. ZIKV-induced trophoblast apoptosis was significantly prevented with the treatment of palmitoleate, an omega-7 mono-unsaturated fatty acid. We also observed that Zika viral-RNA copy number was dramatically decreased in cell media of palmitoleate-treated cells compared to ZIKV-alone infected trophoblast culture media. To further, substantiate the protective role of palmitoleate against ZIKV-induced trophoblast apoptosis; we treated ZIKV-infected placental trophoblasts cells with palmitate a saturated free fatty acid and found that palmitate did not protect ZIKV-induced trophoblast apoptosis. In conclusion, palmitoleate protects against ZIKV-induced placental trophoblast apoptosis. The mechanism of palmitoleate protection against ZIKV-induced trophoblast apoptosis are now under investigation.

16. Dioxin-Activated Aryl Hydrocarbon Receptor Signaling Promotes Adaptations in Hemochorial Placentation. Khursheed Iqbal¹, Pramod Dhakal¹, Katherine F. Roby¹, Stephen Pierce¹ and Michael J. Soares^{1,2} ¹Institute for Reproductive Health and Regenerative Medicine, Departments of Pathology and Laboratory Medicine and Anatomy and Cell Biology, and Pediatrics, University of Kansas Medical Center, Kansas; ²Fetal Health Research, Children's Research Institute, Children's Mercy, Kansas City, MO

The aryl hydrocarbon receptor (AHR) is a cytoplasmic ligand-dependent transcription factor controlling the biological responses to environmental pollutants. Upon binding, pollutants such as 2,3,7,8-tetrachlorodibenzodioxin (TCDD), AHR translocates into nucleus and activates transcription of AHR target genes such as Cyp1a1, encoding a protein important in detoxification of pollutants. The hemochorial placenta serves an essential role in fetal health and is potentially susceptible to environment exposures. Placentation depends upon an intrinsic trophoblast cell differentiation program and interactions of specialized trophoblast cells with uterine versus allantoic structures. The purpose of this study was to explore how exposure to TCDD acting through AHR shapes placental development and to determine site(s) of TCDD action. Pregnant female Holtzman Sprague-Dawley rats were exposed to TCDD at gestational day (gd) 6.5 and placentation sites were collected at gd 13.5. TCDD exposure resulted in a significant upregulation of transcripts for Cyp1a1 in liver, placental, and adjacent maternal tissues. Immunostaining of CYP1A1 in gd 13.5 placentation sites revealed activation of AHR signaling in decidua/metrial gland and in mesenchymal components of the labyrinth zone but not the junctional zone of the chorioallantoic placenta. TCDD treated gd 13.5 placentation sites exhibited deep intrauterine trophoblast invasion characterized by cytokeratin positive endovascular trophoblast cells lining uterine spiral arteries, whereas oil treated controls exhibited limited penetration of endovascular trophoblast cells into the uterine compartment. We next generated an Ahr null rat model that failed to express AHR and to induce CYP1A1 enzyme expression following TCDD exposure. TCDD-induced placental adaptations were AHR dependent. As a first step in determining the site(s) of TCDD actions, we evaluated the effects of TCDD administration during pregnancy in wild type females mated with wild type males, Ahr null females mated with Ahr null males, and Ahr null females mated with wild type males. Mating schemes that resulted in disruption of AHR activity in maternal tissues interfered with TCDD-activated placentation site adaptations. Additionally, to explore the role of CYP1A1 in TCDD-activated placental adaptations we generated Cyp1a1 null rats using CRISPR/Cas9 genome editing. The Cyp1a1 mutation consisted of a 2224 bp deletion, which included the P450 domain, and successfully transmitted through the germline. Collectively, these findings indicate that at least some of TCDD effects on placental development are mediated through its actions on the mother. In summary, we have identified a developmental window of sensitivity to environmental pollutants affecting hemochorial placentation with the potential of impacting fetal and postnatal health. (Supported by NIH grants HD020676, HD079363; Sosland Foundation)

17. Effects of FOXA2 Conditional Overexpression on Female Reproduction in Mice. Peng Wang¹, Kelsey E. Brooks¹, San-Pin Wu², Franco J. Demayo², and Thomas E. Spencer¹. ¹Division of Animal Sciences, University of Missouri, Columbia, MO; ²Reproductive & Developmental Biology Laboratory, National Institute of Environmental Health Sciences, Research Triangle, NC.

Forkhead box a2 (FOXA2) is a pioneer transcription factor which is expressed specifically in the glandular epithelium (GE) of the uterus and critical for GE differentiation and function in mice. A mouse model (Foxa2LsL) for conditional overexpression of FOXA2 was generated by targeting a minigene into the Rosa26 locus consisting of a ubiquitous CAGGS promoter, floxed STOP cassette (LsL) and mouse Foxa2 coding sequence. In Study One, Foxa2LsL mice were crossed with Pgr-Cre mice in which Cre is robustly expressed in the uterus only after birth. The bigenic OE females (PgrCre/+Foxa2LsL/+) are completely infertile. In the bigenic OE uteri, FOXA2 protein was observed in the luminal epithelium (LE), GE, stroma and inner layer of the myometrium of uteri on postnatal day 30 (PD 30), which phenocopies PGR expression. The bigenic OE uteri has fewer number of glands and lower uterine weight than the control. Moreover, the bigenic OE uteri contains KRT14- and TP63-positive basal cells. Thus, overexpression of FOXA2 in uterine stroma and epithelium of the neonatal uterus impairs uterine growth, decreases GE development, and promotes epithelial stratification, causing infertility in the adult. In Study Two, Foxa2LsL mice were crossed with Ltf-iCre mice in which Cre is robustly expressed in epithelia of the uterus only during and after puberty. In adult bigenic OE

mice (LtfiCre/+Foxa2LsL/+), the uterus was histologically normal with Foxa2 mRNA and FOXA2 protein undetectable in the LE. The bigenic OE female mice have normal fertility. The lack of or maintenance of FOXA2 overexpression in the uterine LE of the adult uterus suggests that genetic and epigenetic mechanisms may regulate aberrant Foxa2 expression in the LE but not GE of the uterus. Indeed, FOXA2 has an important role in endometrial tumorigenesis and is increased in GE hyperplasia and then mutated or lost upon progression to adenocarcinoma.

18. Ovarian Cortex from High A4 Cows Secretes Excess A4, and Exhibits Increased Oxidative Stress, and Arrested Follicle Development Which can be Partially Rescued by Angiogenic VEGFA Isoforms.

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We have identified a population of cows within the UNL physiology herd with excess androstenedione (A4) in follicular fluid and 17% reduction in calving rate. We hypothesized that folliculogenesis would be disrupted in High A4 cows; and vascular endothelial growth factor (VEGFA) isoform treatments could rescue disrupted folliculogenesis. Ovarian cortical pieces were collected from High A4 (n = 9) and Low A4 (n = 11) cows at ovariectomy and treated with 1) PBS; 2) VEGFA165 (50 ng/ml); 3) VEGFA165b (50 ng/ml); or 4) VEGFA165+VEGFA165b (50 ng/ml each) for 7 days. Uncultured ovarian cortex from High A4 cows had more primordial follicles and fewer primary, secondary and antral follicles (P = 0.04) when compared to Low A4 (control) cows. After 7 days of culture in PBS, Low A4 cow ovarian cortex had more follicles that developed to later stages while High A4 ovarian cortex had more primordial follicles indicating that culture conditions did not relieve the follicular arrest observed in High A4 ovarian cortex. Treatment with VEGFA165 increased follicular progression in ovarian cortex from High A4 cows to a greater extent than Low A4 cows in the early primary, primary, and secondary follicle (P = 0.05) stages. Ovarian cortex from High A4 cows also secreted greater amounts of A4 (P = 0.01; 42-fold higher) in the culture media compared to Low A4. Treatment with VEGFA165 dramatically reduced the amount of A4 secreted by the ovarian cortex of High A4 cows. Further, ovarian cortex from High A4 cows had increased positive staining for 4HNE (oxidative stress marker) and CD68 (macrophage marker). Taken together these results indicate that ovarian cortex from High A4 cows secrete greater concentrations of A4 which may contribute to increased oxidative stress and macrophage activation leading to follicular arrest. Angiogenic VEGFA isoform treatment can partially rescue follicle development and reduce A4 secretion. Thus, VEGFA165 may be a potential therapeutic to restore the ovarian microenvironment and enhance follicular maturation. This research was funded through a USDA grant 2013-67015- 20965. USDA is an equal opportunity provider and employer.

19. Global Repression of Transposable Elements in the Overgrown Placentas Dwarf Hamster Hybrids.

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The mammalian placenta represents a battleground for diverse evolutionary conflicts. In particular, evolutionary conflict between embryonic maternal and paternal genomes establishes a tension over maternal resource allocation to the developing fetus. The placenta lies at the frontline of this conflict. Evolutionary theory has shown that genomic imprinting in the placenta can be explained by contrasting levels of investment, between males and females, in fetal growth relative to future reproductive output. This form of conflict has been proposed to explain differences in placental growth in reciprocal species hybrids. In some cases, there is a significant difference between placental growth in reciprocal crosses. This is predicted by evolutionary theory when there are species level differences in levels of mating with multiple individuals. In light of this conflict, it is striking that transposable elements and retroviruses also play an important part of placental function. First, endogenous retrovirus env proteins have been repeatedly recruited to facilitate cell-cell fusion at the maternal interface. Second, expression of endogenous retroviruses can be very high in the placenta. Finally, TEs

themselves can aid in the establishment of imprinting since mechanisms of TE silencing can spread in cis to genes. In light of these conflicts, we investigated the hypothesis that overgrown placentas in one, but not the other, cross direction between two closely related dwarf hamsters would be associated with increased TE and endogenous retrovirus expression. To our surprise, we found the opposite to be true. Overall, overgrown placentas in dwarf hamster hybrids show lower levels of global TE expression. This suggests that the average effect of selfish element expression may be to restrain placental growth, rather than to have a role in promoting placental growth.

20. (TRAINEE ORAL PRESENTATION) Ovarian Inflammation and Oxidative Stress Associated with Diet Induced Obesity (DIO) Impacts RNA-Binding Protein Expression and mRNA Stability in the Murine Oocyte. Kelsey Timme, Fang Xie, Katie L. Bidne, John S. Davis, and Jennifer R Wood. Department of Animal Science, University of Nebraska-Lincoln, Lincoln, NE. OB/Gyn Department, University of Nebraska Medical Center, Omaha, NE

Tumor necrosis factor alpha (Tnfa) mRNA and NF B signaling are increased in ovaries collected from mice fed a high fat diet. Inflammation can produce oxidative stress. Thus, in the current study, the impact of oxidative stress on oocyte mRNA abundance, an important determinant of oocyte quality, was determined. Ovaries and ovulated oocytes were collected from C57BL/6 mice fed one of two diets; normal rodent chow (ND) or Western diet (WD), which is high in fat and sucrose. Ovaries and oocytes were collected 16 hours after ovulatory stimulation using exogenous gonadatropins. Body weight (ND = 21.150g +/- 0.750; WD = 24.396g +/- 0.699) and abdominal adipose tissue weight (ND = 0.237g +/- 0.020; WD = 0.596g +/- 0.090) was increased in WD compared to ND controls. However, there was no difference in ovulation rate (ND, 7 +/- 2; WD, 12 +/- 3). Real-time PCR of cDNA derived from whole ovary showed increased expression of glutathione peroxidase (Gpx1) and superoxide dismutases (Sod1, Sod2). Cryopreserved ovarian sections also had increased staining for 4-hydroxynonenal (4-HNE), a protein marker of oxidative stress. We previously demonstrated that DIO mice have increased abundance of developmental pluripotency-associated protein 3 (Dppa3) and POU domain class 5 homeobox 1 (Pou5f1) in ovulated oocytes. In vitro treatment of oocytes with hydrogen peroxide during in vitro maturation demonstrated increased Dppa3 and Pou5f1 abundance in the resulting MII oocytes suggestive of changes in post-transcriptional regulation of these oocyte mRNAs. RNA binding proteins (RBPs) are important post-transcriptional regulators of mRNAs. Furthermore, the RBPs, ELAVL1 and ZFP36L1/2, regulate inflammatory cytokine expression through interaction with AU-rich elements within the 3'UTR of target mRNAs. ELAVL1 was detected in both ND and WD ovary samples but was decreased in WD ovaries. Both ELAVL1 and ZFP36L1/2 were also expressed in ovulated oocytes from ND and WD mice. ELAVL1 was significantly decreased, whereas ZFP36L1/2 levels were significantly increased in ovulated oocytes from WD mice. Together, these data suggest that oxidative stress impacts the expression of RNA binding proteins, which have the potential to alter post-transcriptional regulation of important mRNAs that contribute to the developmental competence of the oocyte.

21. (TRAINEE ORAL PRESENTATION) Maternal Glucose Intolerance Increases Offspring Adipose Mass and Insulin Signaling in Mice. Omonseigho Talton, Keenan Bates, Kylie Hohensee and Laura Schulz. Division of Biological Sciences and Department of Ob, Gyn & Women's Health, University of Missouri, Columbia, MO.

Gestational diabetes mellitus (GDM) increases the risks of obesity and diabetes in offspring. As the incidence of GDM rises globally, so does the need for studies outlining how these offspring outcomes are programmed. We previously developed a mouse model of GDM in which dams exhibit glucose intolerance and reduced insulin response to glucose challenge only during pregnancy, without accompanying obesity. Here, we examined how gestational glucose intolerance affects offspring risk of metabolic dysfunction.

At 4, 12, 20, and 28 weeks, offspring were placed in metabolic cages that recorded metabolism over three days. One cohort of offspring was sacrificed at 19 weeks, and half of the offspring in the second cohort were placed on high-fat high-sucrose diet (HFHS) at 23 weeks, prior to sacrifice at 31 weeks. We examined weight, body composition, glucose tolerance, adipose and liver gene expression, liver and serum triglycerides, serum insulin and leptin in offspring.

Exposure to maternal glucose intolerance in utero increased weights ($p=0.0002$) of HFHS-fed offspring independent of sex. Offspring of GDM dams exhibited higher body fat percentages at 4, 12 and 20 weeks of age ($p=0.001$). At 28 weeks, GDM offspring fed the HFHS but not the CD also had higher body fat percentages than offspring of CON ($p=0.026$). Exposure to GDM increased the respiratory quotient (CO_2 produced / O_2 consumed) in male offspring at 20 weeks ($p=0.0098$) and in offspring of both sexes on either diet at 28 weeks ($p=0.0042$). Real-time PCR in subcutaneous adipose tissue revealed increased mRNA levels of Pparg ($p=0.0134$) and Adipoq ($P=0.0018$) in 31 week old CD-fed male offspring, and increased mRNA levels of Insr ($p=0.0011$) and Lpl ($p=0.0465$) in 31 week old male offspring on both diets. In liver at 31 weeks, mRNA levels of Ppara ($p=0.04032$) were elevated in CD-fed male offspring of GDM dams, and male offspring of GDM dams exhibited higher mRNA levels of Insr on both diets ($p=0.0325$). Neither fasting insulin nor glucose tolerance was affected by exposure to GDM.

Our findings show that GDM comprising glucose intolerance only during pregnancy programs increased adiposity in offspring, and increases the insulin sensitivity of subcutaneous adipose tissue.

22. Role of a Rare Variant of BHLHB9 in an Undiagnosed Pediatric Neurological Disorder. Jay L.

Vivian¹, Michelle Winter¹, Jennifer Pace¹, Sarah Tague¹, Merlin G. Butler¹, Sarah Soden², Neil Miller², Kenneth E. McCarson¹, and Peter G. Smith¹ ¹Kansas Intellectual and Developmental Disabilities Research Center, University of Kansas Medical Center, Kansas City KS. ²Children's Mercy Center for Pediatric Genomic Medicine, Kansas City MO

A male patient enrolled in the NIH Undiagnosed Diseases Program (UDP), anonymized as UDP1757, exhibited congenital progressive neurological dysfunction including motor deficits, impaired cognition, brain atrophy, and death at age 9. Exome sequencing of UDP1757 and family members identified a rare missense variant (C318R) in the X-linked BHLHB9 locus. Previous studies suggested a role for BHLHB9 in neuronal survival, differentiation, and cell signaling. We hypothesize that the UDP1757 clinical phenotype is caused by a defective BHLHB9 variant; testing in experimental models is underway.

Mouse models of a null allele of Bhlhb9 and the C318R variant were rapidly produced via CRISPR/Cas9 genome editing in vivo. Mice lacking Bhlhb9 function show a strain-dependent reduction in neonatal viability. Surviving null juvenile males display low body weight, and reduced strength and locomotion. In adulthood, Bhlhb9 null males and heterozygous females exhibit increased adipose accumulation. In contrast, mice harboring the Bhlhb9 C318R variant exhibit only subtle phenotypes, including a modest reduction in body weight. These analyses indicate essential and pleiotropic roles for BHLHB9 in neonatal viability and homeostasis. The distinct phenotypes of these mutant alleles suggest the C318R variant is a mild hypomorph, and that this mutation by itself does not ostensibly recapitulate the neurological deficits of UDP1757. Ongoing studies include a molecular analysis of Bhlhb9-null neural tissues. High quality patient-specific induced pluripotent stem cells from UDP1757 dermal fibroblasts have also been generated. Questions remain as to the degree to which other variants may contribute to the UDP1757 phenotype. This work is supported by the UDP (R21 GM114647), Frontiers CTSA (UL1 TR000001), and the Kansas IDDRC (U54 HD090216).

23. Studying Early Onset Preeclampsia (EOPE) in a Model for Early Stage Human Placental

Trophoblast. Megan Sheridan¹, Y Yang², A Lyons², Y Tian², DJ Schust³, LC Schulz³, T Ezashi², RM Roberts^{1,2} ¹Department of Biochemistry, ²Division of Animal Sciences, and ³Department of Obstetrics, Gynecology and Women's Health, University of Missouri-Columbia

Early onset preeclampsia (EOPE) is a disease affecting about 0.4% of pregnancies, with grave consequences for both the baby and mother. The disease is characterized by impaired trophoblast (TB) invasion, which results in a poorly perfused placenta. We aimed to study how early placental development may differ in pregnancies affected by EOPE. We derived induced pluripotent stem cells (iPSC) from umbilical cords of infants born to mothers who had EOPE and from infants born after a normal pregnancy. These iPSC were then converted to TB, by exposing them to BMP4 along with signaling inhibitors of Activin and FGF2, under two different O₂ atmospheres (5% and 20%). We hypothesized that the 20% O₂ condition would act as a stressor and that the EOPE-TB would be more susceptible to this stress. Two embryonic stem cell lines (hESC), 8

control (CTL) iPSC and 14 EOPE iPSC were tested to assess how well the differentiated trophoblast cells invaded through a Matrigel-coated membrane. We found that 1) Under 5% O₂, invasiveness of CTL and EOPE lines were equivalent 2) Under 20% O₂, invasiveness of EOPE was lower than CTL TB ($p=0.024$); 3) invasiveness of CTLs was not influenced by 20% O₂; and 4) invasiveness of EOPE lines as a group was significantly inhibited by 20% O₂ ($p=0.008$). To test whether the difference in the number of invasive cells was a consequence of proliferation, total DNA was collected from 2 hESC, 4 CTL, and 4 EOPE cell lines under both O₂ conditions and no significant differences were noted. Release of progesterone and hCG increased in 20% when compared to 5% O₂ in both CTL and EOPE TB lines, indicating a similar differentiation profile. Production of placental growth factor (PGF) was significantly increased in 20% vs 5% O₂ in 5 out of 6 CTL lines tested ($p<0.05$), while none of the EOPE TB lines ($n=4$) significantly upregulated the release of PGF in response to O₂. Transcriptomic analysis is underway to define genes and gene networks that might be responsible for the increased sensitivity of EOPE TB cell invasion to O₂. Supported by NIH grants HD067759 and HD077108

24. Na,K-ATPase $\alpha 4$ and Not $\alpha 1$ is Essential for Sperm Function, but its Ouabain Binding Site is Not Required for Male Fertility. Gustavo Blanco, Jeff P. McDermott, Gladis Sánchez, and Liu Lijun. Dept. of Medicine, College of Medicine and Life Sciences, University of Toledo and Dept. of Molecular and Integrative Physiology, University of Kansas Medical Center. Kansas City, USA.

Spermatozoa express two different Na,K-ATPase isoforms, the testis specific $\alpha 4$ (NKA $\alpha 4$) and the ubiquitous $\alpha 1$ (NKA $\alpha 1$) proteins, which in mice have significant differences in ouabain affinity. The importance of the ouabain binding site, as well as the relative contribution of each isoform to sperm motility and male fertility remains unclear. Here, we explored this by knockin expression of NKA $\alpha 1$ and NKA $\alpha 4$ isoforms in mice with switched sensitivity to ouabain. Wild type and three mouse lines were generated to produce all possible combinations of ouabain sensitive or insensitive NKA $\alpha 1$ and NKA $\alpha 4$ isoforms, by exchanging two critical amino acids (H/D and N/R) in the first extracellular loop of the NKA isoforms ($\alpha 1R$ - $\alpha 4S$, $\alpha 1R$ - $\alpha 4R$, $\alpha 1S$ - $\alpha 4S$, and $\alpha 1S$ - $\alpha 4R$). Immunoblot analysis of mouse sperm samples showed proper expression levels of each α isoform, both at the mRNA and protein levels. Sperm NKA activity levels were similar in all mouse lines and dose response curves for the inhibition of NKA activity to ouabain showed the expected changes in sensitivity of the mutated NKA isoforms. Ouabain (1 μM) increased intracellular sodium mainly in sperm from mice expressing ouabain sensitive NKA $\alpha 4$. In addition, ouabain inhibited total, progressive sperm motility, and sperm hyperactivation in $\alpha 1R$ - $\alpha 4S$ and $\alpha 1S$ - $\alpha 4S$ mice, but not in $\alpha 1S$ - $\alpha 4R$ or $\alpha 1R$ - $\alpha 4R$ mice. Testis size and morphology was normal in all mouse types and all of them showed similar sperm production and male fertility. Altogether, these results indicate that the ouabain affinity site of sperm NKA $\alpha 1$ and NKA $\alpha 4$ isoforms is not an essential requirement for male fertility; and that sperm function is highly dependent on the NKA $\alpha 4$, but not the NKA $\alpha 1$ isoform.

25. Investigating the Role of Type I Collagen in Mouse Uterine Function. Jenna DeCata, Arin K. Oestreich, Janae Judon, Charlotte L. Phillips, Laura C. Schulz. University of Missouri, Columbia, MO

Type I collagen functions as a structural extracellular matrix protein and is a heterotrimeric molecule composed of two $\alpha 1(I)$ chains intertwined with one $\alpha 2(I)$ chain. These heterotrimers cross-link and provide tensile strength to tissues. Type I collagen in the uterus is remodeled during embryo implantation. We hypothesized that type I collagen plays an essential role in uterine function, and therefore, mutations in the genes that code for type I collagen, COL1A1 and COL1A2, as is present in the Osteogenesis Imperfecta model mouse (oim), will result in impaired reproductive capacity. Oim/oim mice are functional null for the $\alpha 2(I)$ chain and synthesize only homotrimeric $\alpha 1(I)$ collagen. We bred wildtype and oim/oim dams to wildtype sires and examined litter size, pup weights and days to delivery. There was an approximate 30% decrease (Student's t-test, $p=0.01$) in the number of pups born to oim/oim dams ($n=16$) as compared to wildtype dams. To determine when embryos were lost, corpora lutea were counted and compared to viable embryo numbers at two gestational ages: E6.5 ($n=9$) and E10.5 ($n=10$). There was no difference in the number of viable embryos at E6.5, but there was a reduction in the ratio of viable embryos to corpora lutea (Fisher's exact test, $p<0.0001$) in oim/oim dams at E10.5. Thus, ovulation and implantation appeared to occur normally, but uterine support of pregnancy was inadequate post-implantation. In addition, the days to parturition for the oim/oim dams was normal, suggesting no irregularities in estrus cycles or time to conception. Morphological analysis of the

implantation sites is ongoing to detect irregularities within the uterus during early-mid gestation. Preliminary data suggest greater numbers of uterine glands in virgin oim/oim (33.9 ± 8.2 , $n=4$) than in wildtype mice (24.8 ± 6.2 , $n=4$) (t-test, $p=0.13$), indicating a potential role of COL1 in gland formation and/or remodeling. This project shows a role for collagen in uterine development that may have clinical significance for individuals suffering from Osteogenesis Imperfecta and other connective tissue diseases.

26. Maternal Obesity Affects Fetal Growth with Maternal Obesity Associated Growth Restriction Attributed to Decreased 11 β -Hydroxysteroid Dehydrogenase Expression. Andrea R. McCain, Kristin A. Beede, Dustin T. Yates, Jennifer R. Wood.

Maternal obesity alters fetal development due to potential changes in lipid exposure due to altered placental nutrient delivery and/or hormone synthesis. Altered fetal development, referred to as adaptive developmental programming, contributes to increased progression of offspring toward obesity and metabolic syndrome during adulthood. The current goal was to identify mechanistic links between altered fetal growth and placental development and function in the context of maternal obesity. Lethal Yellow (LY) mice, a model which replicates the phenotype of obese, pre-diabetic individuals, were used for the study. Specifically, seventeen-week-old control (C57BL/6, B6) and LY females were mated to B6 or LY males, respectively yielding B6 (female) x LY (male) pregnancies representing paternal obesity and LY (f) x B6 (m) pregnancies representing maternal obesity. Additionally, B6 (f) x B6 (m) crosses produced lean control pregnancies. Dams were necropsied at 12.5 days of gestation (E12.5) and fetuses with corresponding placenta collected. The gender and phenotype (LY or B6) of each embryo was determined using digital droplet PCR (ddPCR) for the SRY gene and agouti mRNA, respectively. We did not detect any gender dependent differences in any of the physiological measurements taken at this gestational time point. Alternatively, the average embryo weight, placenta weight and ratio of embryo to placenta weight was decreased in LYxB6 but not B6xLY compared to B6xB6 matings. To determine potential mechanisms associated with the intrauterine growth restriction associated with maternal obesity, RNA was collected from placentas and ddPCR performed using primers against corticosterone regulating enzymes 11 β -hydroxysteroid dehydrogenase type 1 (Hsd11b1) and type 2 (Hsd11b2). There was no significant difference in Hsd11b1 expression in LYxB6 or B6xLY placentas compared to B6xB6 controls. Alternatively, Hsd11b2 mRNA abundance was decreased 3-fold in LYxB6 placenta whereas there was no significant difference in B6xLY placenta compared to B6xB6 control. Together these data indicate that intrauterine growth restriction is associated with maternal obesity and this effect may be due to increased fetal glucocorticoid exposure.

27. Conceptus Elongation in Beef Heifers with Superior Uterine Capacity for Pregnancy. Joao G.N. Moraes¹, Thomas W. Geary², Peter J. Hansen³, Holly Neibergs⁴, Susanta Behura¹, Thomas R. Hansen⁵, Thomas E. Spencer¹ ¹Division of Animal Sciences, University of Missouri, Columbia, Missouri ²USDA-ARS, Fort Keogh Livestock and Range Research Laboratory, Miles City, MT ³Department of Animal Sciences, University of Florida, Gainesville, FL ⁴Department of Animal Sciences and Center for Reproductive Biology, Washington State University, Pullman, WA ⁵Animal Reproduction and Biotechnology Laboratory, Colorado State University, Fort Collins, CO

Infertility and subfertility represent major problems in domestic animals and humans. To select animals with intrinsic differences in pregnancy loss, beef heifers were subjected to serial embryo transfer and classified based on day 28 pregnancy rates as high fertile (HF=100%), subfertile (SF=25-33%), or infertile (IF=0%). Studies using in vivo-produced embryos established that preimplantation conceptus survival and growth to day 14 was not compromised in the SF and IF heifers (Geary, Biol Reprod, 95:47 2016). Thus, the observed difference in fertility was hypothesized to manifest during conceptus elongation and pregnancy recognition. Two in vivo-produced embryos were transferred into HF ($n=21$), SF ($n=10$), and IF ($n=5$) heifers on day 7. On day 17, the uterus was flushed and endometrium collected. Conceptus recovery rate was higher ($P<0.05$) in HF (71%) and SF (90%) than IF (20%) heifers. Interferon tau (IFNT) in the uterine flush was quantified by ELISA. Conceptus length was positively ($P<0.01$) correlated ($R=0.79$) with IFNT in the flush. IFNT was greater ($P<0.05$) in uterine flush from pregnant HF (148 ± 54 ng/mL) compared to SF (74 ± 67 ng/mL) and IF (0 ng/mL) heifers. Conceptuses from HF ($\bar{x}=10.6$ cm, range=1.2-32.2 cm) were longer ($P<0.01$) than SF ($\bar{x}=4.7$ cm, range=1.5-13.5 cm) or IF (<0.1 cm) heifers. Total RNA was sequenced ($n=5$ per group) from day 17 endometria

of open or nonpregnant (NP) HF, SF and IF heifers and pregnant (P) HF and SF heifers as well as 17 HF conceptuses and 10 SF conceptuses. There were 96 differentially expressed genes (DEGs; FDR $P < 0.05$) in NP endometrium; several DEGs encoded proteins involved in immune responses or present in immune cells. Comparison of P and NP endometrium in HF or SF heifers found 3,422 and 1,095 DEGs, respectively. The endometrium response to pregnancy was significantly diminished in SF heifers. There were 1,287 DEGs between HF and SF conceptuses. Many of the down-regulated genes in SF conceptuses are associated with embryonic lethality in other species. These studies support the idea that the uterine environment directly affects conceptus survival and elongation during the establishment of pregnancy and asynchronous conceptus-endometrial interactions result in pregnancy loss. Supported by NIH R01 HD072898.

28. Estrogen Receptor 2 Regulates the Granulosa Cell Genes Critical for Gonadotropin Induced Preovulatory Follicle Maturation and Ovulation. Vincentaben Khristi, Prabhakar Singh, Subhra Ghosh, Archit Pramanik, Shaon Borosha, Khyati Dalal, Katherine F. Roby, Michael W. Wolfe and M.A. Karim Rumi. Institute for Reproductive Health and Regenerative Medicine, Department of Pathology and Laboratory Medicine, Department of Anatomy and Cell Biology, Department of Molecular and Integrative Physiology, University of Kansas Medical Center, Kansas City, KS.

Estrogen receptor 2 (ESR2) plays a critical role in folliculogenesis and ovulation. Disruption of ESR2 function in rats results in female infertility due to failure of ovulation. Ovulation failure occurred in two distinct models, ESR2 null mutants (exon3 deletion, ESR2 Δ E3) and ESR2 DNA-binding-domain mutants (exon 4 deletion, ESR2 Δ E4) indicating that transcriptional regulation by ESR2 is indispensable for ovulation. To define the regulatory role of ESR2 in preovulatory follicular maturation and ovulation, we investigated responsiveness to exogenous gonadotropins. 4-week-old ESR2 mutant females were treated with gonadotropins, and ovarian weights and oocyte yield were evaluated. Gonadotropin stimulated ovarian weight gain was reduced in the mutants and they failed to ovulate. ESR2 mutant ovaries exhibited numerous antral follicles containing trapped oocytes and a complete absence of corpora lutea. As granulosa cells (GCs) play a vital role in follicle maturation and ovulation, and ESR2-dependent estrogen signaling is predominant in GCs, we further examined the differential expression of gonadotropin induced genes in GCs. Of 32,623 genes detected by RNA-sequencing, 1696 were differentially expressed in ESR2 mutant rats (790 downregulated, and 906 upregulated, absolute fold change 2, FDR $p < 0.05$). These included genes involved in folliculogenesis, follicle maturation, and ovulation. Molecular pathway analyses suggested their potential roles in steroidogenesis and steroid metabolism, cytokine and growth factor signaling, inflammation and angiogenesis, cell-cell contacts and extracellular remodeling, and transcriptional regulation. Our findings indicate that ESR2 regulates key genes in GCs that are essential for follicle maturation and ovulation.

29. Autophagy: A Non-hormonal Contraceptive Target. Arin Oestreich, Ran Xu, Stephan, Gary Silverman, Stephen Pak, Kelle Moley. Washington University School of Medicine.

In 2011, an estimated 45% of pregnancies in the US were unplanned and often led to poor fetal and pediatric health outcomes. Although hormonal contraceptives are effective, women at risk of cardiac events cannot use them because they increase the risks of thrombotic events, and other women discontinue use due to unwanted side effects. Thus, to reduce the rate of unintended pregnancies, there is a need to develop new, highly effective, non-hormonal methods of reversible contraception. Endometrial stromal cell (ESC) decidualization is a process by which the uterus becomes receptive to embryo implantation. As this process is critical for the establishment of pregnancy, the molecular mechanisms that regulate it are potential contraceptive targets. Recent evidence suggests that decidualization of endometrial stromal cells (ESCs) is accompanied by activation of autophagy. Furthermore, our work using mice with a hypomorphic mutation in the autophagy gene Atg16L1 which have diminished autophagic flux have an impaired ability to undergo artificial decidualization. Therefore, we hypothesized that inhibiting autophagy could act as a non-hormonal contraceptive to prevent pregnancy by impairing ESC decidualization. First, we identified FDA approved compounds that inhibited autophagy using a *C. elegans* based high throughput drug screen of the LOPAC1280 library of 1280 pharmacologically active compounds from Sigma. To see if pharmacological inhibition of the autophagy pathway would impair ESC decidualization, we cultured and treated immortalized human ESCs with one of the identified compounds, Zafirlukast, a leukotriene receptor antagonist. Cells were treated with

a vehicle or Zafirlukast along with medroxyprogesterone-17- acetate and N6,2'-O-dibutyryl adenosine cAMP sodium salt to stimulate decidualization. In a preliminary dose response curve, cells treated with Zafirlukast had decreased expression of the decidualization marker PRL than cells treated with vehicle ($P \leq 0.05$; $n=4$ 1-way ANOVA with Tukey's multiple comparison test). These data suggest that inhibiting autophagy impairs ESC decidualization in both mice and human cells. We conclude that autophagy is a potential non-hormonal contraceptive target. The experiments described in this abstract were supported by NIH grant R01HD065435 awarded to KHM.

30. Progesterone Effects on Extracellular Vesicles in the Sheep Uterus. Gregory W. Burns¹, Kelsey E. Brooks^{1,2}, Eleanore V. O'Neil¹, Darren E. Hagen³, Susanta K. Behura¹, and Thomas E. Spencer¹
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Progesterone (P4) acts via the endometrium to modify the uterine environment and promote conceptus growth for pregnancy establishment. Many cells release membrane-bound vesicles of endosomal and plasma membrane origin that can be collectively termed extracellular vesicles (EVs). In other tissues EVs represent an important mode of intercellular communication by transferring select RNAs, proteins, and lipids between cells. Thus, EVs are hypothesized to be a novel form of communication between the uterus and conceptus. In sheep, EVs are found in the uterine lumen, and endometrial-derived EVs can traffic to the conceptus trophectoderm. This study tested the hypothesis that P4 regulates production of EVs by the ovine uterus. Uterine luminal and glandular epithelia were identified as a source of EVs by electron microscopy. Size exclusion chromatography and nanoparticle tracking analysis (NTA) found that total EVs in the uterine lumen increased 5.4-fold from day 10 to 14 in cyclic sheep. Using an ovariectomy and hormone replacement model, NTA found that progesterone increased EV number by 2.7-fold and vesicle diameter by 12 nm in the uterine lumen. Endometrial transcriptome analysis revealed that P4 regulated 1,611 transcripts (931 increased and 680 decreased). Small RNA sequencing of endometrium and EVs from the uterine lumen detected expression of 768 miRNAs and found that P4 regulated 9 endometrial and 7 EV miRNAs. This study supports an expanded role for EVs in P4's actions on the uterus to establish and promote an embryotrophic environment. Supported by USDA NIFA AFRI 2015-67015-23678 and 2016-67015-24741.

31. (TRAINEE ORAL PRESENTATION ONLY - NO POSTER) Identification of RPLP1 as a Novel Target of miR-451a Whose Expression Is Elevated in Endometriotic Lesion Tissue and Correlates with Endometriotic Lesion Tissue and Cell Proliferation. Zahraa Alali, Tommaso Falcone, Warren B Nothnick. Molecular and Integrative Physiology, University of Kansas Medical Center, Kansas City, KS, USA; Obstetrics, Gynecology and Women's Health Institute, Cleveland Clinic, Cleveland, OH, USA

Endometriosis is a disease common in women of reproductive age where endometrial tissue establishes and survives in ectopic locations. However, how these lesions establish and survive is unknown. We have recently identified ribosomal protein large P1 (RPLP1; which is a modulator of cell proliferation) as a potential target of miR-451a expressed in endometriotic epithelial 12Z cells. The objective of the current study was to determine the expression of RPLP1 in human endometriotic lesion tissue, examine the function of RPLP1 in modulating cell survival/proliferation and miR-451a regulation of RPLP1. To achieve this, RPLP1 mRNA and protein levels were examined in paired endometriotic lesion tissue and eutopic endometrium from women with stage III/IV endometriosis (N=35) as well as tissue from women without symptoms of endometriosis (controls; N=20 for localization studies). Collectively, data indicated that the net expression of RPLP1 mRNA was significantly higher in ectopic lesion tissue compared to paired eutopic endometrium (3.72 fold increase; $P < 0.01$) and immunohistochemical localization revealed predominant localization to epithelial cells (lesion > endometriosis eutopic > control eutopic; $P < 0.05$). As RPLP1 is proposed to drive cellular proliferation, we assessed the correlation between lesion RPLP1 mRNA expression and that of cyclinE1 and observed a positive correlation between both markers (Pearson $r = 0.571$; $P < 0.01$; N=35). To further demonstrate functionality, we generated a stable endometriotic epithelial cell line in which RPLP1 was deleted and found that loss of RPLP1 expression was associated with a highly significant reduction in cell number/survival ($P < 0.001$; N=3). We further

demonstrated that over-expression of miR-451a via transient transfection of 12Z cells resulted in a significant ($P < 0.05$; $N = 3$) reduction in RPLP1 expression as well as that of cyclinE1. In conclusion, these studies reveal that RPLP1 is a novel target of miR-451a and that RPLP1 expression and its regulation by miR-451a are associated with cell proliferation and survival.

32. Conceptus Derived Prostaglandin Synthase 2 (PTGS2) Regulates Embryonic Development in Sheep. Eleanore V. O'Neil, Joshua Benne, Gregory Burns, Kelsey Brooks and Thomas E. Spencer. Division of Animal Sciences, University of Missouri-Columbia

During the period of pregnancy recognition and establishment in sheep, the luminal epithelium of the endometrium and the trophectoderm of the elongating conceptus produces prostaglandins (PGs). Biosynthesis of PGs in both the ovine endometrium and conceptus is dependent on the enzyme PG-endoperoxide synthase 2 (PTGS2). Infusion of a selective PTGS2 inhibitor into the uterine lumen of pregnant sheep on days 8 to 14 prevented conceptus elongation, and subsequent studies found that PGs enhance expression of conceptus elongation- and implantation-related genes in the endometrium. However, the specific role of conceptus-derived PGs in pregnancy establishment is not known in ruminants. This study tested the hypothesis that conceptus PTGS2 has a biological role in conceptus elongation during early pregnancy in sheep using CRISPR-Cas9 technology. Two guide RNAs (gRNAs) were designed to target exon 2 or exon 3 of the *Ovis aries* PTGS2 gene. Rambouillet ewes were superovulated and bred to a fertile ram. Zygotes were collected from the oviducts at 36 h post-estrus and injected with either Cas9 mRNA as a control or with Cas9 mRNA and sgRNAs to target PTGS2. Injected zygotes were cultured and resulting embryos were then transferred into the oviduct or uterus of synchronized recipient ewes ($n = 3-6$ embryos per ewe) and were recovered by gently flushing the uterine lumen on day 14 post-estrus. In total, 112 embryos (39 Control, 73 PTGS2 targeted) were transferred into recipient ewes. A higher proportion of the control embryos were recovered ($P < 0.05$) as conceptuses (48%) compared to the PTGS2 targeted embryos (24%) on day 14. For PTGS2 targeted conceptuses, genotyping revealed that 18% were not edited, 52% had one allele edited (monoallelic), and 30% had two alleles edited (biallelic) with mutations that interrupted splice sites or introduced frameshift mutations in the PTGS2 gene. Conceptuses with mutated PTGS2 averaged 8 mm in length ($n = 5$) while control conceptuses averaged 15 mm ($n = 19$). These results support the idea that PTGS2 is important for blastocyst hatching from the zona pellucida and/or trophectoderm survival and development during early pregnancy. This project was supported by grants 2009-65203-31188 and 2012-67015-23999 from the USDA National Institute of Food and Agriculture.

33. RNA Editing in Mammalian Oocytes. Pavla Brachova, Nehemiah S. Alvarez, Keith E. Latham, David F. Albertini, Lane K. Christenson. Molecular and Integrative Physiology, University of Kansas Medical Center, Kansas City, Kansas, USA; Pathology and Laboratory Medicine, University of Kansas Medical Center, Kansas City, Kansas, USA; Department of Animal Science, Michigan State University, East Lansing, Michigan, USA; Center for Human Reproduction, New York, New York, USA.

Successful reproduction depends on high quality oocytes that develop and are competent for fertilization and embryo development. During oocyte growth, the epigenetic state allows permissive expression from repetitive genomic elements. Mouse models that increase repetitive RNA transcription or have defects in repetitive RNA degradation display oocyte defects. However, the role the RNA sensing machinery has in the regulation of repetitive RNA abundance remains poorly understood. A central component of the RNA sensing machinery is adenosine deaminases acting on double stranded RNA (ADAR). ADAR can bind double stranded RNA (dsRNA) generated from repetitive genomic loci and deaminate adenosines into inosines. In somatic cells, loss of ADAR causes a buildup of un-edited RNA species and can trigger inflammation, autoimmunity, and cell death. The role of RNA editing has not been examined in the context of oocyte quality. Our goal was to identify an RNA editing signature in transcriptionally active and inactive mouse and human oocytes. To assess RNA editing in transcriptionally active oocytes, we collected postnatal day 12 oocytes and performed RNAseq. Transcriptionally inactive oocyte RNA-seq data from fully grown germinal vesicle (GV) and MII oocytes of mouse and human samples was available from previous publications. We utilized a computational approach to compare RNA-seq data to whole genome SNP databases of mice and humans. Confocal and fluorescence microscopy were used to examine ADAR1 localization in individual mouse and human oocytes and in ovarian

sections of mature mice. RNA-seq analysis revealed expression of ADAR1, ADAR2, and ADAR3 in mouse and human oocytes. Immunofluorescence staining of ADAR1 in human and mouse oocytes appears as cytoplasmic puncta. Our RNA editing pipeline revealed that 1,396 genes were commonly edited between growing and mature oocytes. These genes were enriched in meiosis GO terms. Many edits were found to occur in endogenous retroviral fusion genes. Our studies identify prevalent RNA editing in mouse and human oocytes. ADAR1 is prevalent in the oocyte, and also in the granulosa cells of mouse ovaries. Through our studies, we hope to gain insight into this novel post-transcriptional gene regulation pathway and into mechanisms that govern high egg quality.

34. Aberrant Secretion of 10 Gonadal Steroids in Gonadotropin-releasing Hormone II Receptor Knockdown Boars. Amy T. Desaulniers¹, Rebecca A. Cederberg¹, Clay A. Lents² and Brett R. White¹
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Paradoxically, the second mammalian GnRH isoform (GnRH-II) and its receptor (GnRHR-II) are not physiological regulators of gonadotropin secretion. Instead, data from our laboratory suggests that both are abundantly produced in the porcine testis and mediate testosterone secretion independent of luteinizing hormone (LH). To further study the role of GnRH-II and its receptor in pigs, our laboratory generated a GnRHR-II knockdown (KD) swine line with 70% lower testicular GnRHR-II mRNA levels compared to littermate control boars. During pubertal development, testosterone concentrations tended to be reduced in transgenic versus littermate control boars, yet LH concentrations were unaffected. The objective of this study was to compare the secretory patterns of testosterone and circulating concentrations of 16 other steroids in adult GnRHR-II KD (n = 5) and littermate control (n = 5) males. Boars were fit with indwelling jugular cannulae and blood was collected every 15 min for 8 h. Serum was assayed for testosterone concentration via radioimmunoassay. Samples (1/animal) were also subjected to high performance liquid chromatography tandem mass spectrometry at Biocrates Life Sciences AG (Innsbruck, Austria). Transgenic boars tended to produce fewer pulses of testosterone than littermate controls (P < 0.10). Amplitude of pulses was reduced in transgenics (P < 0.05) but pulse duration was unaffected (P > 0.10). GnRHR-II KD boars also tended to have lower minimum, maximum and mean concentrations of testosterone (P < 0.10). Likewise, area under the curve tended to be reduced in transgenics (P < 0.10). Mass spectrometry revealed that production of corticosteroids was largely unaffected in GnRHR-II KD boars; however, gonadal steroids were dramatically impacted. Serum concentrations of progestogens (17 α -hydroxyprogesterone and progesterone), androgens (dehydroepiandrosterone, dihydrotestosterone and androsterone) and estrogens (estrone and 17 β - estradiol) were reduced (P < 0.05) in transgenic compared to littermate control boars. In addition, concentrations of testosterone, dehydroepiandrosterone sulfate and androstenedione tended to be lower in GnRHR-II KD boars (P \leq 0.10). Ultimately, these data demonstrate that GnRH-II and its receptor are critical modulators of steroidogenesis within porcine Leydig cells. Partially supported by USDA NIFA AFRI ELI predoctoral fellowship (2017-67011-26036; ATD) and AFRI (2017-67015- 26508; BRW) funds. USDA is an equal opportunity provider and employer.

35. Addition of Palmitate to Porcine Embryo Culture Improves the Number of Nuclei in the Resulting Blastocyst Stage Embryos. C. A. Pfeiffer^{1*}, B. K. Redel¹, L. D. Spate¹, R. S. Prather¹ ¹Division of Animal Sciences, University of Missouri, Columbia, MO, U.S.A.

The use of pigs for human health research is highly dependent on the success of porcine embryonic culture and in vitro fertilization. To increase the developmental competence of in vitro produced embryos, the embryonic culture medium must be improved. Cancer cells, rapidly proliferating somatic cells, and early stage embryos have similar metabolisms and rely on many of the same nutrients for growth. For example, cancer cells depend on fatty acids for cellular growth. The synthesis of new membranes in proliferating fibroblast cells has been shown to require palmitate, a fatty acid that can be synthesized from nutrients or can be taken up from the extracellular environment. For this reason, we hypothesized that in vitro produced embryos may benefit from supplemental palmitate in culture. Slaughterhouse derived cumulus oocyte complexes were matured for 42 hours in maturation medium containing FGF2, LIF, and IGF1. Selected metaphase II oocytes were fertilized in modified tris buffered medium for 4 hours. To determine the optimal concentration of palmitate to add to culture, a concentration curve was completed. Palmitate was dissolved in chloroform as a carrier

and supplemented to MU2 medium. Five different treatments, MU2, MU2 + Chloroform, MU2 + 25 μ M palmitate, MU2 + 50 μ M palmitate, and MU2 + 100 μ M palmitate, were then used to assess the effect palmitate had on the percent of zygotes that developed to the blastocyst stage as well as the number of nuclei in the resulting blastocysts. A Proc Genmod in SAS 9.4 (Cary, NC) was used to determine if blastocyst percentages were significantly different among treatments. An analysis of variance was used to determine if differences existed between treatments in respect to total cell number. While the addition of palmitate did not increase the percentage of blastocyst development ($24.9 \pm 3.9\%$, $25.6 \pm 3.0\%$, $23.1 \pm 3.1\%$, $21.2 \pm 3.1\%$, and $21.8 \pm 2.1\%$, respectively, $P > 0.05$), it did increase the number of nuclei ($37.4 \pm 5.6a$, $43.5 \pm 13.3a,b$, $37.7 \pm 8.2a$, $48.0 \pm 13.0b$, and $37.4 \pm 6.6a$, respectively $P < 0.04$). In the future, we will elucidate the best time to add palmitate to culture and determine if palmitate cultured embryos are competent to establish a pregnancy. Funded by Food for the 21st Century

36. Epigenetic and transcriptional changes in rat trophoblast stem cells exposed to hypoxia. Nehemiah S. Alvarez, Kesiuke Kozai, Damayanti Chakraborty, and Michael J. Soares. Institute for Reproductive Health and Regenerative Medicine, Departments of Pathology and Laboratory Medicine and Pediatrics, University of Kansas Medical Center, Kansas City, KS; Fetal Health Research, Children's Research Institute, Children's Mercy, Kansas City, MO

In placental mammals, successful pregnancy depends on proper embryo implantation into the uterine wall. Embryo implantation is dependent on cells on the surface of the embryo (trophoblast cells), which directly interact with the uterus. After implantation, trophoblast cells differentiate into specialized cell types that make up the placenta and are required for establishing the maternal-fetal interface. Defects in trophoblast lineage development can reduce the chances of a successful pregnancy in humans by causing pathological conditions such as preeclampsia, intrauterine growth restriction, and pre-term birth. As such, deficiencies in trophoblast differentiation are a major contributing factor to early pregnancy loss, but the factors contributing to trophoblast deficiencies remain poorly understood. One possible cause is the reduced ability of trophoblast cells to respond to environmental signals such as oxygen tension or nutrient status. Here we investigated the effects of hypoxia on epigenetic and transcriptional regulatory networks in rat trophoblast stem (TS) cells. After 24 h exposure of TS cells to 0.5% oxygen, we observed genome-wide alterations, including changes in repressive histone marks, a decrease in global DNA methylation, and alterations in transcript profiles. We also detected upregulation of several families of retroelements, including LINEs, SINEs, and LTRs after exposure to hypoxia. We propose that TS cells undergo genome-wide epigenetic alterations in low oxygen that activate transcriptional networks necessary for adaptations. (Supported by NIH grants HD020676, HD079363; Sosland Foundation)

37. wtf Causes Aneuploid Gametes. María Angélica Bravo Núñez¹, Nicole Nuckolls¹, Sarah Zanders^{1,2}, 1Stowers Institute for Medical Research, Kansas City; 2Department of Molecular and Integrative Physiology, University of Kansas Medical Center, Kansas City

During meiosis, two rounds of chromosome segregation reduce ploidy from diploid to haploid. When this process fails, aneuploid gametes that have the wrong number of chromosomes can form. Aneuploidy is the leading cause of miscarriages and congenital birth defects in humans. It is commonly thought that the frequency of aneuploidy in gametes is entirely dependent on the frequency of chromosome mis-segregation during meiosis. We have discovered an additional mechanism that can lead to a 10-fold increase in the frequency of aneuploidy, without affecting the fidelity of chromosome segregation. This novel mechanism stems from competition between selfish genes found throughout eukaryotes that are known as gamete-killing meiotic drivers. These meiotic drivers act by destroying the gametes that do not inherit them. Using newly discovered wtf meiotic drive genes from fission yeast, we show that competition between diverged gamete killers at allelic loci can increase the frequency of aneuploid gametes to as high as 95% by destroying haploid gametes. This work will expand our understanding of meiosis and will shed light into how meiotic drivers cause infertility and aneuploidy.

38. Effect of Aromatase (CYP19A1) Deletion on Pre-implantation Embryo Development and Conceptus Elongation in Pigs. A.E. Meyer, R. D. Geisert, T.E. Spencer, R.S. Prather, K.E. Brooks, C. Murphy, L. Spate, J. Benne, S. Murphy, and R. Cecil. Division of Animal Sciences, University of Missouri, Columbia, MO, USA.

Embryo mortality in pigs is greatest during the peri-implantation period, when the conceptus undergoes elongation, attaches to the endometrium, and establishes pregnancy. The elongating conceptus secretes estrogen (E2), which is the signal for maternal recognition of pregnancy. Conceptus estrogen synthesis increases from day 11 to 12 as the conceptus rapidly elongates from a tubular to filamentous form. Production of E2 by the conceptus is dependent on aromatase (CYP19A1). To understand the role of E2 in conceptus elongation and establishment of pregnancy, a loss-of-function study was conducted by mutating CYP19A1 using CRISPR/Cas9 technology. Briefly, guide RNAs (gRNAs) were designed to target exon 2 of the CYP19A1 gene. Fetal fibroblast cells were transfected with a construct expressing Cas9 and gRNAs and biallelic deletions were identified using Sanger Sequencing. Wild-type (WT) and edited (CYP19A1-null) fibroblast cells were used to create embryos through somatic cell nuclear transfer (SCNT). SCNT-derived embryos were cultured in vitro for 7 days. Consequently, 30 to 50 blastocysts were transferred into synchronized recipient gilts (n=8) on day 4 of the estrous cycle. The reproductive tract was collected from recipient gilts on day 12 or 14 post-estrus. Conceptuses were recovered by flushing the uterine lumen. There was no difference in the conceptus development of WT and CYP19A1-null embryos. Total E2 was substantially higher in the uterine flushing of gilts gestating WT embryos than CYP19A1-null embryos ($P = 0.06$). Results indicate that inactivation of CYP19A1 inhibits the large increase in E2 synthesis during conceptus rapid elongation. These results support the idea that conceptus E2 is not essential for pre-implantation embryo development nor rapid conceptus elongation. Future research will utilize the same approach to understand the biological roles of conceptus E2 in pregnancy recognition, conceptus survival, and development of the placenta. Research supported by grant 2017-12211054 from the USDA National Institute of Food and Agriculture.

39. Tissue Factor Pathway Inhibitor Regulation of Endovascular Trophoblast Cell Development and Uterine Spiral Artery Remodeling at the Placentation Site. Masanaga Muto, Damayanti Chakraborty, Regan L Scott, and Michael J Soares. Institute for Reproductive Health and Regenerative Medicine, Departments of Pathology and Pediatrics, University of Kansas Medical Center, Kansas City, Kansas; Fetal Health Research, Children's Research Institute, Children's Mercy, Kansas City, Missouri.

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 possessing 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 controlling the development of 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 components of the coagulation pathway, including thrombomodulin and tissue factor pathway inhibitor (Tfpi), which are recognized anti-coagulation factors of endothelial cells. 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 utilized rat trophoblast-specific lentiviral delivery of Tfpi shRNAs (LV-Tfpi shRNA). Placental weights of LV-Tfpi shRNA transduced embryos were significantly decreased at gestational day 15.5 compared with LV-control shRNA treated placentas. Immunohistochemical analysis using cytokeratin antibody to identify trophoblast cells revealed that the depth of intrauterine trophoblast invasion was significantly less within placentation sites of LV-Tfpi shRNA transduced rat embryos. Furthermore, fibrinogen deposition was prominently observed in uterine spiral arterioles associated with LV-Tfpi shRNA transduced placentation sites. These results implicate Tfpi as a potential regulator of endovascular trophoblast cell invasion, uterine spiral artery remodeling, and hemostasis at the maternal-fetal interface. (Supported by a Lalor Foundation Postdoctoral Fellowship; NIH HD020676, HD079363)

40. (TRAINEE ORAL PRESENTATION) Forkhead box a2 (FOXA2) and Endometrial Glands are Essential for Uterine Function and Fertility. Andrew M. Kelleher, Susanta Behura, and Thomas E. Spencer. Division of Animal Sciences, 158 ASRC, 920 East Campus Drive, University of Missouri, Columbia 65211

Forkhead box A2 (FOXA2) is a critical regulator of endometrial gland development and differentiated function in the adult uterus. Available data in mice and humans support the hypothesis that endometrial glands and FOXA2 have essential biological roles in endometrial physiology and pregnancy biology. In these studies, FOXA2 was conditionally deleted in the adult mouse uterus using the lactotransferrin Cre (Ltf-Cre) model and in the neonatal mouse uterus using the progesterone receptor Cre (Pgr-Cre) model. The uteri of adult FOXA2-deleted mice were morphologically normal and contained glands, whereas the uteri of neonatal FOXA2-deleted mice lack uterine glands. Both neonatal and adult FOXA2-deleted mice were infertile and displayed defects in blastocyst implantation and stromal cell decidualization. Of note, leukemia inhibitory factor (Lif) expression was absent on gestational day (GD) 4 (day of implantation) in both FOXA2-deleted models. The absence of FOXA2 and/or uterine glands did not affect the formation of specialized implantation chambers (crypts) that form from evaginations of the uterine luminal epithelium (LE) towards the antimesometrial (AM) pole of the GD 4 uterus. Despite normal embryo localization within crypts, heparin-binding epidermal growth factor (Hbegf) and prostaglandin-endoperoxide synthase 2 (Ptgs2) were not upregulated in the AM LE or stroma around the implanting embryo in FOXA2-deleted females. Interestingly, injections of recombinant mouse LIF on GD 4 resulted in increased expression of Hbegf and Ptgs2 within crypts around the implanting embryo in FOXA2-deleted females. Histologically normal implantation sites were observed in LIF-replaced neonatal and adult FOXA2-deleted mice on GD 6. Pregnancy was maintained to term in LIF-replaced uterine gland-containing adult Foxa2-deleted mice, but failed by GD 10 in glandless neonatal FOXA2-deleted mice. RNA-seq analysis of GD 6 IS from WT and LIF-replaced FOXA2-deleted mice revealed expression of 36 factors, known to be involved in decidualization, were uniquely altered in glandless mice (Alpl, Angpt1, Angpt4, Fkbp5, Foxo1, Id1, Ptgs2, Vegfa). Collectively, these findings suggest that FOXA2 regulates glandular Lif expression for blastocyst implantation and that uterine glands and, by inference, their secretions impact stromal cell decidualization for pregnancy establishment. Supported by NIH1R21HD076347.

41. IL33 and the Female Reproductive Tract: Analysis and Establishment of Genetic Rat Models.

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Interleukin 33 (IL33) is a novel member of the IL1 family. IL33 is expressed in epithelial cells, possesses a barrier function, and contributes to Th2 type immune responses and innate immunity. Roles of IL33 in the female reproductive tract are poorly understood. In the present study, we explore aspects of the biology of IL33 in the female reproductive tract and describe the generation of mutant IL33 signaling rat models. Initially, we examined the regulation of IL33 expression in the female reproductive tract. The acute effects of ovarian steroid hormones on IL33 expression in the uterus were investigated using ovariectomized (OVX) rats. Treatment with progesterone significantly increased IL33 expression, whereas the treatment with estrogen significantly decreased IL33 expression. Next, we examined whether IL33 is associated with decidualization, a progesterone-dependent event. We treated OVX rats with an empirically determined hormone regimen, including both estrogen and progesterone, known to prepare the uterus for embryo implantation. Decidualization was induced by damaging the antimesometrial endometrial surface of one uterine horn. In contrast to the acute actions of progesterone on the uterus of the OVX rat, decidualization was associated with a significant decrease in IL33 expression. IL33 expression was also examined in the midgestation placentation site. We observed that IL33 expression was significantly higher in the metrial gland than in the junctional and labyrinth zones of the gestation day 13.5 placentation site. To explore the role of IL33 signaling in the female reproductive function, we generated a series of IL33 mutant rat models and an IL33 receptor (IL1rl1) mutant rat model using clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR-associated protein 9 (Cas9)-mediated genome editing. We generated three independent IL33 mutant rat lines possessing deletions including: i) exon 3; ii) exons 3 to 8; iii) exons 5 to 8 and an IL1rl1 mutant rat strain. Founders with each of the mutations were backcrossed to wild type rats and the genotypes of offspring analyzed. IL33 and IL1rl1 mutations

were successfully transmitted through the germline. In summary, IL33 signaling is a potential contributor to the regulation of female reproductive physiology. Future work will be directed toward dissecting a role for IL33 in female reproductive function using our mutant IL33 signaling rat models. (Supported by a postdoctoral fellowship from the American Heart Association, NIH grants HD020676, HD079363, and the Sosland Foundation)

42. Placental Hematopoiesis in the GATA Light. Pratik Home, Bhaswati Bhattacharya, Soma Ray and Soumen Paul. 1 Department of Pathology and Laboratory Medicine and Institute for Reproductive Health and Regenerative Medicine, University of Kansas Medical Center, Kansas City, KS USA.

Of all the major organs that act as sites for hematopoietic stem cell (HSC) generation, the placenta is an important one. It has been shown that mid-gestation mouse placenta plays a significant role in the HSC development where it provides a temporary niche for definitive HSC pool. GATA family of transcription factors have previously been implicated in the development of HSCs in other organs, and we have shown previously that GATA2 and GATA3 are involved in the trophoblast development and differentiation. Recently we demonstrated that simultaneous knockout of both Gata2 and Gata3 in trophoblast lineage severely affected placental development. Also, the double knock-out resulted in significant developmental defects in the embryo proper leading to very early embryonic lethality. These developmental defects were accompanied by severe blood loss in the placenta, yolk sac and the embryo proper. Moreover, we established dual conditional Gata2 and Gata3 knockout trophoblast stem cells and used ChIP-seq and RNA-seq analyses to define independent and shared global targets of GATA2 and GATA3. We found that several pathways associated with the hematopoietic development are targets of both the transcription factors. Here using trophoblast giant cell (TGC)-specific conditional knockout mouse model we show that GATA factor loss in the TGC layers affects HSC population in the placenta and embryonic liver. As the endothelial cells in the placental labyrinth have been shown to provide a niche for the placental HSC and progenitor development, it is critical to define how the cross-talk between the TGC and the labyrinth takes place in this context. This study aims to shed light on the GATA-dependent signaling mechanism by which trophoblast giant cells regulate hematopoiesis in the mouse placenta.

43. Complex Modes of Transgenerational Gene Silencing by piRNA. Kelley Van Vaerenberghe¹, Danny E. Miller^{2,3}, Celeste Cummings¹, Marilyn Barragan¹, Alexandra Erwin¹ and Justin P. Blumenstiel¹
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Selfish elements such as transposable elements (TEs) pose a significant threat to genome stability. As such, mechanisms of genome defense based on piRNAs have evolved to limit TE proliferation in the germline. The production of TE piRNAs is commonly driven by TEs residing in piRNA clusters, but TE insertions also have the capacity to induce piRNA cluster formation at de novo insertions. While this mechanism ensures robust TE silencing, it also has the capacity to induce piRNA biogenesis targeting genes flanking the TE insertion. Since piRNA silencing has the capacity to be transmitted maternally to the next generation, this can also lead to off-target gene silencing that is propagated across generations. Here we examine the dynamics of piRNA mediated transgenerational gene silencing induced by TE insertions that flank genes. We identify one case in which genic piRNA biogenesis can be transmitted across generations, even in the absence of the original silencing allele. This can be considered a novel case of paramutation. In contrast, we also identify a case whereby robust piRNA biogenesis is associated with gene silencing that lacks the capacity to be transmitted maternally. Interestingly, in the latter case, we have also identified a revertant allele that maintains genic piRNA biogenesis but re-establishes gene expression. These results highlight significant complexity in the mechanisms of transgenerational off-target gene silencing by piRNA. Future studies aim to identify the factors that determine why some off-target piRNAs can silence across generations, but others do not.

44. Transcriptomic Profiling of Trophoblast Cells Within the Hemochorial Placentation Site. Regan L. Scott¹, Masanaga Muto¹, Kaela M. Varberg¹, Damayanti Chakraborty¹, Jeremy Chien², and Michael J. Soares^{1,3}. ¹Institute for Reproductive Health and Regenerative Medicine, Departments of Pathology & Laboratory Medicine and Pediatrics, University of Kansas Medical Center, Kansas City, KS; ²Division of Molecular Medicine, Department of Internal Medicine, University of New Mexico School of Medicine, Albuquerque, NM; ³Fetal Health Research, Children's Research Institute, Children's Mercy, Kansas City, MO.

The hemochorial placenta is composed of specialized trophoblast cell types that interact with uterine spiral arteries. These trophoblast cells are endowed with invasive properties allowing them to exit the developing placenta and direct changes in the uterine vasculature that promote the effective delivery of nutrients to the placenta. Furthermore, this migratory trophoblast cell population is undermined in diseases of pregnancy such as preeclampsia, intrauterine growth restriction, and early pregnancy loss. However, their location within the uterine wall precludes their routine analysis in human placentation sites. The rat exhibits deep intrauterine trophoblast invasion and represents an effective animal model for investigating the biology of trophoblast invasion and uterine spiral artery remodeling. The purpose of this investigation was to profile the transcriptome of trophoblast cells isolated from the rat placentation site. Transgenic male rats constitutively expressing enhanced green fluorescent protein (GFP) were mated with wild type female rats. On gestation day 18.5, placentation sites were dissected into metrial gland (site of intrauterine trophoblast invasion) and junctional zone (site of invasive trophoblast progenitors and other differentiated trophoblast lineages) compartments. GFP-positive tissues were enzymatically dissociated and GFP-positive trophoblast cells collected by flow cytometry and cell sorting. RNA was isolated from the GFP-positive cells, libraries generated, and sequenced to generate 100 bp paired-end reads. Bioinformatic and pathway analyses were performed. Striking differences in gene expression were observed in invasive trophoblast cells and junctional trophoblast cells. Transcript expression profiles were validated by qRT-PCR on independent macrodissections of metrial gland and junctional zone tissues and from laser capture microdissected specimens isolated from invasive trophoblast cells of the metrial gland and trophoblast cells of the junctional zone. Collectively, the datasets provide a platform to uncover candidate regulators for in vivo investigation of pathways controlling placentation and trophoblast cell lineage development. (Supported by a postdoctoral fellowship from the Lalor Foundation, NIH grants HD020676 and HD079363, and the Sosland Foundation).

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