November 7-8
2019

16th Annual Gilbert S. Greenwald Symposium on Reproduction and Perinatal Research

KU MEDICAL CENTER
The University of Kansas

www.kumc.edu/greenwald

Biography - Gilbert S. Greenwald

The Institute for Reproduction and Perinatal Research at the University of Kansas Medical Center hosts the Annual Gilbert S. Greenwald Symposium on Reproduction and Perinatal Research in honor of 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.

Greenwald Lab, 1975-1977
Pictured from left to right: Gil Greenwald, PhD, Bertalan Varga, MD, PhD (visiting faculty research fellow from Budapest) and his wife, Jack Conner, PhD (postdoc), Paul Terranova, PhD (postdoc), Srinivas Saidapur, PhD (postdoc).

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Sponsors & Volunteers

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

Sponsors

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Pola Gorsky Greenwald
Dr. Richard Peppler
Beth Greenwald Jordan and Jerry L. Jordan
Dept of Molecular and Integrative Physiology
Bohan Visiting Professor Program
Institute for Reproduction and Perinatal Research (IRPR)
NIH R13 HD083029 (Katherine Roby, PI)

Volunteers

September Numata, BS, Graduate Student
Kristen Schwingen, BS, Graduate Student
Keisuke Kozai, PhD, Postdoctoral Fellow
Subhra Ghosh, MS, Research Assistant
Wendena Parkes, BS, Graduate Student
Ross McNally, PhD, Postdoctoral Fellow
V. Praveen Chakravarthi Rahhavulu, PhD, Postdoctoral Fellow
Regan Scott, MS, Graduate Student
Marija Kuna, PhD, Postdoctoral Fellow
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Rikki Nelson, BS, Graduate Student
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Stephen Fulbright, MS, Research Assistant
Ashley Cloud, BS, Graduate Student
Vinay Shukla, PhD, Postdoctoral Fellow
Ananya Ghosh, MS, Graduate Student
Bhaswati Bhattacharya, MS, Graduate Student
Kaela Varberg, PhD, Postdoctoral Fellow
Fatimah Aljubran, MS, Graduate Student
Xiaoyu Zhang, PhD, Postdoctoral Fellow
Kacey Grooms, BA, Research Assistant
Mae Winchester, MD, MFM Fellow
Mikaela Simon, MS, Graduate Student
Ayushi Vashisht, MS Graduate Student

Organizing Committee

COMMITTEE MEMBERS:

Katherine F. Roby, PhD (Chair)
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Associate Professor of Obstetrics and Gynecology

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Assistant Professor of Molecular and Integrative Physiology

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Research Assistant Professor of Pathology and Laboratory Medicine

Kaela Varberg, PhD
Postdoctoral Fellow, Pathology and Laboratory Medicine

Bhaswati Bhattacharya, MS
Graduate Student, Pathology and Laboratory Medicine

Fatimah Aljubran, MS
Graduate Student, Molecular and Integrative Physiology

EVENT SUPPORT STAFF:

Institute for Reproduction and Perinatal Research

Brandi Miller, BA, IRPR Administrative Assistant

Stacy Oxley, BA, IRPR Associate Director of Administration

Symposium History

Plenary Speakers

2004

Harry Weitlauf, MD
Texas Tech University
Osborn Address

James Cross, PhD
University of Calgary

B. Anne Croy, DVM, PhD
University of Guelph

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

Kevin Osteen, PhD
Vanderbilt University

Richard Stouffer, PhD
Oregon Health & Science University

Neena Schwartz, PhD
Northwestern University

2005

Shyamal K. Roy, PhD
University of Nebraska
Osborn Address

Sally Camper, PhD
University of Michigan

Thaddeus Golos, PhD
Wisconsin Regional Primate Center

Matthew Hardy, PhD
Population Council

Joy Pate, PhD
Ohio State University

John Robinson, PhD
Ohio State University

2006

Geula Gibori, PhD
University of Illinois at Chicago
Osborn Address

Robert Braun, PhD
University of Washington

Susan Fisher, PhD
University of California-San Fransisco

Fred Karsch, PhD
University of Michigan

John Schimenti, PhD
Cornell University

Teresa Woodruff, PhD
Northwestern University

2007

John J. Eppig, PhD
The Jackson Laboratory
Osborn Address

Indrani Bagchi, PhD
University of Illinois-Champaign

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

Patricia Hunt, PhD
Washington State University

Mark S. Roberson, PhD
Cornell University

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

Bruce D. Murphy, PhD
University of Montreal

2008

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

Jon Levine, PhD
Northwestern University
Evanston, IL

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

John Peluso, PhD
University of Connecticut
Farmington, CT

Miles Wilkinson, PhD
MD Anderson Cancer Center
Houston, Texas

Nasser Chegini, PhD
University of Florida
Gainesville, Fl

2009

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

Alberto Darszon PhD
National Autonomous University of Mexico

Louis DePaolo, PhD
Eunice Kennedy Shriver NICHD, NIH

Keith Latham, PhD
Temple University

Ajay Nangia, MD
University of Kansas Medical Center

2009 *(continued)*

Stephanie Seminara, MD
Massachusetts General Hospital, Harvard Medical School

Thomas Spencer, PhD
Texas A&M University

2010

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

Romana A. Nowak, PhD
University of Ilinois

Susan S. Suarez, MS, PhD
Cornell University

John Davis, PhD
University of Nebraska Medical Center

Sergio R. Ojeda, DVM
Oregon National Primate Research Center

Stephen A. Krawetz, PhD
Wayne State University

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

Symposium History

Plenary Speakers

2011

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

Blanche Capel, PhD, Duke University Medical Center

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

Asgi T. Fazleabas, PhD, Michigan State University

Yaacov Barak, PhD, University of Pittsburgh

Tony M. Plant, PhD, University of Pittsburgh

2012

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

Kyle Orwig, PhD, University of Pittsburgh

Bruce D. Murphy, PhD, University of Montreal

Francesco DeMayo, PhD, Baylor College of Medicine

Yoel Sadovsky, PhD, University of Pittsburgh

2013

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

Frederick vom Saal, PhD, University of Missouri-Columbia

Mary Hunzicker-Dunn, PhD, Washington State University

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

Derek Boerboom, DVM, PhD, University of Montreal

Shoukhrat Mitalipov, PhD, Oregon Health and Science University

2014

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

Marisa S. Bartolomei, PhD, University of Pennsylvania

Suzanne Moenter, PhD, University of Michigan

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

David Zarkower, PhD, University of Minnesota

2015

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

William Kinsey, PhD, University of Kansas Medical Center

Amy Ralston, PhD, MIchigan State

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

James A. MacLean, PhD, Southern Illinois University

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

Qinglei Li, PhD, Texas A&M University

2016

David A. Haig, PhD, Harvard University Keynote Lecturer

Alex Bortvin, MD, PhD, Carnegie Institution for Science

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

Sarah Kimmis, PhD, McGill University

Donald F. Conrad, PhD, Washington University

Deborah M. Sloboda, PhD, McMaster Univeristy

Kathleen M. Caron, PhD, University of North Carolina

2017

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

Hugh Clarke, PhD, McGill University

Diana Laird, PhD, University of California - San Francisco

Liang Ma, PhD, Washington University - St. Louis

James Pru, PhD, Washington State University

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

Mellissa Mann, PhD, Magee-Womens Research Institute

2018

Sandra T. Davidge, PhD, University of Alberta Keynote Lecturer

Paul S. Cooke, PhD, University of Florida

Rebecca A. Simmons, MD, University of Pennsylvania

Satoshi H. Namekawa, PhD, Cincinnati Children's Hospital Medical Center

Todd. S. Macfarlan, PhD, NICHD

Ramakrishna Kommagani, PhD, Washington University, St. Louis

Joan S. Jorgensen, DVM, PhD, University of Wisconsin

Program Schedule

THURSDAY, November 7 — **University of Kansas Medical Center, 3901 Rainbow Blvd., Kansas City, KS 66160**

3:00 p.m.	**Registration Opens**, 1006 Wahl West (Auditorium)
4:00 p.m.	Welcome from **Greenwald Symposium Trainee Elevator Pitch Organizer Kaela Varberg, PhD,** 1006 Wahl West (Auditorium)
4:00 - 4:50 p.m.	**Trainee Elevator Pitches**, 1006 Wahl West (Auditorium)
5:00 - 5:01 p.m.	Welcome from **Center for Reproductive Sciences Director Warren Nothnick, PhD, HCLD**
5:01 - 5:02 p.m.	Welcome/Opening Remarks from **School of Medicine Senior Associate Dean for Research and Graduate Education Peter Smith, PhD**
5:02 - 5:05 p.m.	Brief History of the Greenwald Symposium/Dr. Greenwald from **Paul F. Terranova, PhD, Emeritus Professor**
5:05 - 5:07 p.m.	Keynote Lecturer Introduction, **Soumen Paul, PhD, Professor**
5:07 - 6:12 p.m.	**Keynote Lecture: Serdar E. Bulun, MD, Northwestern University** ***"Stem Cells, Epigenetic Regulation, and Progesterone Action in Uterine Fibroids"***
6:30 - 8:30 p.m.	**Reception and Poster Session**, 5202 Health Education Building (HEB), Ad Astra Room - **Poster Session A: 7-7:45 p.m.; Session B: 7:45-8:30 p.m.**

FRIDAY, November 8 — **Kansas City Public Library - Central (Downtown), 14 West 10th St., Kansas City, MO 64108, Helzberg Auditorium, 5th Floor**

BRING IN YOUR PARKING TICKET

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

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

Session I

8:35 - 9:05 a.m. *(Q&A 9:00-9:05 a.m.)*	**Ov D. Slayden, PhD, Oregon Health and Science University** *(Ashley Cloud, BS, introducing)* *"Endometriosis in Nonhuman Primates"*
9:05 - 9:20 a.m. *(Q&A 9:17-9:20 a.m.)*	**Bhaswati Bhattacharya, MS, Graduate Student, University of Kansas Medical Center** *(Warren Nothnick, PhD, HCLD, introducing)* *"Atypical Protein Kinase C iota (PKCiota) is Essential for the Establishment of the Maternal-Fetal Exchange Interface during Mammalian Development"*
9:20 - 9:35 a.m. *(Q&A 9:32-9:35 a.m.)*	**Harriet Fitzgerald, PhD, Postdoctoral Fellow, University of Missouri** *(Ning Wang, PhD, introducing)* *"The Development of a Uterine Gland 3D Culture Model to Understand Pregnancy Establishment in Women"*
9:35 - 10:05 a.m. *(Q&A 10:00-10:05 a.m.)*	**Monica P. Colaiacovo, PhD, Harvard Medical School** *(Fatimah Aljubran, MS, introducing)* *"Germline Exposure to Our Chemical Landscape: Mechanistic Insights from C. Elegans"*

Program Schedule

10:05 - 10:25 a.m. **Morning Break**

Session II

10:25 - 10:55 a.m.
(Q&A 10:50-10:55 a.m.)
David Natale, PhD, Queen's University, Ontario, Canada
(Kaela Varberg, PhD, introducing)
"Let's Be Friends: Trophoblast Interactions Critical in Placental Development"

10:55 - 11:10 a.m.
(Q&A 11:07-11:10 a.m.)
Alison Ermisch, BS, Graduate Student, University of Nebraska-Lincoln
(Pratik Home, PhD, introducing)
"Oxidative Stress Alters the Expression Profile of Dppa3 in Oocytes and Decreases Di-Methylation of Histone H3K3 in the Pre-Implantation Embryo"

11:10 - 11:25 a.m.
(Q&A 11:22-11:25 a.m.)
Kaela Varberg, PhD, Postdoctoral Fellow, University of Kansas Medical Center *(Vargheese Chennathukuzhi, PhD, introducing)*
"ASCL2 Reciprocally Controls Key Trophoblast Lineage Decisions During Hemochorial Placenta Development"

11:25 - 11:55 a.m.
(Q&A 11:50-11:55 a.m.)
Kaylon L. Bruner-Tran, PhD, Vanderbilt University Medical Center
(Marija Kuna, PhD, introducing)
"Developmental Dioxin Exposure and the Paternal-Derived Risk to Preterm Birth"

11:55 a.m. - 12:40 p.m. **LUNCH** (Speakers and Trainees go through food line first; Trainee Speaker Interaction is from 11:55-12:40 p.m.)

12:40 - 1:20 p.m. **LUNCH Continued and Mingle Time**

1:20 - 1:30 p.m. **Trainee Awards Presentation**

Session III

1:30 - 2:00 p.m.
(*Q&A 1:55-2:00 p.m.)*
Thomas R. (Tod) Hansen, PhD, Colorado State University
(Ananya Ghosh, MS, introducing)
"Endocrine Action of Early Pregnancy in Ruminants"

2:00 - 2:15 p.m.
(Q&A 2:12-2:15 p.m.)
Elisabeth Bauerly, BS, Graduate Student, Stowers Institute for Medical Research *(Michael Wolfe, PhD, introducing)*
"Building a Tail: Dissecting the Role of Axonemal Proteins During Spermatogenesis"

2:15 - 2:30 p.m.
(Q&A 2:27-2:30 p.m.)
Ashley Cloud, BS, Graduate Student, University of Kansas Medical Center *(Lane Christenson, PhD, introducing)*
"Loss of REST in Uterine Leiomyoma Leads to an Altered Progesterone Response"

2:30 - 2:45 p.m.
(Q&A 2:42-2:45 p.m.)
Sangappa Chadchan, PhD, Postdoctoral Fellow, Washington University - St. Louis *(Lane Christenson, PhD, introducing)*
"GREB1 Acts as a Progesterone Receptor (PR) Co-Activator to Promote Uterine Receptivity for Embryo Implantation"

2:45 - 3:15 p.m.
(Q&A 3:10-3:15 p.m.)
Brian P. Hermann, PhD, University of Texas, San Antonio
(Xiaoyu Zhang, PhD, introducing)
"Exploring Spermatogonial Stem Cell Biology at the Single-Cell Resolution"

3:15 - 3:30 p.m. **Closing comments - meeting adjourned**

KUMC Campus Map

16th Annual Gilbert S. Greenwald Symposium on Reproduction and Perinatal Research

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

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

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

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

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

Event parking

Elevator

Event locations

Accessible parking spaces

Walking route to event locations

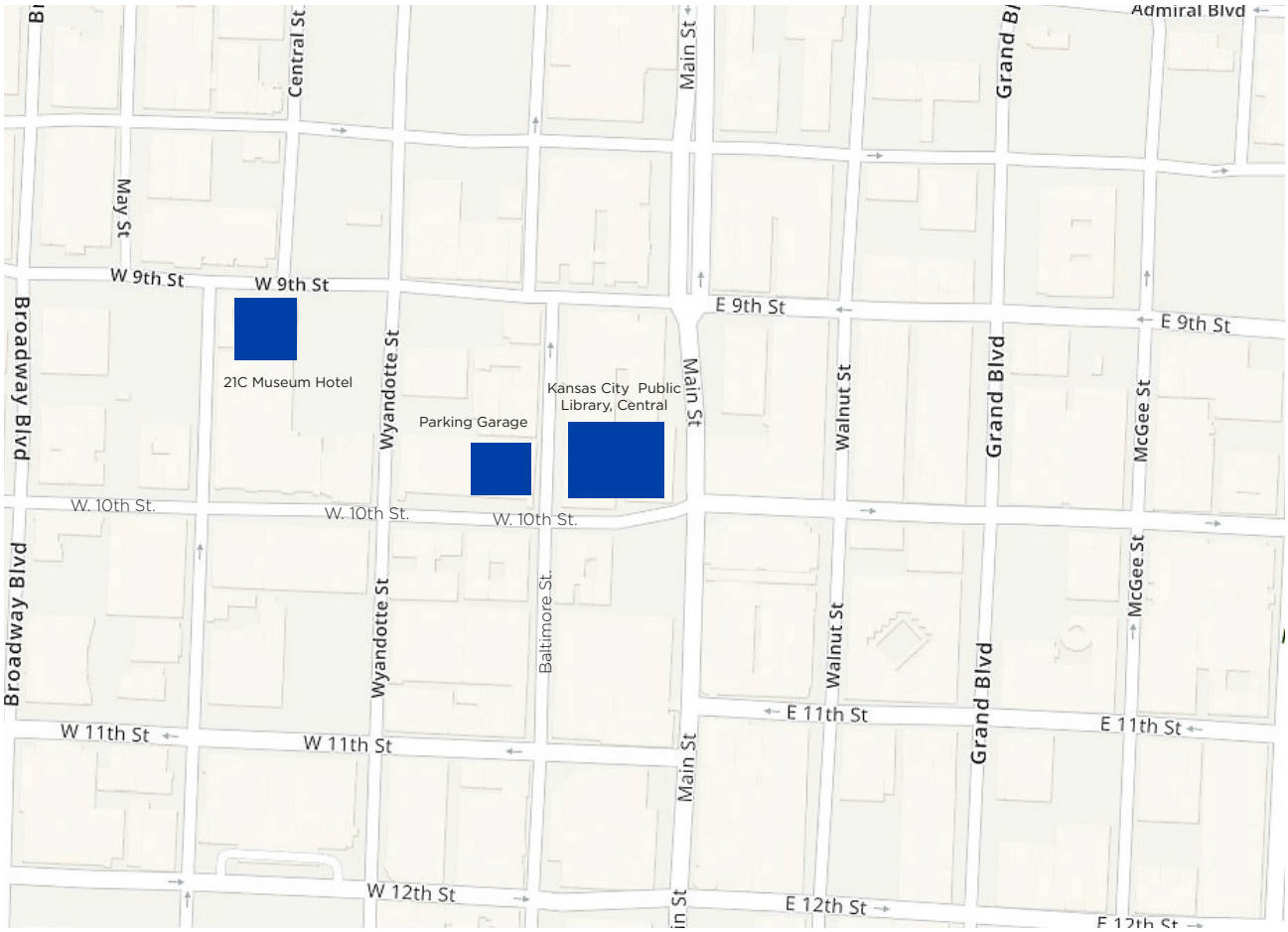
KU MEDICAL CENTER
The University of Kansas

Kansas City Map

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

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

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



Venue Information

The Kansas City Public Library - Central

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

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

Facts About the Library

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

Helzberg Auditorium

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

Gladys Feld Helzberg

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

Trainee Elevator Pitch Session

Science communication is a critically important skill that can help researchers effectively distill a message. The message is often the importance of the research being conducted and how it may benefit others/society. A polished elevator pitch can help facilitate new connections to build a professional network, spark a new professional collaboration, or even land a job interview. Trainees attending the Greenwald Symposium are encouraged to participate in the elevator pitch session by preparing a concise, clear explanation of their research project that can be easily understood by non-experts. Trainees include information about the big scientific question they or their lab is focused on answering and the potential impact of their work. An elevator pitch consists of a brief (2 minutes or less) project overview and can include one slide as a visual aid.

NEW THIS YEAR: PEOPLE'S CHOICE AWARD: Elevator Pitch Session attendees are asked to vote for their top 3 favorite pitches (ranked #1-3). Voting will take place through anonymous ballots turned in immediately following the session. The individual with the most votes will win a People's Choice Award prize to be presented at the awards ceremony on Friday.

Elevator Pitch Presenters *(in order of presentation)*

#	First Name	Last Name	Cred	Position Title	Institution / University
1	Marija	Kuna	PhD	Postdoctoral Fellow	University of Kansas Medical Center
2	Philma Glora	Muthuraj	MS	Graduate Research Assistant	University of Nebraska-Lincoln
3	Gwendalyn	Krekeler	BS	Research Technician I	Washington University, St. Louis
4	Asmaa	Alsousi	PhD	Post Doctoral Research Scholar	Children's Mercy
5	Xiaoman	Hong	MD	Senior Research Associate (STAFF)	University of Kansas Medical Center
6	Rowan	Karvas	BS	PhD Candidate	University of Missouri
7	Kerri	Bochantin	BS	Graduate Research Assistant	University of Nebraska-Lincoln
8	Ayesha	Hasan	MD	Maternal-Fetal Medicine Fellow	University of Kansas Medical Center
9	Amanda	Schmelzle	BA	Master's student	University of Missouri
10	Ananya	Ghosh	MS	Graduate student	University of Kansas Medical Center
11	Regan	Scott	MS	Graduate Student	University of Kansas Medical Center
12	Bailey	Bye	BS	Research Assistant (STAFF)	University of Kansas Medical Center
13	Madison	Kraus	BS	Undergraduate Student	University of Nebraska-Lincoln
14	Kaela	Varberg	PhD	Postdoctoral Fellow	University of Kansas Medical Center
15	Xiaoyu	Zhang	PhD	Postdoctoral Fellow	University of Kansas Medical Center
16	Bailey	McGuire	BS	Graduate Research Student	Iowa State University
17	Keisuke	Kozai	PhD	Postdoctoral fellow	University of Kansas Medical Center
18	Elisabeth	Bauerly	BS	PreDoctoral Researcher	Stowers Institute for Medical Research
19	Bhaswati	Bhattacharya	MS	Graduate Research Assistant	University of Kansas Medical Center
20	Wendena	Parkes	BS	Graduate Student	University of Kansas Medical Center
21	Jovana	Rajovic	BS	Graduate Student	University of Kansas Medical Center
22	Katie	Bidne	MS	Graduate Research Assistant	University of Nebraska - Lincoln
23	Pooja	Popli	PhD	Post-doctorate Research Associate	Washington University, St. Louis
24	Mae	Winchester	MD	Maternal-Fetal Medicine Fellow	University of Kansas Medical Center
25	Pauline	Xu	BS	Graduate Research Assistant	University of Nebraska Medical Center
26	Ashley	Cloud	BS	Graduate Student	University of Kansas Medical Center
27	Vinay	Shukla	PhD	Postdoctoral Fellow	University of Kansas Medical Center

Speaker Information

Keynote Lecturer

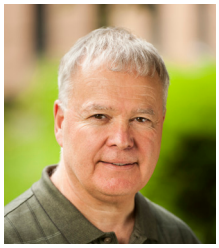
Serdar E. Bulun, MD

John J. Sciarra Professor
Department of Obstetrics and Gynecology
Feinberg School of Medicine
Northwestern University

"Stem Cells, Epigenetic Regulation, and Progesterone Action in Uterine Fibroids"

Dr. Serdar Bulun is the John J Sciarra Professor of Obstetrics and Gynecology, Chair of the Department of Obstetrics and Gynecology at Northwestern University and Obstetrician and Gynecologist-in-Chief at Prentice Women's Hospital at Northwestern Memorial Hospital. He was trained as an obstetrician-gynecologist at SUNY at Buffalo, subspecialized in reproductive endocrinology-infertility in UT Southwestern Medical Center at Dallas where he worked as an Assistant Professor for 7 years, and thereafter served as the Director of REI at University of Illinois at Chicago for 4 years. In 2003, Serdar moved to Northwestern University and NMH and, since then, has recruited numerous MD or PhD faculty, some of whom focus on steroid hormone-related pathology of endometriosis, uterine fibroids, and intrauterine growth retardation. His research team has introduced aromatase inhibitors as a new class of drugs to treat endometriosis and pelvic pain and been awarded over a total of 60 million dollars of research funding in the areas of uterine, breast and placental disorders. Bulun's exceptional achievements have earned many notable recognitions including his election to the National Academy of Medicine in 2015. He has been serving as the Chair of the Department of Obstetrics and Gynecology at Northwestern University since 2012. Subsequently, the clinical, training and research programs of the Department have been substantially expanded and are widely acknowledged.

Session I



Ov D. Slayden, PhD

Associate Professor
Devision of Reproductive and Developmental Sciences
Oregon Health and Science University

"Endometriosis in Nonhuman Primates"

Dr. Slayden received his Ph.D. in Biochemistry and Animal Science at Oregon State University. He moved to the Oregon Primate Center in 1991 after being awarded a Reproductive Biology Training Fellowship through the Department of Physiology at OHSU. His laboratory conducts research relating to contraception and reproductive tract disorders including irregular menstrual bleeding, menorrhagia, endometriosis, and polycystic ovarian syndrome (PCOS). His lab utilizes nonhuman primates (NHPs; macaques and baboons) as research models to bridge the gap between bench research and clinical trials in women. His broad premise is that a better understanding of reproductive tract disorders in NHPs can be leveraged to develop new therapies and improve women's reproductive health. In recent studies he has developed a model for inducing endometriosis in disease-free rhesus macaques and is conducting studies on new technologies to image and ablate endometriotic lesions during gynecologic surgery. His laboratory manages the NHP Core for a National Center for Translational Research in Reproduction and Infertility (NCTRI) Center (P50 HD071836).

Monica P. Colaiacovo, PhD

Professor
Department of Genetics
Harvard Medical School

"Germline Exposure to Our Chemical Landscape: Mechanistic Insights from C. Elegans"

Dr. Monica Colaiacovo received her PhD in Molecular and Cell Biology from Brandeis University in Waltham, MA. She did her postdoctoral work in the laboratory of Dr. Anne M. Villeneuve at Stanford University. Dr. Colaiacovo joined the Department of Genetics at Harvard Medical School in late 2003, where she is currently Professor of Genetics. Dr. Colaiacovo's laboratory investigates how different environmental exposures and perturbations to normal gene functions can affect the mechanisms underlying accurate meiotic chromosome segregation, using the nematode Caenorhabditis elegans as a model system. These studies are of vital importance for understanding the causes of miscarriages, stillbirths, birth defects such as Down syndrome, and tumorigenesis in humans. Their studies have led to fundamental new scientific discoveries at the forefront of the meiosis and germline maintenance fields, and the development of innovative new strategies for using C. elegans in scientific research. Dr. Colaiacovo is a member of the Molecular Genetics A (MGA) Study Section, NIGMS/NIH, and is an Associate Editor of PLoS Genetics.

Session II

David Natale, PhD
Associate Professor
Department of Obstetrics and Biomedical and Molecular Sciences
Queen's University, Canada

"Let's Be Friends: Trophoblast Interactions Critical in Placental Development"

Dr. David R. C. Natale received his BSc (Hons) in Genetics and PhD in Physiology and Developmental Biology from the University of Western Ontario in London, Canada studying trophectoderm and blastocyst development. He then went to the University of Calgary for a postdoctoral fellowship in the laboratory of Dr. Jay Cross and studied mouse placental development and trophoblast biology. He has recently moved from the University of California San Diego to take up a position as Associate Professor in Obstetrics & Gynaecology at Queen's University in Kingston, Canada. His research program focuses on understanding the role of trophoblast stem and progenitor cells in the development of placental pathologies and in the adaptive potential of the placenta to stress during pregnancy.

Kaylon L. Bruner-Tran, PhD
Professor
Department of Obstetrics and Gynecology
Vanderbilt University Medical Center

"Developmental Dioxin Exposure and the Paternal-Derived Risk to Preterm Birth"

Kaylon L. Bruner-Tran, PhD, Professor of Obstetrics and Gynecology at Vanderbilt University Medical Center in Nashville, TN (USA). She received her PhD in reproductive pathology from Vanderbilt University in 1995. For her post-doctoral training, Dr. Bruner-Tran completed a dual-track program at Thomas Jefferson Medical College in Philadelphia which included basic science in molecular endocrinology in the laboratory of Gerald Litwack, PhD and specialized training in gynecologic histopathology with Fred Gorstein, MD. Following these studies, she returned to Vanderbilt where she established a strong collaborative research program with Dr. Kevin Osteen. As Co-Director the Women's Reproductive Health Research Center at Vanderbilt, she directs the Disease Modeling Core Facility, which is utilized by numerous NIH-sponsored investigators as well as for Industry-sponsored research. Working with Dr. Osteen, she has developed experimental mouse models of endometriosis as well as a model of in utero toxicant exposure which mimics the human endometriosis phenotype. Her laboratory is focused on the impact of early life toxicant exposures on maintenance of pregnancy, with a particular emphasis on paternal exposures associated with preterm birth and adverse fetal outcomes. A major goal of her laboratory is to examine the effectiveness of nutritional modification to reduce the incidence of reproductive failure following early life toxicant exposure.

Session III

Thomas R. (Tod) Hansen, PhD
Traubert Professor
Department of Biomedical Sciences
Director, Animal Reproduction and Biotechnology Laboratory
Colorado State University

"Endocrine Action of Early Pregnancy in Ruminants"

Dr. Thomas R. (Tod) Hansen is the Mabel I. and Henry H. Traubert Professor of Animal Genetics and Director of the Animal Reproduction and Biotechnology Laboratory, which includes the Equine Reproduction Laboratory as a Program of Research and Scholarly Excellence at Colorado State University (CSU). He also serves as Director of the CSU Biomedical Sciences Foothills Campus. He earned the BS degree in Animal Sciences at CSU and the MS and PhD degrees in Reproductive Physiology at Texas A&M University. After completing post-doctoral studies in Molecular Biology at the University of Missouri, he served as Professor at the University of Wyoming and then was recruited to CSU in the Department of Biomedical Sciences. His research focuses on: 1) embryo-maternal signaling with intent to reduce early embryo mortality (i.e., miscarriage); 2) implantation of the embryo and development of the placenta to better understand and manage intrauterine growth restriction of the fetus; and 3) maternal infection with virus during pregnancy to discover how maternal viral infections impair development of the fetal immune system and post-natal immune responses to secondary infections. His research has been funded by the NIH-NICHD, NIH-INBRE, USDA-NIFA, American Cancer Society and biotechnology/biopharma companies. He teaches Human and Animal Reproduction to undergraduate and graduate Biomedical Sciences students.

Brian P. Hermann, PhD
Associate Professor
Departmnet of Biology
Director, Genomics Core
University of Texas, San Antonio

"Exploring Spermatogonial Stem Cell Biology at the Single-Cell Resolution"

Dr. Hermann received his PhD in 2005 from the University of Kansas Medical Center under the supervision of Leslie Heckert where he studied transcriptional regulation of the FSH-receptor and Steroidogenic factor-1 genes. He then completed postdoctoral training in lab of Dr. Kyle Orwig at the Magee-Womens Research Institute, University of Pittsburgh where he performed the first definitive spermatogonial stem cell (SSC) transplantation in non-human primates. With support from an NIH K99/R00 award, Dr. Hermann started his lab at the University of Texas at San Antonio (UTSA) in 2011. The Hermann lab studies the mechanisms regulating SSC fate, SSCs fate specification during testis development, and potential SSC-based therapeutic strategies for male infertility. Dr. Hermann also directs the UTSA Genomics Core, which specializes in single-cell methodologies, and has applied those approaches to understanding the identity of SSCs and their regulatory framework.

Abstract Titles

1. Dioxin Induced Adaptations at the Maternal-Fetal Interface

Khursheed Iqbal[1,2], Pramod Dhakal[1,2], Katherine F. Roby[1,3], Stephen H. Pierce[1], Regan Scott[1,2], Carrie A. Vyhlidal[1,4,5], and Michael J. Soares[1,2,5,6] [1]Institute for Reproduction and Perinatal Research, [2]Department of Pathology and Laboratory Medicine, [3]Anatomy and Cell Biology, University of Kansas Medical Center, KS; [4]Division of Clinical Pharmacology and [5]Center for Perinatal Research, Children's Research Institute, Children's Mercy, Kansas City, MO; [6]Departments of Pediatrics and Obstetrics and Gynecology, University of Kansas Medical Center, Kansas City, KS

2. Uterine Gland Influence on Development of the Placenta and Fetus

Pramod Dhakal[1], Susanta Behura[1], Harriet Fitzgerald[1], Andrew Kelleher[1] and Thomas E. Spencer[1,2] [1]Division of Animal Sciences, University of Missouri, Columbia, MO [2]Department of Obstetrics, Gynecology and Women's Health, University of Missouri, Columbia, MO

3. Role of IGF2 in Regulating Rat Hemochorial Placental Development

Ayesha Hasan[1,3], Khursheed Iqbal[1,2], Regan L. Scott[1,2], Stephen H. Pierce[1,2], Masanaga Muto[1,2], Keisuke Kozai[1,2], Michael J. Soares[1,2,3,4,5] [1]Institute for Reproduction and Perinatal Research, Departments of [2]Pathology and Laboratory Medicine, [3]Obstetrics and Gynecology, and [4]Pediatrics, University of Kansas Medical Center, Kansas City, Kansas; [5]Center for Perinatal Research, Children's Research Institute, Children's Mercy, Kansas City, MO

4. Luteinizing Hormone Enhances Glucose Metabolism by Small Luteal Cells Leading to *de novo* Lipogenesis

Emilia Przygrodzka[1], Fatema Binderwala[2], Pan Zhang[1], Hou Xiaoying[1], Robert Powers[2], John S. Davis[1,3]. [1]Olson Center for Women's Health, Department of Obstetrics and Gynecology, University of Nebraska Medical Center; [2]Department of Chemistry, University of Nebraska-Lincoln, 722 Hamilton Hall, Lincoln, NE 68588-0304 and [3]VA Medical Center, Omaha, NE; [3]VA Medical Center, Omaha, NE

5. Genetic Sex Determination from RNA Using Rbm31 Gametologs

Cecil Terrell and Laura Schulz. Department of Obstetrics, Gynecology, and Women's Health, University of Missouri-Columbia, Columbia, MO.

6. A Gatekeeping Role of ESR2 in Primordial Follicle Preservation

V. Praveen Chakravarthi[1], Subhra Ghosh[1], Katherine F. Roby[2], and M. A. Karim Rumi[1]. Department of Pathology and Laboratory Medicine, Department of Anatomy and Cell Biology, Institute for Reproduction and Perinatal Research, University of Kansas Medical Center, Kansas City, Kansas

7. Pig Conceptus Expression of Type I Interferon Delta and Type II Interferon Gamma During Early Pregnancy

D.N. Johns, C.G. Lucas, C.A. Pfeiffer, L.D. Spate, J.A. Benne, R.F. Cecil, K.M. Wells, T.E. Spencer, R.S. Prather, and R.D. Geisert. Division of Animal Sciences, University of Missouri, Columbia, MO USA

8. Genetic Variants Identified in Cows with an Excess Androgen Ovarian Microenvironment Provides Clues to Women with Polycystic Ovary Disease

Alexandria P. Snider[1], Sarah Nafziger[1], Jeff Bergman[1], Scott G. Kurz[1], John S. Davis[2], Jennifer R. Wood[1], Jessica L. Petersen[1], Andrea S. Cupp[1] [1]Department of Animal Science, University of Nebraska–Lincoln; [2]Obstetrics and Gynecology, University of Nebraska Medical Center

9. Autophagy Protein Beclin 1 is Critical for Mouse Embryo Implantation and Decidualization
Pooja Popli[1&2], Sangappa B. Chadchan[1&2], Rucker EB 3[rd3] and Ramakrishna Kommagani[1&2] [1]Department Obstetrics and Gynecology, [2]Center for Reproductive Health Sciences, Washington University School of Medicine, St. Louis, MO, 63110, USA. [3]Department of Biology, University of Kentucky, Lexington, KY 40506.

10. Trophoblast Paracrine Signaling Regulates Placental Hematoendothelial Niche
Pratik Home[1, 2], Ananya Ghosh[1], Avishek Ganguly[1], Bhaswati Bhattacharya[1], Soma Ray[1], Soumen Paul[1, 2] [1] Department of Pathology and Laboratory Medicine, [2] Institute for Reproduction and Perinatal Research, University of Kansas Medical Center, Kansas City, KS USA.

11. Specialized Pro-Resolving Lipid Mediator, RvD2 Induces GPR18 Membrane Localization and Differentially Regulates Inflammatory Cytokines in Placental Trophoblasts
Prakash Kumar Sahoo, Sathish Kumar Natarajan. Nutrition and Health Sciences, University of Nebraska-Lincoln, NE

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

13. CITED2 Regulation of Embryonic and Placental Development: Species Differences
Marija Kuna[1, 2], Pramod Dhakal[1, 2], Lindsey N. Kent[1, 2], Regan L. Scott[1, 2], Khursheed Iqbal[1, 2] and Michael J. Soares[1, 2, 3, 4, 5] [1]Institute for Reproduction and Perinatal Research, Departments of [2]Pathology and Laboratory Medicine, [3]Obstetrics and Gynecology, and [4]Pediatrics, University of Kansas Medical Center, Kansas City, Kansas; [5]Center for Perinatal Research, Children's Research Institute, Children's Mercy, Kansas City, MO

14. Effects of Bovine Pregnancy-Associated Glycoproteins on Gene Transcription in Bovine Endometrial Explants
Amanda L. Schmelzle, Ky G. Pohler, Michael F. Smith, Jonathan A. Green, Division of Animal Sciences, University of Missouri; Columbia, MO

15. Na, K-ATPase α4 Inhibitors as Agents for Male Contraception
[1]**Lacey Greve**, [2]Courtney Marsh, [1]Gladis Sanchez, [3]Ajay Nangia, [4]Shameem Sultana, [4]Gunda Georg and [1]Gustavo Blanco. [1]Department of Molecular and Integrative Physiology, The University of Kansas Medical Center, Kansas City KS; [2]Department of Obstetrics and Gynecology, The University of Kansas Medical Center, Kansas City KS; [3]Department of Urology, The University of Kansas Medical Center, Kansas City KS; and [4]Department of Medicinal Chemistry, University of Minnesota, Minneapolis, MN

16. Inhibiting an Inhibitor: Effects of Myostatin Deficiency During Pregnancy on the Placenta
Alyssa Tipler[1], Jenna DeCata[2], and Laura C. Schulz[2] [1]Truman State University, Kirksville MO [2]University of Missouri, Columbia, MO

17. TRAINEE ORAL PRESENTATION ONLY (NO POSTER)
GREB1 Acts as a Progesterone Receptor (PR) Co-Activator to Promote Uterine Receptivity for Embryo Implantation
Sangappa B. Chadchan[1&2], Pooja Popli[1&2], Marina Rowan[1&2], Eryk Andreas[1&2], Charles D. Foulds[3], Denise Lanza[3], Jason D. Heaney[3], John P. Lydon[3], Kelle H. Moley[1&2], Emily S. Jungheim[1&2], Bert W. O'Malley[3], and Ramakrishna Kommagani[1&2] [1]Department of Obstetrics and Gynecology, [2]Center for Reproductive Health Sciences, Washington University, School of Medicine, St. Louis, MO, 63110, USA. [3]Department of Molecular and Cellular Biology, Baylor College of Medicine, Houston, TX, 77030, USA.

18. TRAINEE ORAL PRESENTATION AND POSTER

ASCL2 Reciprocally Controls Key Trophoblast Lineage Decisions During Hemochorial Placenta Development

Kaela M. Varberg[1,2], Regan L. Scott[1,2], Masanaga Muto[1,2], Khursheed Iqbal[1,2], Keisuke Kozai[1,2], Elin Grundberg[3], Michael J. Soares[1,2,4,5,6]. [1]Institute for Reproduction and Perinatal Research, University of Kansas Medical Center, Kansas City, KS [2]Department of Pathology and Laboratory Medicine, University of Kansas Medical Center, Kansas City, KS [3]Center for Pediatric Genomic Medicine, Children's Mercy, Kansas City, MO [4]Department of Pediatrics, University of Kansas Medical Center, Kansas City, KS [5]Department of Obstetrics and Gynecology, University of Kansas Medical Center, Kansas City, KS [6]Center for Perinatal Research, Children's Research Institute, Children's Mercy, Kansas City, MO

19. TRAINEE ORAL PRESENTATION ONLY (NO POSTER)

The Development of a Uterine Gland 3D Culture Model to Understand Pregnancy Establishment in Women

Harriet C. Fitzgerald, Pramod Dhakal, Susanta K. Behura, Daniel J. Schust, Thomas E. Spencer. Division of Animal Sciences, University of Missouri, Columbia, MO; Department of Obstetrics, Gynecology and Women's Health, University of Missouri, Columbia, MO

20. Low Dose of Cisplatin Induces Oocyte Death in Primordial Follicles of Mouse Ovary

Maya M. Eldani, Pauline C. Xu, Wend K.R. Ouedraogo, So-Youn Kim. Olson Center for Women's Health, Department of Obstetrics and Gynecology, College of Medicine, University of Nebraska Medical Center, Omaha, NE

21. Determining Impacts of Heat Stress on the Luteal JAK-STAT Pathway in Gilts

Crystal M. Roach, Katie L. Bidne, Matthew R. Romoser, Jason W. Ross, Lance H. Baumgard, Aileen F. Keating . Department of Animal Science, Iowa State University

22. Labyrinth Trophoblast Specific Role of GATA2 AND GATA3 in Mouse Placental Development

Ananya Ghosh, Pratik Home and Soumen Paul. Department of Pathology and Laboratory Medicine, Institute for Reproduction and Perinatal Research (IRPR), University of Kansas Medical Center, USA

23. Western Diet Consumption Alters Lipid Profiles in Dam Circulation, Placenta, and Fetus

[1]**KL Bidne**, [2]AL Rister, [1]AR McCain, [2]ED Dodds, and [1]JR Wood. Department of Animal Science, University of Nebraska – Lincoln, Lincoln, Nebraska, USA [2]Department of Chemistry, University of Nebraska – Lincoln, Lincoln, Nebraska, USA

24. TRAINEE ORAL PRESENTATION ONLY (NO POSTER)

Building a Tail: Dissecting the Role of Axonemal Proteins During Spermatogenesis

Elisabeth Bauerly[1] and Matthew C. Gibson[1,2,*] [1] Stowers Institute for Medical Research, Kansas City, MO 64110, USA. [2] Department of Anatomy and Cell Biology, The University of Kansas School of Medicine, Kansas City, KS 66160, USA.

25. A-to-I RNA Modifications are Enriched in Oocyte Ribosome Associated RNA

Pavla Brachova[1*], Nehemiah S. Alvarez[1,2*], Lane K. Christenson[1.] [1] Department of Molecular and Integrative Physiology, University of Kansas Medical Center, Kansas City, KS 66160, [2] De Novo Genomics, Kansas City, KS, [*] These authors contributed equally to this work

26. A Role for Malignant Brain Tumor Domain-containing protein 1 in Human Endometrial Stromal Cell Decidualization

Sangappa B. Chadchan[1,2], **G. L. Krekeler**[1,2], E.S. Jungheim[1,2], and Ramakrishna Kommagani[1,2]
[1]Department of Obstetrics and Gynecology [2]Center for Reproductive Health Sciences
Washington University School of Medicine St Louis, MO, 63110, USA

27. Characterization and Regulation of Extracellular Vesicles in the Lumen of the Ovine Uterus
Eleanore V. O'Neil, Gregory W. Burns, and Thomas E. Spencer. Division of Animal Sciences, University of Missouri-Columbia

28. PLAC1 Regulation of Hemochorial Placenta Development
Jovana Rajovic[1,2], Khursheed Iqbal[1], Jackson Nteeba[1], Regan L. Scott[1], Marija Kuna[1], Andjelka Celic[2], Masanaga Muto[1], Keisuke Kozai[1], Michael J. Soares[1,3,4] [1]Institute for Reproduction and Perinatal Research, Department of Pathology and Laboratory Medicine, University of Kansas Medical Center, Kansas City, KS; [2]Reproductive Biology Program, University of Novi Sad, Novi Sad, Serbia, [3]Departments of Obstetrics and Gynecology, and Pediatrics, University of Kansas Medical Center, Kansas City, KS; [4]Center for Perinatal Research, Children's Research Institute, Children's Mercy, Kansas City, MO

29. Pancreatic Ductal Adenocarcinoma Highly Expresses Inhibin βA Subunit
Pauline C. Xu, Maya Eldani, So-Youn Kim. Olson Center for Women's Health, Department of Obstetrics and Gynecology, College of Medicine, University of Nebraska Medical Center, Omaha, NE

30. Aryl Hydocarbon Receptor Signaling in Trophoblast Development
Vinay Shukla[1], Khursheed Iqbal[1], Kacey A. Grooms[1], Carrie A. Vyhlidal[2,3], and Michael J. Soares[1,3,4] [1]Institute for Reproduction and Perinatal Research and Department of Pathology and Laboratory Medicine, University of Kansas Medical Center, Kansas City, KS; [2]Division of Clinical Pharmacology and [3]Center for Perinatal Research, Children's Mercy, Kansas City, MO; [4]Departments of Pediatrics and Obstetrics and Gynecology, University of Kansas Medical Center, Kansas City, KS

31. Entinostat Induces PARPi Sensitivity Across Three Different Ovarian Cancer Models via Alteration of Homologous Recombination Pathway
Vijayalaxmi Gupta[1], Shariska Petersen[1], Jeff Hirst[1], Katherine Roby[2],Harsh Pathak[4,5], Meghan Kusch[1] Andrew Wilson[3], Andrew Godwin[4,5], Dineo Khabele[1,5] [1]Division of Gynecologic Oncology, Department of Obstetrics & Gynecology, The University of Kansas Medical Center, Kansas City, KS; [2]Department of Anatomy and Cell biology, The University of Kansas Medical Center, Kansas City, KS, [3]Department of Obstetrics and Gynecology, Vanderbilt University Medical Center, Nashville, Tennessee, [4]Department of Pathology, The University of Kansas Medical Center, Kansas City, KS, [5]The University of Kansas Cancer Center, Kansas City, KS.

32. Impact of High Fat Diet-Induced Obesity on Ovarian DNA Damage Repair Proteins in Rats
Bailey C. McGuire[1], M. Estefanía González Alvarez[1], Karl Kerns[2], Peter Sutovsky[2,3], Aileen F. Keating[1] [1]Department of Animal Science, Iowa State University [2]Division of Animal Sciences, University of Missouri [3]Department of Obstetrics, Gynecology and Women's Health, University of Missouri

33. Ovarian Influences on Postnatal Mouse Uterine Development
Jessica Milano-Foster, Pramod Dhakal, Thomas E. Spencer. Division of Animal Science and Department of Obstetrics, Gynecology and Women's Health, University of Missouri-Columbia

34. AKT1 Regulates Fetal and Placental Development and Postnatal Growth
Keisuke Kozai[1,2], Mae-Lan Winchester[1,3], Khursheed Iqbal[1,2], Masanaga Muto[1,2], and Michael J. Soares[1,2,3,4,5] [1]Institute for Reproduction and Perinatal Research, Departments of [2]Pathology and Laboratory Medicine, [3]Obstetrics and Gynecology, and [4]Pediatrics, University of Kansas Medical Center, Kansas City, KS; [5]Center for Perinatal Research, Children's Research Institute, Children's Mercy, Kansas City, MO.

35. TRAINEE ORAL PRESENTATION AND POSTER
Oxidative Stress Alters the Expression Profile of *Dppa3* in Oocytes and Decreases Di-Methylation of Histone H3K9 in the Pre-Implantation Embryo
Alison F. Ermisch, Kelsey R. Timme, Jennifer R. Wood. Department of Animal Science, University of Nebraska-Lincoln, Lincoln, NE

36. Codon Identity in Human Oocytes Reveals Age-Associated Defects in mRNA Decay
Nehemiah S. Alvarez[1,2], Pavla Brachova[1], Lane K. Christenson[1.] [1] Department of Molecular and Integrative Physiology, University of Kansas Medical Center, Kansas City, KS 66160, [2] De Novo Genomics, Kansas City, KS

37. University of Na, K-ATPase α4 Controls Glucose Uptake in Sperm via the Sodium Glucose Transporter
September Numata and Gustavo Blanco. Department of Molecular and Integrative Physiology, The University of Kansas Medical Center, Kansas City KS.

38. Pluripotent Stem Cell Models in the KUMC Transgenic Facility
Julia Draper, Katelin Gibson, Illya Bronshteyn, Jay L. Vivian, and Melissa Larson. Transgenic and Gene Targeting Institutional Facility, University of Kansas Medical Center, Kansas City, KS.

39. TRAINEE ORAL PRESENTATION ONLY (NO POSTER)
Loss of REST in Uterine Leiomyoma leads to an Altered Progesterone Response
Ashley Cloud, Michelle McWilliams, Faezeh Koohestani, Sornakala Ganeshkumar, Sumedha Gunewardena, Vargheese Chennathukuzhi. Department of Molecular and Integrative Physiology, University of Kansas Medical Center, Kansas City, KS.

40. Zika Virus Infection Induces Endoplasmic Reticulum Stress and Apoptosis in Placental Trophoblasts
Philma Glora Muthuraj, Aryamav Pattnaik, Prakash Kumar Sahoo, Asit Pattnaik and Sathish Kumar Natarajan. Department of Nutrition and Health Sciences, University of Nebraska-Lincoln, NE

41. Women's Attitudes Toward Vaccination During Preconception Care
Elise Foley and Courtney Marsh. Advanced Reproductive Care, Department of Reproductive Endocrinology and Infertility, University of Kansas Medical Center, Kansas City, KS.

42. Early Reduced Growth Rates Predict Delayed or Altered Puberty and May Adversely Affect Reproductive Longevity in Beef Heifers
Jessica Keane[1], Sarah Nafziger[1], Mohamed A. Abedal-Majed[1], Sarah Tenley[1], Mariah Hart[1], Jeff Bergman[1], Scott Kurz[1], Jennifer Wood[1], Adam Summers[2], and Andrea S. Cupp[1] Department of Animal Science, University of Nebraska-Lincoln, Lincoln, Nebraska2 Department of Animal Science, New Mexico State University, Las Cruces, New Mexico

43. TRAINEE ORAL PRESENTATION ONLY (NO POSTER)
Atypical Protein Kinase C iota (PKCiota) is Essential for the Establishment of the Maternal-Fetal Exchange Interface during Mammalian Development
Bhaswati Bhattacharya and Soumen Paul. Department of Pathology and Laboratory Medicine, Institute for Reproduction and Perinatal Research, University of Kansas Medical Center, Kansas City, KS.

44. The Function of ACTC1 in an in vitro Model of Human Placentation
Rowan M. Karvas[1], Juliann Leak[1], Toshihiko Ezashi[2], Danny Schust[3], R. Michael Roberts[2,4], and Laura C. Schulz[3.] 1- University of Missouri, Biological Sciences; 2- University of Missouri, Animal Sciences; 3- University of Missouri, Obstetrics, Gynecology, and Women's Health; 4-University of Missouri, Biochemistry

45. Single Cell Interrogation of the Maternal-Placental Interface
Regan L. Scott[1,2], Khursheed Iqbal[1,2], and Michael J. Soares[1,2,3,4,5] [1]Institute for Reproduction and Perinatal Research, Departments of [2]Pathology and Laboratory Medicine, [3]Obstetrics and Gynecology, and [4]Pediatrics, University of Kansas Medical Center, Kansas City, Kansas; [5]Center for Perinatal Research, Children's Research Institute, Children's Mercy, Kansas City, MO

46. Impact of High Fat Diet-Induced Obesity on Ovarian Chemical Metabolism Proteins in Rats
M. Estefanía González Alvarez[1], Bailey McGuire[1], Karl Kerns[2], Peter Sutovsky[2,3], Aileen F. Keating[1.]
[1]Department of Animal Science, Iowa State University [2]Division of Animal Sciences, University of Missouri
[3]Department of Obstetrics, Gynecology and Women's Health, University of Missouri

47. Increased Circulation of Pro-Inflammatory Cytokines Alters Steroidogenesis in Ovarian Somatic Cells in Beef Cows
KA Bochantin, AP Snider, SA Springman, SG Kurz, JA Keane, S Nafzinger, JW Bergman, RM McFee, AS Cupp, JR Wood. Department of Animal Science, University of Nebraska-Lincoln

48. Na,K-ATPase α4 Undergoes Phosphorylation During Sperm Capacitation
Kristen M. Schwingen and Gustavo Blanco. Department of Molecular and Integrative Physiology, The University of Kansas Medical Center, Kansas City, KS.

49. Development of Novel Mouse Models Using CRISPR Genome Editing Approaches
Melissa A. Larson, Katelin Gibson, Illya Bronshteyn, Julia Draper, and Jay L. Vivian. Transgenic and Gene-Targeting Institutional Facility, University of Kansas Medical Center, Kansas City, KS.

50. Effects of GnRH-II on Spermatogenic Function of Swine
Megan A. Ebrecht[1], Caitlin E. Ross[2], Rebecca A. Cederberg[2], Kyle W. Lovercamp[1], Amy T. Desaulniers[1] and Brett R. White[2.] [1]University of Central Missouri, Warrensburg, MO [2]University of Nebraska-Lincoln, Lincoln, NE

51. Cigarette Smoke Exposure Activated Aryl Hydrocarbon Receptor Signaling in Human Trophoblasts and Altered Markers of Growth and Differentiation
Asmaa Alsousi[1], Rebecca Biswell[1], Jeffrey Johnston[1], Elin Grundburg[1], Michael J. Soares[2], and Carrie A. Vyhlidal[1]. Children's Mercy Hospital, Kansas City, MO [1] and University of Kansas Medical Center, Kansas City, Kansas [2].

52. A Subcompartment Analysis of Oxidative Stress in Ovarian Reproductive Aging
Wendena S. Parkes1, September Numata1, Farners Amargant2, Francesca E. Duncan2, Michele T. Pritchard1 1Department of Pharmacology, Toxicology and Therapeutics, University of Kansas Medical Center, Kansas City, KS, 2Department of Obstetrics and Gynecology, Feinberg School of Medicine, Northwestern University, Chicago IL

Full Abstracts

1. Dioxin Induced Adaptations at the Maternal-Fetal Interface

Khursheed Iqbal[1,2], Pramod Dhakal[1,2], Katherine F. Roby[1,3], Stephen H. Pierce[1], Regan Scott[1,2], Carrie A. Vyhlidal[1,4,5], and Michael J. Soares[1,2,5,6] [1]Institute for Reproduction and Perinatal Research, [2]Department of Pathology and Laboratory Medicine, [3]Anatomy and Cell Biology, University of Kansas Medical Center, KS; [4]Division of Clinical Pharmacology and [5]Center for Perinatal Research, Children's Research Institute, Children's Mercy, Kansas City, MO; [6]Departments of Pediatrics and Obstetrics and Gynecology, University of Kansas Medical Center, Kansas City, KS

The actions of dioxins, such as 2,3,7,8-tetrachlorodibenzodioxin (TCDD), are mediated by the aryl hydrocarbon receptor (AHR), a ligand-dependent transcription factor. Dioxin-AHR interaction results in the transcriptional activation of target genes such as *Cyp1a1*. TCDD has been reported to affect pregnancy and possibly development of the hemochorial placenta. The purpose of this study was to investigate TCDD actions on pregnancy and placentation using the rat as a model. High TCDD exposures resulted in pregnancy failure; however, lower TCDD exposures resulted in prominent adaptations at the maternal-fetal interface. Gestation day (gd) 13.5 placentation sites from TCDD-treated pregnant rats exhibited deep intrauterine endovascular trophoblast invasion and uterine spiral artery remodeling, which was not observed in oil treated controls. Immunostaining for CYP1A1 in gd 13.5 placentation sites revealed specific activation of AHR signaling in endothelial cells lining small diameter blood vessels at the uterine-placental boundary (metrial gland) and in endothelial cells within the extraembryonic mesenchymal cores of the labyrinth zone but not in the junctional zone of the placenta. Single cell RNA-Seq analysis of the metrial gland of pregnant rats revealed a high level of expression of *Ahr* in endothelial cells; however, minimal expression in intrauterine invasive trophoblast cells. The importance of AHR and CYP1A1 in the placentation site adaptive responses to TCDD were investigated in *Ahr* and *Cyp1a1* null rat models. We found that TCDD-induced intrauterine trophoblast invasion and uterine spiral artery remodeling was AHR-dependent but not affected by CYP1A1. We next evaluated the importance of AHR signaling in maternal versus embryonic/extraembryonic tissues following TCDD treatment. The presence of AHR in maternal tissues was essential for TCDD-induced adaptations at the placentation site. Placentation site adaptations were not affected by embryonic/extraembryonic AHR expression. RNA-Seq, RT-qPCR, and immunostaining of the metrial gland revealed that TCDD dysregulated uterine natural killer (NK) cell specific transcript expression without affecting overall NK cell numbers, indicating that TCDD treatment affected the uterine NK cell phenotype. Uterine NK cells have a prominent restraining effect on intrauterine trophoblast invasion, which may be modified by TCDD. In summary, exposure to dioxin during pregnancy induces robust AHR-dependent structural changes within the uterine-placental interface. Most interestingly, our findings indicate that at least some of the TCDD effects on placentation are mediated through its actions on the mother and not directly on trophoblast cells. (Supported by NIH grants ES028957, ES029280; Sosland Foundation)

2. Uterine Gland Influence on Development of the Placenta and Fetus

Pramod Dhakal[1], Susanta Behura[1], Harriet Fitzgerald[1], Andrew Kelleher[1] and Thomas E. Spencer[1,2] [1]Division of Animal Sciences, University of Missouri, Columbia, MO [2]Department of Obstetrics, Gynecology and Women's Health, University of Missouri, Columbia, MO

Forkhead box a2 (FOXA2) is a gland-specific transcription factor critical for postnatal uterine gland development and adult uterine gland function. In the mouse uterus, Foxa2 regulates a large number of hormone-regulated, gland-specific genes, including the critical implantation factor leukemia inhibitory factor (Lif). Foxa2 conditional knockout (cKO) mice, generated using lactotransferrin (Ltf)-iCre and floxed Foxa2 mice, are infertile due to defects in blastocyst implantation, however injections of Lif on gestational day (GD) 4 restored fertility with birth of live pups at term (*PNAS* 2017; 114:E1018). Although fertility was restored, subtle differences in decidual marker gene expression were observed on GD 6 and 10 in Lif-replaced uterine Foxa2 cKO mice. The goal here was to begin testing the hypothesis that Foxa2-deficient uterine glands will impact placental and fetal growth. First, placentas from Lif-repleted wildtype control and Foxa2 cKO mice were assessed on GD 15. Placentas were not histologically different. RNA-Seq anlaysis found 385 genes were decreased (FDR P<0.05) in placentas from uterine Foxa2 cKO mice, including prolactin (Prl) family members and cyclins, but no genes were increased in Foxa2 cKO mice. Next, a littermate study was conducted using

bred Control and Foxa2 cKO female mice. On GD 12.5, implantation site number was lower (P<0.05) in the Foxa2 cKO as compared to Control dams (7.3±1.8 vs 9.0±1.1). Placentae of female pups, but not male pups, weighed 15.2% less (P<0.001) in Foxa2 cKO dams. Male and female fetuses from Foxa2 cKO dams weighed 13.8% and 22.2%, respectively, less (P<0.001) than from Control dams. These results support the idea that Foxa2-regulated factors produced by the uterine glands directly or indirectly, via the decidua, impact placental and fetal growth in a sex-dependent manner. Supported in part by NICHD Grants R21 HD076347 and R01 HD096266.

3. Role of IGF2 in Regulating Rat Hemochorial Placental Development

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The development of the placenta is central to favorable pregnancy outcomes for both the mother and the fetus. Complex pathways of cellular proliferation, migration and differentiation must occur for this organ to function properly. Imprinted genes have been shown to be important in the development of the placenta and the fetus. *Igf2* is a maternally imprinted gene, meaning its expression in the fetus is paternally derived. This gene is found to be highly expressed in the placenta in numerous cell types and likely has a key function in placental development. While it has previously been demonstrated that mouse pregnancies devoid of *Igf2* expression produce growth restricted offspring, these results may not be generalization to human pregnancies because, unlike humans, mice placentation involves shallow trophoblast invasion. Given that rats possess deep trophoblast invasion, similar to humans, this model was selected to investigate the impact of selectively knocking out *Igf2* expression on fetal growth and placental development. A mutant rat was generated using Crispr/Cas9-mediated genome edited deletion of Exons 2, 3 and 4, which eliminated the core of the IGF2 protein and resulted in a frame-shift mutation. Breeding schemes were generated to produce offspring with the mutant allele being paternally transmitted *(Igf2*$^{+/pat}$*)* or maternally transmitted (*Igf2*$^{mat/+}$). Wild type (*Igf2*$^{+/+}$) females were crossed with *Igf2*$^{+/pat}$ males or alternatively, Igf2$^{mat/+}$ females were crossed with *Igf2*$^{+/+}$ males. Fetal and placental weights were obtained from gestation days 15.5, 18.5 and 20.5. Placentas were separated so that the labyrinth and junctional zones could be independently weighed. Progeny with paternal transmission of mutated the *Igf2* allele exhibited a disruption in placental and fetal development, whereas maternal transmission of the mutated *Igf2* allele generated placentas and offspring indistinguishable from wild type conceptuses. *Igf2*$^{+/pat}$ fetal and placental weights were significantly smaller when compared to *Igf2*$^{+/+}$ littermates at each gestation day examined. Placental compartments were differentially affected by the paternally transmitted mutant *Igf2* allele. Labyrinth zones of *Igf2*$^{+/pat}$ placentas were significantly growth restricted, whereas no significant differences were observed between junctional zone compartments of *Igf2*$^{+/pat}$ versus *Igf2*$^{+/+}$ placentas. In the second breeding scheme, *Igf2*$^{mat/+}$ fetal and placental weights did not significantly differ from *Igf2*$^{+/+}$ fetal and placental weights. Single cell RNA-seq of the rat maternal-placental interface demonstrated that IGF2 is abundantly and specifically expressed in trophoblast cells invading the uterine parenchyma. This attribute of rat invasive trophoblast cells is shared with human invasive extravillous trophoblast cells. However, IGF2 expression status did not adversely affect trophoblast invasion. *Igf2*$^{+/pat}$ and *Igf2*$^{+/+}$ invasive trophoblast cells showed similar spatial patterns of intrauterine trophoblast cell invasion. In summary, these findings reveal IGF2 as a conserved regulator of hemochorial placental development. We have also established a new in vivo tool for exploring the biology of IGF2 signaling in the intrauterine invasive trophoblast lineage. (Supported by an AHA fellowships to MM and KK, NIH grants HD020676; HD079363, ES028957 and the Sosland Foundation)

4. Luteinizing Hormone Enhances Glucose Metabolism by Small Luteal Cells Leading to *de novo* Lipogenesis

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Production of progesterone by the corpus luteum (CL) is fundamental for establishment and maintenance of pregnancy. Luteinizing hormone (LH) is crucial for the formation, function and maintenance of the CL, but the cellular metabolic changes induced by LH remains unclear. Recently, we found that LH stimulates glucose uptake and glycolysis in bovine luteal cells. In the current study we examined: (AIM 1) metabolic changes induced by glucose and LH in luteal cells; (AIM 2) the effects of LH and PKA on the phosphorylation

of enzymes involved in *de novo* lipogenesis and (AIM 3) the effect of inhibition of *de novo* lipogenesis on LH-stimulated progesterone production. AIM 1**:** Primary small luteal cells were isolated form the mature bovine CL and incubated with C^{13}-labeled glucose (control) and C^{13}-labeled glucose + LH (10 ng/ml) for 1 and 4h. Cells and post-incubation media were harvested to determine metabolomics changes using NMR. AIM 2**:** Small luteal cells were treated with different doses of LH (1-100 ng/ml) for 30 min; activator of adenylyl cyclase- forskolin (FSK) for 2, 10 and 30 min; inhibitor of protein kinase A (H89) and LH (10 ng/ml) for 4h. Afterward, luteal cells were collected in order to determine the phosphorylation of proteins associated with *de novo* fatty acid synthesis. AIM 3**:** Small luteal cells were pretreated with inhibitor of ATP citrate lyase (ACYL)- BMS 303141 and then incubated with LH (10 ng/ml) for 4h. Data were analyzed using t-student test or one-way ANOVA with Dunnett's *post hoc* test. Treatment with LH increased glucose utilization as evidenced by decreased ($P<0.05$) concentrations of glucose and fructose-6-phosphate and increased ($P<0.05$) concentrations of lactate and pyruvate, the main metabolites involved in glycolysis and TCA cycle. Simultaneously, lower ($P<0.05$) concentrations of carnithine, coenzyme A and enhanced ($P<0.05$) content of acetate were observed in cells treated with LH, indicating enhanced oxidative phosphorylation and *de novo* fatty acids synthesis. Additionally, LH increased ($P<0.05$) the content of uridine, cytidine/uridine triphosphate and uridine diphosphate N-acetylglucosamine suggesting changes in the penthose phosphate and hexosamine biosynthesis pathways. Both LH and FSK enhanced ($P<0.05$) phosphorylation of ACLY at Ser455, a residue specific for protein kinase A, while pretreatment with H89 diminished LH-mediated effects on ACLY phosphorylation. LH and FSK inhibited ($P<0.05$) the phosphorylation of ACC1 (Acetyl-CoA carboxylase 1) at Ser79, which is responsible for inactivation of that enzyme. Inhibition of ACLY abolished ($P<0.05$) stimulatory effect of LH on progesterone production. The results show that LH enhances glucose metabolism in small luteal cells leading to its utilization in different metabolic pathways associated with ATP production, synthesis of nucleotides, glycosylation of proteins and *de novo* synthesis of fatty acids, all of which constitute an important source of energy for maintenance of luteal cell function. Supported by NIFA USDA 2017-67015-26450, VA and NIH R01HD092263.

5. Genetic Sex Determination from RNA Using Rbm31 Gametologs

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When studying prenatal development, it is important to determine the genetic sex of the fetus. Sexual dimorphism presents early in gestation, and both the fetus and placenta may respond differentially to perturbations like nutrition, toxicants and disease based on sex. For example, some disease symptoms arise earlier and with greater severity in male placentas. Additionally, the National Institutes of Health now requires that sex be considered as a relevant biological variable in funded studies. The sex of a fetus, unlike that of an adult or juvenile mouse, is difficult to ascertain visually. Thus, a common strategy for determining fetal sex is PCR amplification of divergent X and Y chromosome gametologs, but this generally requires the use of DNA, and an extra isolation step. The goal of this study was to develop an RT-PCR based sexing protocol, such that RNA, already isolated for gene expression studies, might also be used for sexing of placental or fetal samples. We searched whole-genome microarray data to identify gametologs expressed in the mouse placenta, and identified RNA-binding motif 31, X-linked (Rbm31x) and RNA-binding motif 31, Y-linked (Rbm31y). PCR amplification of cDNA gives two distinct products, corresponding to the X and Y homologs. Rbm31x has an 84bp deletion not present in Rbm31y, giving strong resolution of bands on an agarose gel. Using this method on placenta, as well as fetal limbs, we have shown the ability to differentiate males and females from RNA samples.

6. A Gatekeeping Role of ESR2 in Primordial Follicle Preservation

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Over the entire mammalian reproductive lifespan, the only source of mature oocytes is a fixed number of primordial follicles present in the ovary. While most primordial follicles are maintained in a dormant state, a small fraction are progressively activated to generate mature oocytes. Uncontrolled and excessive induction of primordial follicles leads to premature ovarian insufficiency, which causes infertility in 1-2% of all women of reproductive age in addition to estrogen deficiency. Maintenance of primordial follicle dormancy and steady activation are independent of gonadotropins, but the molecular mechanisms responsible remain largely unknown. We recently made a novel observation that estrogen receptor β (ESR2) plays a gatekeeping role during the recruitment of primordial follicles. In the absence of ESR2, an increased number of primordial follicles develop into primary follicles in *Esr2*-null rats. Primordial follicle activation was also increased in *Esr2* mutants lacking the DNA binding domain, suggesting a role for the canonical transcriptional activation function of ESR2 in maintaining dormancy. Furthermore, the disruption of ESR2-signaling with a selective antagonist increased

the number of activated follicles in wildtype rats, whereas a selective agonist deceased follicle activation. As expected, the accelerated recruitment of primordial follicles in *Esr2*-null females resulted in the loss of their follicle reserve. *Esr2*-null females exhibited markedly reduced levels of serum AMH and estradiol, suggesting premature ovarian senescence. A candidate approach was employed to elucidate the molecular mechanisms involved. We observed that primordial follicles express ESR2 abundantly, suggesting a direct regulatory role by ESR2 within the follicle. Disruption of ESR2 signaling markedly upregulated activation of the AKT and ERK pathways. This was also associated with activation of the mTOR pathway. In *Esr2*-null rat ovaries, expression of *Kitlg, Gdf9,* and *Bmp15* were markedly upregulated, which might have facilitated the PI3K and AKT activation and resulted in primordial follicle activation. Our findings indicate that while exposure to endocrine disruptors that inhibit ESR2-signaling pose a significant risk for accelerated follicle loss, ESR2-antagonists can be useful for *in vitro* primordial follicle activation.

7. Pig Conceptus Expression of Type I Interferon Delta and Type II Interferon Gamma During Early Pregnancy

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Establishment and maintenance of pregnancy in the pig requires a complex process that relies on adequate communication between the conceptus and maternal uterine epithelium. Directly before the time of attachment to the uterine surface epithelium, the conceptus undergoes a dramatic morphological change to rapidly elongate throughout the uterine horn between days 10 and 12 of pregnancy. During this time, the conceptuses release several biological factors into the uterine lumen that allow the uterine epithelium to become receptive to the attaching conceptuses as well as promote proper conceptus development. Previous studies indicate that without the unique expression of a cytokine called interleukin-1 beta 2 rapid elongation would not be achieved. The conceptuses also secrete estrogens between days 11 to 15 which are thought to redirect the release of prostaglandin F2α, the luteolytic hormone, into the uterine lumen where it is metabolized. Following elongation, the conceptus is known to secrete large quantities of two different types of interferons between days 12 and 20 of pregnancy with peak interferon production between days 14 and 15. The porcine conceptus is unique from other mammals in that it secretes both type I (interferon delta, *IFND*), and type II (interferon gamma, *IFNG*), interferons from the trophectoderm during the peri-implantation period. *IFNG* is the only type II interferon whereas type I *IFND* consists of 11 different genes. It is unlikely that these interferons are involved in maternal recognition of pregnancy, however, their function in establishment and maintenance of pregnancy is unknown. The objective of the present study was to determine conceptus expression of *IFND* and *IFNG* on day 14, 17 and 30 of pregnancy. One primer was designed to target *IFNG* and three primers were designed to target groupings of the 11 different *IFND* genes. The different *IFND* genes were grouped together based on high similarity to each other. These primers were used to amplify complementary DNA synthesized from conceptus RNA to identify their expression. *IFND-1*, *IFND-2* and *IFNG* show expression on day 14, 17, and 30 of pregnancy. *IFND-3, IFND-4, and IFND-10* show expression only at day 30 of pregnancy. *IFND-5, IFND-6, IFND-7, IFND-8, IFND-9,* and *IFND-11* showed no expression across day 14, 17 and 30. Although pig conceptus *IFND* expression has been well known, this research indicates that of the 11 different *IFND* genes found in the current database, five of them appear to be expressed by the conceptus during early pregnancy.
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8. Genetic Variants Identified in Cows with an Excess Androgen Ovarian Microenvironment Provides Clues to Women with Polycystic Ovary Disease

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A naturally-occurring cow model of androgen excess (High Androstenedione; High A4) shares many metabolic and molecular phenotypes of Polycystic Ovary Syndrome (PCOS). High A4 cows have irregular estrous cycles, anovulation, and reduced calving rates but wean calves that are 24 kg heavier. Since producers retain females with heavier offspring to remain in the herd, it is possible High A4 cows have been preferentially selected. Thus, we hypothesize females with a PCOS-like phenotype have genomic variation linked to steroidogenic and metabolic phenotypes comprising the High A4 phenotype. To test this hypothesis, we genotyped 200 individuals with the GeneSeek Genomic Profiler Bovine 150K SNP array. While no loci achieved a genome-wide significance threshold determined by FDR of 0.01, 70 genes within 25 kb of genetic variants associated (raw $p<0.01$) with the High A4 phenotype were prioritized for investigation. Additionally, approximately 17 million variants were identified in whole-genome sequence of 15 individuals (8 High A4, 7 Control). Annotation with SNPEff found 4,600 of these with predicted high impact. High impact variants were identified in seven of

the 70 genes identified in the initial GWAS. We have assayed expression of these, *CARNS1*, *CCR6*, *GPR31*, *ALKBH6*, *CLIP3*, *SREBP1a* and *SREBP1c,* via ddPCR in ovarian cortex, theca, and granulosa cells, in High A4 compared to controls cows. In High A4 ovarian cortex, *SREBP1c* and *CLIP3* were significantly upregulated compared to controls ($p \leq 0.05$). There was a tendency ($p \leq 0.10$) for *CARNS1* and *CCR6* to be downregulated in High A4 granulosa cells. These genes are involved in inflammation or oxidative stress, two processes upregulated in the High A4 phenotype. Understanding genetic variants that predict the High A4 phenotype can provide a potential selection tool for producers. Also, these genetic variants could allow us to better understand metabolic, growth and reproductive trait interactions in human disease such as PCOS.

9. Autophagy Protein Beclin 1 is Critical for Mouse Embryo Implantation and Decidualization

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Between 40% and 70% of miscarriages are unexplained and are due implantation failure owing to defective endometrial receptivity. The endometrial receptivity require the stromal cells to transdifferentiate into decidual cells that secrete factors necessary for embryo survival and trophoblast invasion. Although much of the molecular events involved in endometrial receptivity and decidualization are well known, the role of autophagy related proteins in endometrial receptivity is not yet recognized. Using a conditional knockout genetic mouse model, we demonstrate that Beclin-1, a key autophagy protein, is critical for facilitating the endometrial receptivity and decidualization. We generated conditional knockout of Beclin in the uterus by crossing $Beclin^{flox/flox}$ mice with mice expressing Cre recombinase under control of the progesterone receptor promoter ($PR^{cre/+}$). We found that conditional deletion of *Beclin1* (*Beclin* cKO) in uterus resulted in infertility in female mice owing to defective embryo implantation. Further, in *Beclin* cKO mice responsiveness of the uterus to a deciduogenic stimulus was severely curtailed with marked abrogation in the decidualization promoting genes (Wnt4 and Bmp2). Taken together, we demonstrate that autophagy protein Beclin1 is crucial for the endometrial receptivity and decidualization. Thus, autophagy-stimulating strategies may improve pregnancy outcomes in women with recurrent pregnancy loss condition. This work was supported by NIH grants R01HD065435, R00HD080742, and Washington University, School of Medicine start-up funds to Dr. Kommagani.

10. Trophoblast Paracrine Signaling Regulates Placental Hematoendothelial Niche

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The placenta acts as a major organ for hematopoiesis, and it has been hypothesized that placental hematopoietic stem and progenitor cells (HSPCs) migrate to the fetal liver to ensure optimum hematopoiesis in a developing embryo. The labyrinth vasculature in a mid-gestation mouse placenta provides a niche for definitive hematopoietic stem cell (HSC) generation and expansion. It has been proposed that these processes are regulated by several paracrine factors secreted by trophoblast giant cells (TGCs) at the maternal-fetal interface. However, the molecular mechanisms by which the TGCs regulate the hematoendothelial niche within the developing placenta is yet to be defined. Using a TGC-specific *Gata2* and *Gata3* double knockout mouse model, we show that the loss of GATA2 and GATA3 in the TGC layer leads to fetal growth retardation and embryonic death due to disruptions in the delicate hematopoietic-angiogenic balance in the developing placenta. Using single-cell RNA-Seq (scRNA-seq) analyses, we also show that the loss of GATA factors in the TGCs results in the loss of HSC population within the placental labyrinth and is associated with defective placental angiogenesis. Interestingly, we also found that this TGC-specific GATA factor-loss leads to impaired differentiation and distribution of trophoblast progenitor cells. Our study helps to define the GATA-dependent non-autonomous signaling mechanisms of the primary parietal trophoblast giant cells by which it regulates the delicate hematopoietic-angiogenic balance in the developing placenta.

11. Specialized Pro-Resolving Lipid Mediator, RvD2 Induces GPR18 Membrane Localization and Differentially Regulates Inflammatory Cytokines in Placental Trophoblasts

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Omega-3 fatty acids are important to pregnancy and neonatal development and health. One mechanism by which omega-3 fatty acids exert their protective effects is through serving as substrates for the generation of

specialized pro-resolving lipid mediators (SPM) that potently limit and resolve inflammatory processes. We recently identified that SPM levels are increased in maternal blood at delivery as compared to umbilical cord blood, suggesting the placenta as a potential site of action for maternal SPM. To explore this hypothesis, we obtained human placental samples and stained for the SPM resolvin D2 (RvD2) receptor GPR18 via immunohistochemistry. In so doing, we identified GPR18 expression in placental vascular smooth muscle and extravillous trophoblasts of the placental tissues. Using *in vitro* culturing, we confirmed expression of GPR18 in these cell types and further identified that stimulation with RvD2 led to significantly altered responsiveness (cytoskeletal changes and pro-inflammatory cytokine production) to lipopolysaccharide inflammatory stimulation in human umbilical artery smooth muscle cells and placental trophoblasts. Taken together, these findings establish a role for SPM actions in human placental tissue.

12. Loss of Adenosine Deaminase Acting on RNA (*Adar*) in Granulosa Cells Causes Infertility

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Post-transcriptional regulation is critical to the overall expression of a gene. Acuity at this step contributes to the cell's ability to maintain or respond to its physiological environment by altering gene expression without transcriptional reprogramming at the level of the nucleus. RNA sequencing has highlighted the abundance of non-encoded polymorphisms in RNA sequences and the potential for RNA editing to contribute to post-transcriptional gene regulatory networks. Both coding and noncoding regions of mRNA can be edited resulting in altered codons, altered splice sites, changes in transcript stability, and changes in translation efficiency. Adenosine deaminases acting on RNA (ADAR) catalyze adenosine to inosine (A-to-I) editing, and comprise one family of RNA editing enzymes. There are two catalytically active adenosine deaminases, ADAR1 (*Adar*), with three distinct transcript variants, and ADAR2 (*Adarb1*), that also has three transcript variants. The third adenosine deaminase, ADAR3 (*Adarb2*), has two transcript isoforms both lacking catalytic activity. The periovulatory period provides a landscape for evaluating the role of post-transcriptional regulation as the somatic cells are undergoing differentiation and integrating signals from the maturing oocyte. Analysis of published granulosa cell RNA-seq datasets indicates that *Adar* is the highest expressed adenosine deaminase (10.66 ± 0.02 fragments per kilobase of transcript per million mapped reads) compared to *Adarb1* (2.11 ± 0.17) and *Adarb2* (0.05 ± 0.02). An organism-wide *Adar* deletion is embryonic lethal in mice, so a granulosa cell specific *Adar* depleted model was created to examine the role of ADAR1 in ovarian function. $ADAR^{FL/FL}$/Aromatase-Cre (n=5) and wild-type control littermate (n=6) female mice were bred to wild-type males for fertility evaluation over a 5 month period. To assess follicular development and ovulation, $ADAR^{FL/FL}$/Arom-Cre (n=3) and control (n=5) females were administered 5IU of PMSG, 5IU of hCG 46 hours after PMSG, and eggs were collected from oviducts 16 hours following hCG. In the mating trial, control females had 7 ± 1 pups/litter while $ADAR^{FL/FL}$/Arom-Cre females were infertile. Hormonal stimulation resulted in the recovery of no ovulated eggs in the $ADAR^{FL/FL}$/Arom-Cre females, while control mice had 44 ± 8 ovulated eggs. Ovarian histology following PMSG + hCG stimulation revealed that antral follicles developed but lacked evidence of luteinization following hCG administration. Ongoing studies are evaluating the temporal expression of the three *Adar* specific transcripts in granulosa cells as well as assessing the effect of *Adar* deletion on female cyclicity and expression of genes relating to follicular development, ovulation, and luteinization. These studies provide the foundation for identifying the mechanism by which *Adar* impacts ovarian function.

13. CITED2 Regulation of Embryonic and Placental Development: Species Differences

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CBP/p300-interacting transactivator with glutamic acid/aspartic acid-rich carboxyl terminal domain 2 (CITED2) is a member of the CITED protein family and has been shown to possess critical roles in cellular development and differentiation. CITED2 is an important regulatory gene during prenatal development and is crucial for placenta development and trophoblast cell differentiation. CITED2 regulates the recruitment of CBP/p300, histone 3, lysine 27 acetyltransferases, to transcription factors such as TFAP2C and HIF1. The activity of some transcription factors is enhanced by CITED2 (e.g. TFAP2C), whereas the activity of others is repressed (e.g. HIF1). Evidence indicates that CITED2 is a conserved regulator of both rodent and human placentation. In the human placentation site, CITED2 is prominently expressed in the invasive trophoblast lineage, referred to as extravillous trophoblast (EVT). In the rat, CITED2 is prominently expressed in the junctional zone, site of invasive trophoblast cell progenitors, and in trophoblast cells invading into the uterus. Trophoblast cells of the junctional zone exhibit characteristic patterns of genome accessibility, which are potentially influenced

by CITED2. To study the role of CITED2 in trophoblast cell differentiation and placentation, our laboratory generated a rat model possessing a deletion of the complete coding sequence of CITED2 using Crispr/Cas9 genome editing and acquired a mutant CITED2 mouse model previously generated by homologous recombination (PNAS 99:10488-10493, 2002). CITED2 disruptions were investigated on outbred genetic backgrounds (rat: Holtzman Sprague-Dawley; mouse: CD1). Heterozygous males and females of each species were mated, and embryonic and placental development examined at various stages of gestation. CITED2 deficiencies in the mouse and rat similarly exhibited intrauterine fetal growth restriction, dysmorphic lung development, and deficits in placentation. Prominent species differences were also observed. CITED2 disruption in the mouse resulted in prenatal lethality, exencephaly, and adrenal gland agenesis. In contrast, in the rat, CITED2 null fetuses progressed through pregnancy and died immediately after birth with intact adrenal glands and without signs of exencephaly. Comparison of mouse and rat models of CITED2 deficiency demonstrated some conserved roles for CITED2 in embryonic and placental development, and also unique roles for CITED2 in each species. CITED2 is probably not unique. Thus, caution is warranted in generalizing gene regulatory actions from observations of gene disruption in a single species. (Supported by HD020676, HD079363, HD099638; Sosland Foundation)

14. Effects of Bovine Pregnancy-Associated Glycoproteins on Gene Transcription in Bovine Endometrial Explants

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Pregnancy-associated glycoproteins (PAGs) are a complex gene family, whose members are expressed by trophoblasts of ruminants and related species. In cattle, the PAGs accumulate at the trophoblast-uterine interface and many can enter the maternal circulation. However, very little is known about the role they play in pregnancy although preliminary results suggest that PAGs at the placenta-uterine interface play roles involving matrix turnover and chemokine release. This study was designed to provide further insight into the biological roles of bovine PAGs by measuring changes in endometrial transcript abundance for some matrix metalloproteinases (MMPs) and chemokines/cytokines. PAGs for these experiments were purified from mid-gestation bovine placental extracts by affinity chromatography. Heifers were synchronized and bred by artificial insemination. Heifers were slaughtered at day 18 post-insemination and the reproductive tracts were obtained and flushed to determine if a conceptus was present. Endometrial explants were collected and split between 4 groups: pregnant with and without 15 µg/ml PAG (n=10) and not-pregnant with and without 15 µg/ml PAG (n=9). Endometrial explants were cultured for up to 96 hours at 37°C and 5% CO_2 and samples were harvested at 24 h time points for extraction of RNA. Transcript abundance for ten target genes was analyzed in the endometrial tissue by quantitative PCR. The normalization control transcript was PPIA. Significant increases in CXCL5 and MMP12 were measured in the PAG-treated endometrium from pregnant and non-pregnant animals ($P<0.05$). There was also a significant increase in message for CCL2 and MMP13 in the pregnant PAG-treated group but not in the non-pregnant groups ($P<0.05$). These results indicate that PAGs are capable of inducing changes in transcript abundance in bovine endometrial explants, which suggests that this model system might be useful to assess PAG function at the placenta-uterine interface. Funded by the MU Research Board.

15. Na, K-ATPase α4 Inhibitors as Agents for Male Contraception

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Male contraception still remains as a highly desired unmet goal. The finding of sperm specific proteins that play an essential role in male fertility provides appealing targets for the development of a male contraceptive. We discovered a testis specific isoform of the Na,K-ATPase ion transport system, known as NAKα4, which is highly expressed in the sperm flagellum and is required for sperm motility, sperm hyperactivation and male fertility. NAKα4 has the unique property of having high affinity for the specific inhibitor of Na,K-ATPase, ouabain. Taking advantage of this characteristic, we synthesized a series of derivatives, which specifically bind to the NAKα4 ouabain binding site, as proven by *in silico* docking analysis. These compounds selectively inhibit NAKα4 activity over the other NAK isoforms and reduce the motility of mouse sperm. Here, we extended our study to test the effect of NAKα4 inhibitors on human sperm. The activity of the compounds was tested on different motility parameters of sperm isolated from ejaculates of healthy donors. After swim-up, sperm samples were subjected

to different concentrations of the compounds and sperm motility was determined by computer assisted sperm analysis (CASA). Our results show that NAKα4 inhibitors had different inhibitory potency, with some blocking total and several parameters of sperm motility by ~60%. This value is in good agreement with what the World Health Organization (WHO) considers as low parameters for sperm fertility. Therefore, our data supports the idea that our compounds are attractive chemical scaffolds for the development of a novel non-hormonal male contraceptive agent. [Supported by NIH R01 HD080423].

16. Inhibiting an Inhibitor: Effects of Myostatin Deficiency During Pregnancy on the Placenta

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Myostatin is a protein secreted by muscle tissue and is an inhibitor of muscle growth. Previous studies have shown that maternal myostatin deficiency during pregnancy increases body mass of wildtype fetuses. This suggests that myostatin-deficient dams can affect the development of their offspring during gestation, but the pathway through which maternal myostatin affects offspring is unknown. Previously, we have shown that maternal myostatin cannot cross the placenta to act directly on the fetus. The placenta could potentially play a role in myostatin-deficient dams by transporting more nutrients to the offspring, resulting in a higher body mass. We hypothesize that myostatin inhibits blood flow into the placenta, thus decreasing nutrient transport. The labyrinth zone of the placenta is responsible for the exchange of nutrients and gases from maternal to fetal blood and the junctional zone is responsible for producing hormones, growth factors and cytokines. Based on our hypothesis, we predict that a dam heterozygous for a myostatin mutation (*Mstn/-*) mated with a WT male will have placentas with a larger than normal labyrinth zone, resulting in a more efficient exchange of nutrients and gases between the mother and fetus. In this study, we mated reciprocal crosses of WT and myostatin deficient parents. On day 17.5 of gestation, the placentas were collected. The junctional and labyrinth zone, along with maternal and fetal blood spaces within the labyrinth were imaged and their cross-sectional areas were analyzed via ImageJ. The placentas were then analyzed by using PCR for fetal genotype and sex. There were no statistically significant differences in the labyrinth and junctional zone areas between WT dams and *Mstn/-* dams.

17. TRAINEE ORAL PRESENTATION ONLY (NO POSTER)

GREB1 Acts as a Progesterone Receptor (PR) Co-Activator to Promote Uterine Receptivity for Embryo Implantation

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Successful establishment of pregnancy requires that uterus become receptive to embryo implantation. Up to 37% of conceptions fail to advance beyond 20 weeks of gestation owing to defective embryo implantation. The Embryo implantation is a highly complex process, governed through exquisite crosstalk between the competent blastocyst and receptive endometrium, which is tightly regulated by the steroid hormones estrogen and progesterone. Nevertheless, the full spectrum of the downstream effects of estrogen and progesterone signaling has not been precisely defined. Here, we focused on Growth Regulation by Estrogen in Breast Cancer 1 (GREB1), an early estrogen-responsive gene in breast cancer cells and an androgen-responsive gene in prostate cancer cells. We focus on GREB1 since in our previous work; we showed that siRNA-mediated knockdown of GREB1 significantly impaired in-vitro decidualization of both immortalized as well as primary human endometrial stromal cells. Here, we generated Greb1 knockout mice (Greb1 KO) and found that homozygous female mice were severely sub-fertile owing to defective embryo implantation. Whereas estrogen-mediated signaling was intact in the endometrium of Greb1 KO mice, however, endometrial response to progesterone was compromised and the absence of Greb1 leads to impaired decidualization in mice. Further, GREB1 physically interacts with PR and is required for progesterone-mediated gene expression in primary human endometrial stromal cells. Collectively, our results demonstrate that GREB1 acts as a novel PR transcriptional co-activator to control steroid hormone responses in the endometrium to promote embryo implantation and decidualization. This work may have further implications for endometrial pathologies such as recurrent pregnancy loss and endometriosis. This research work supported by NIH grants R01HD065435 and R00 HD080742; and Washington University, School of Medicine start-up funds to Dr. Kommagani.

18. TRAINEE ORAL PRESENTATION AND POSTER

ASCL2 Reciprocally Controls Key Trophoblast Lineage Decisions During Hemochorial Placenta Development

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The invasive trophoblast cell lineage is critical to spiral artery remodeling and placentation. Insufficient trophoblast invasion, and subsequent vascular remodeling, can lead to pregnancy disorders including preeclampsia, preterm birth, and intrauterine growth restriction. Previous studies in the mouse identified Achaete-scute family bHLH transcription factor 2 (ASCL2) as essential to placental development, including junctional zone morphogenesis. Invasive trophoblast cell lineages arise from progenitors located in the junctional zone. The mouse exhibits shallow trophoblast invasion and is not an optimal model for investigating the trophoblast-uterine interface. In contrast, the rat possesses deep intrauterine trophoblast invasion and spiral artery remodeling similar to human placentation. We hypothesized that ASCL2 is a critical and conserved regulator of invasive trophoblast lineage development. Single cell RNA sequencing analysis of tissue from the rat maternal-fetal interface identified *Ascl2* as specifically and robustly expressed in invasive trophoblast. Further, *Ascl2* binding motifs were identified as enriched in invasive trophoblast cells by single cell ATAC sequencing in the rat. To test our hypothesis, we established an *Ascl2* mutant rat model using *CRISPR/Cas9* genome editing and investigated invasive/extravillous trophoblast (EVT) cell differentiation using a human trophoblast stem (TS) cell model system. *Ascl2*$^{(+/-)}$ x *Ascl2*$^{(+/-)}$ breeding generated 54% wild type (+/+), 46% heterozygous (+/-), and zero null (-/-) live pups (n=14 pregnancies). *Ascl2* nulls died between gestation days 11.5-12.5 and exhibited disruptions in placentation. Rat *Ascl2* is paternally imprinted. *Ascl2*$^{(+/-)}$ females mated to wild type males resulted in pregnancies exhibiting approximately 50% prenatal lethality, which was not observed in offspring generated via transmission of the mutant *Ascl2* allele through the male. Differentiation of human TS cells into EVT cells resulted in significant upregulation of *ASCL2* (n=6; p<0.0001) and several other transcripts indicative of EVT cell differentiation, including major histocompatibility complex, class I, G (n=6, p<0.0001). shRNA-mediated knock down of ASCL2 impaired EVT cell differentiation as indicated by altered cell morphology and gene expression profiles. RNA sequencing analysis of ASCL2-depleted trophoblast cells identified both downregulation of EVT cell-associated transcripts and upregulation of syncytiotrophoblast-associated transcripts. Thus, ASCL2 possesses a key regulatory function in trophoblast development by promoting EVT cell differentiation, while concurrently suppressing syncytiotrophoblast differentiation. Future investigations will seek to determine the position of ASCL2 in the regulatory hierarchy controlling placentation. (Supported by an NRSA postdoctoral F32HD096809 to KMV; HD020676; HD099638, Sosland Foundation)

19. TRAINEE ORAL PRESENTATION ONLY (NO POSTER)

The Development of a Uterine Gland 3D Culture Model to Understand Pregnancy Establishment in Women

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In humans, an unreceptive uterus and disrupted maternal-conceptus interactions can cause infertility due to pregnancy loss or later pregnancy complications. Recent studies in mice revealed that uterine glands and, by inference, their products and secretions impact uterine receptivity, blastocyst implantation, stromal cell decidualization, and placental development. In order to investigate the roles of uterine glands in first trimester human pregnancy, we used an established protocol to generate three-dimensional human endometrial epithelial organoid (EEO) cultures from endometrial biopsies of two different patients. The EEO expand long-term, are genetically stable, differentiate following treatment with reproductive hormones, and can be cryopreserved. After passaging, EEO were grown for 4 days in expansion medium and then treated with estradiol-17β (E2) for 2 days and then either nothing (Control), E2 and medroxyprogesterone acetate (MPA) or E2+MPA+cAMP for a further 6 days (n=3 replicates per patient and treatment). Immunofluorescence analyses found that EEO cells were positive for the gland marker, FOXA2, as well as steroid receptors (ESR1 and PGR). Real-time qPCR analysis found that E2 increased *PGR*, *IHH* and *OLFM4* expression, whereas MPA

increased *HSD17B2*, *PAEP* and *SPP1*. EdgeR robust analysis of RNA-sequencing data revealed that E2 increased 1,093 genes including *OLFM4, PGR and IHH* and decreased 398 genes. Relative to the Control, E2+MPA increased 1,211 genes, such as *PAEP*, *SPP1*, *LIF, HSD17B2* and *STC1,* and decreased 476 genes, whereas E2+MPA+cAMP treatment increased 1,417 and decreased 609 genes. Single-cell RNA sequencing analysis showed that the EEO consist of several different epithelial cell types whose proportion and gene expression changes with hormone treatment, recapitulating changes seen in proliferative and secretory phase endometrium *in vivo*. The EEO model will serve as an important platform for studying gland-decidualizing stromal cell-trophoblast interactions and discovering essential genes involved in human pregnancy establishment. Supported by NIH Grants R01 HD096266 and R21 HD087589.

20. Low Dose of Cisplatin Induces Oocyte Death in Primordial Follicles of Mouse Ovary

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In the mammalian ovary, ovarian damage can result from chemo-, radiation therapy, or environmental toxins, etc. However, we still do not know the exact mechanism of oocyte death by cisplatin on the ovary, one of the detrimental alkylating agents. In this study, we investigated whether the consequence by cisplatin is different dependent on chemotherapeutic dose and schedule. Six-week-old CD1 female mice (n=20) were intraperitoneally (i.p.) injected *in vivo* with DPBS, 2 mg/kg or 5mg/kg cisplatin for 15 days and 2 mg/kg cisplatin for 15 days followed by a period without injection for extra 10 days. Additionally, we cultured postnatal day 5 (PD5) mouse ovaries *in vitro* with DPBS, 1 μM or 4 μM cisplatin once for ninety-six hours as well as 1 mM cisplatin everyday treatment. H&E staining was performed, and total follicles per ovary were counted with serial sections of ovaries. Contrary to previous reports, our results showed that total numbers of primordial, primary, secondary and antral follicles in the mouse ovaries treated with cisplatin significantly decreased compared to those treated with DPBS. Moreover, our *in vitro* studies using PD5 ovaries confirmed that cisplatin induces oocyte death, especially in primordial follicles and granulosa cells within growing follicles. To identify surviving primordial and primary follicles, TAp63 was used as an oocyte biomarker. Our observation using transmission electron microscope (TEM) showed that cisplatin induces damage of intra-organelles inside of primordial follicles, especially mitochondria. In addition, TEM data revealed cisplatin primarily causes oocyte death of primordial follicles without damage in pregranulosa cells or other growing follicles in the ovary. Our results indicate that the effect of cisplatin on the loss of follicles in the mouse ovary is the same between the high dose of injection and consecutive low dose of it. Thus, we conclude fertoprotectants against cisplatin should target molecules that control the apoptotic pathway in the oocyte of primordial follicles. Dr. Kim's Startup Package and 1R01HD096042 (Development of Mechanism-Based Ovarian Reserve Protecting Adjuvant Therapies Against Gonadotoxic Therapeutic Agents) funded this work.

21. Determining Impacts of Heat Stress on the Luteal JAK-STAT Pathway in Gilts

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Heat-stress (HS) occurs when environmental and metabolic heat production exceed heat dissipation. Reproductive dysfunction results from HS in swine and we previously identified HS-induced reduced corpora lutea (CL) weight. In the ovary, prolactin (PRL) influences luteolysis via binding to the PRL receptor (PRLR), phosphorylating and activating janus kinase (JAK2) and signal transducer and activator of transcription (STAT) proteins. We have previously demonstrated that HS elevates circulating PRL in swine, thus, we hypothesized that the CL is hyper-responsive to PRL; a molecular scenario that could contribute to reduced luteal weight. Fourteen post-pubertal crossbred gilts were synchronized and subjected to thermal neutral (TN; 20±1°C; 35-50% humidity; n = 7) or cyclic HS (35 ±1°C for 12h/31.6°C for 12h; 20-35% humidity; n = 7) conditions from 2 days post estrus (dpe) until peak CL function at 12 dpe. Western blotting was performed to quantify abundance of luteal PRLR, pJAK2, JAK2, pSTAT3, STAT3, pSTAT5α/β and STAT5α. No treatment effect on PRLR, pJAK2, JAK2, pSTAT3, pSTAT5α and STAT5α/β proteins were observed ($P > 0.14$). Ovarian STAT3 protein abundance was increased (11%; $P < 0.01$) in the CL of gilts exposed to HS, relative to TN treated gilts. There was no impact of HS on levels of pJAK2 and pSTAT5α/β ($P > 0.05$), however, pSTAT3:STAT3 ratio was decreased ($P < 0.06$) in the CL of HS relative to TN gilts. These data suggest that HS alters ovarian signaling pathways during the luteal phase that could contribute to fertility dysfunction. This project was supported by the Iowa Pork Producers Association.

22. Labyrinth Trophoblast Specific Role of GATA2 AND GATA3 in Mouse Placental Development
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GATA transcription factors GATA2 and GATA3 play an important role in trophoblast lineage differentiation and overall placental development. We have shown that simultaneous knockouts of both *Gata2* and *Gata3* in all the trophoblast cells impair this process and result in severely underdeveloped labyrinth zone and junctional zone of the placenta. This double knockout (DKO) also resulted in gross developmental defects in the embryo proper accompanied with loss of hematopoietic population in both the embryonic and extraembryonic tissues. A fully developed mouse placenta contains distinct layers of differentiated trophoblasts with each subclass having their own unique gene signatures. We thus hypothesized that GATA2 and GATA3 may have a trophoblast subtype specific function that is essential for the labyrinth zone development. To address this we have used trophoblast subtype specific cre mouse models that would specifically ablate *Gata2* and *Gata3* in these trophoblast sub-populations and then study its effect on overall placental and embryonic development. We used a labyrinth SynTII trophoblast specific marker Gcm1 regulated Cre mouse models for these experiments. Our study shows that in $Gcm1^{Cre}$ mediated DKO the loss of these transcription factors together arrest the growth of the embryos at E9.5. There were phenotypic abnormalities in the placenta which are under developed and pale owing to aberrant haematopoiesis and the embryo proper shows significant growth retardation, developmental defects, and blood loss. Single cell RNA-Seq analysis and ultra-structure analysis of the placental samples further revealed the differentiated trophoblast sub-populations that have been affected as well as the altered transcriptomic profile due to the lineage specific loss of these transcription factors.

23. Western Diet Consumption Alters Lipid Profiles in Dam Circulation, Placenta, and Fetus
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Maternal obesity leads to altered postnatal metabolism and health outcomes for the offspring. One potential contributor to altered metabolism is the increased nutrient transfer from maternal to fetal circulation, mediated by the placenta. While studies examining the obesity-dependent nutrient transport alterations in end-of-gestation placentas, little is known about how maternal obesity affects the initial development and function of the placenta. Therefore, we sought to identify changes in lipid profiles within circulation of diet-induced obese dams which are transmitted to the mid-gestation mouse placenta and fetus. Female C57BL/6J mice (5 weeks of age) were placed on either a control diet (normal diet, ND, n=7) or a high-fat, high-sucrose diet (western diet, WD, n=5). After eight weeks, mice were mated with ND C57BL/6J males. Observation of a copulatory plug was considered embryonic day 0.5 (e0.5). Dams were euthanized at e12.5, with weights, blood, tissues, and fetal/placenta pairs collected. Serum lipids were extracted and analyzed via liquid chromatography-mass spectrometry. Mass spectrometry imaging (MSI) was performed to identify and localize lipids in the placenta and fetus. Dams on WD were heavier than their ND counterparts, $P < 0.01$. Female fetuses from ND dams weighed less than the male fetuses, $P < 0.05$. However, there was no weight difference between female and male fetuses from WD dams, $P > 0.05$. In ND dams, female placental weights were also reduced compared to males $P < 0.05$. Similarly, female placentas from WD dams tended to be smaller than their male counterparts, $P < 0.1$. Relative quantitation of dam serum lipids revealed increases in circulating 16:1, 18:1, 20:0, 20:2, and 20:3 lysophosphatidylcholines (LPCs) in WD dams, $P < 0.05$. Analysis of MSI revealed sex-dependent alterations in placental LPCs between WD and ND groups. LPC 18:1 was increased in WD placentas of male and female fetuses ($P < 0.5$, $P < 0.1$, respectively), while 20:3 was increased only in placentas of WD males, $P < 0.05$. Interestingly, differences in fetal LPCs detected by MSI were distinct from LPC profile differences observed in maternal circulation or the placenta. In female WD fetuses, LPC 16:0 and 18:0 were reduced compared to ND counterparts, but no differences were seen in male fetuses. Overall, fetuses from ND but not WD dams had sex-dependent weight differences, suggesting that maternal obesity altered mid-gestation fetal growth. While some changes in placental lipid species mirrored those in dam circulation, others did not. Furthermore, maternal obesity induced differences in female fetal lipid profiles, but these differences were distinct compared to dam circulation and placenta. Taken together, these data suggest that maternal obesity alters placental lipid metabolism, which may have consequences on fetal development.

24. TRAINEE ORAL PRESENTATION ONLY (NO POSTER)
Building a Tail: Dissecting the Role of Axonemal Proteins During Spermatogenesis
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Axonemal dyneins are motor proteins that form the inner and outer arms of the axoneme in cilia and flagella. Defects in the dynein arms are the leading cause of primary ciliary dyskinesia (PCD), which is characterized by chronic respiratory infections, situs inversus, and sterility. Despite the current understanding of pathological features associated with PCD, many of their causative genes still remain elusive. Using *Drosophila*, here we analyze genetic requirements for *wampa* (*wam*), a previously uncharacterized component of the outer dynein arm. While homozygous mutant animals are viable and display no morphological defects, we report that loss of *wam* results in complete male sterility. Transmission electron microscopic analysis of developing spermatids reveals that *wam* homozygous mutants lack outer dynein arms along the axoneme, which leads to a complete loss of flagellar motility. In addition to a role in outer dynein arm formation, we also uncover additional requirements for this gene during spermatogenesis, including the regulation of mitochondrial localization and the shaping of the nuclear head. Due to the conserved nature of axonemal dyneins and their essential role in both PCD and fertility, this study advances our understanding of the pathology of PCD, as well as the functional role of dyneins in axonemal formation and other aspects of spermatogenesis.

25. A-to-I RNA Modifications are Enriched in Oocyte Ribosome Associated RNA

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In growing oocytes, maternal mRNA are transcribed and stored. Stored transcripts support oocyte meiotic maturation and early embryonic development, and then undergo decay. We previously identified adenosine into inosine (A-to-I) RNA editing as a common RNA epitranscriptome modification in GV oocytes and MII eggs. These A-to-I RNA edits were enriched at the third nucleotide of the codon (wobble position), altering codon optimality, which can potentially impact mRNA stability and translation efficiency during the GV-to-MII transition. Due to the codon-specific nature of RNA editing, we hypothesized that A-to-I RNA editing was associated with translational machinery. To test this, we used a computational approach to examine A-to-I RNA editing dynamics in total RNA-seq and polysomal RNA-seq data during meiotic maturation (GV, MI, and MII stages, n=2/stage). During meiotic maturation, there was no difference in the number of A-to-I RNA edited transcripts in total RNA (GV=1750.5±337.5; MI=999.5±109.5; MII=1132±213; means±SEM). In contrast, ribosome associated RNA exhibited a decrease of A-to-I RNA edits during meiotic maturation (GV=1666±30; MI=850.5±5.5; MII=709.5±6.5; $p<0.05$ one-way ANOVA). Efficiency of A-to-I RNA editing also decreased at these stages (GV=83%, MI=38%, and MII=32%). Both total RNA and ribosome associated RNA exhibited an enrichment of editing at the wobble position. In ribosome associated RNA, 18 codons were highly edited in GV oocytes, and declined during meiotic maturation. Overall, we show that oocyte meiotic maturation coincides with a reduction in ribosome associated RNA edits, as well as editing efficiency, indicating that A-to-I RNA modifications are involved in RNA clearance during maternal RNA degradation.

26. A Role for Malignant Brain Tumor Domain-containing protein 1 in Human Endometrial Stromal Cell Decidualization

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A two-way communication between the implantation-competent blastocyst and the receptive uterus is essential for establishing successful pregnancy. Early miscarriage, stemming from defects in maternal endometrial function, affects up to 30% of women attempting to conceive. Progesterone, signaling via its nuclear receptor PR, is indispensable for endometrial stromal cell decidualization; a cellular transformation in which stromal fibroblasts differentiate into decidual cells. Here, we show that Malignant brain tumor domain-containing protein 1 (*MBTD1*) is critical for human endometrial stromal cell decidualization. The mRNA level of *MBTD1* was significantly elevated during the course of *in-vitro* decidualization in both immortalized and primary human endometrial stromal cells. Further, MBTD1 protein was prominently localized in the nucleus of decidualized primary human endometrial stromal cells. Importantly, the siRNA-mediated knockdown of *MBTD1* significantly impaired the *in-vitro* decidualization of both immortalized and primary human endometrial stromal cells. For both types of HESCs, there was a significant reduction in the progesterone-driven decidualization markers, *PRL* and *IGFBP1*. Finally, MBTD1 knockdown significantly reduced the expression of well-established P4 target genes *WNT4*, *FOXOA1,* and *GREB1*. Interestingly, expression of MBTD1 was not under the control of P4-signaling. Collectively, this study provides evidence that MBTD1 contributes to successful *in-vitro* decidualization of human endometrial stromal cells by sustaining progesterone signaling. This work may have further implications in the assistance of new designs of more proactive diagnostic and therapeutic tools for recurrent pregnancy loss. Recent studies

have found recurrent MBTD1-CXorf67 fusion proteins were reported in low-grade endometrial stromal sarcoma. Therefore, the research on MBTD1 could also improve diagnostic and therapeutic tools regarding endometrial sarcomas. This research work is supported by NIH grants R01HD065435 and R00 HD080742; and Washington University, School of Medicine start-up funds to Dr. Kommagani.

27. Characterization and Regulation of Extracellular Vesicles in the Lumen of the Ovine Uterus

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Conceptus elongation is required for successful pregnancy establishment in ruminants, but the underlying mechanisms and regulation of this process is unclear. In vitro studies with embryos and in vivo studies with the uterine gland knockout (UGKO) ewe model support the idea that uterine secretions are essential for conceptus survival and elongation. Extracellular vesicles (EVs) emanate from both the uterine endometrial epithelia and conceptus trophectoderm, are present in the uterine lumen, and contain cargo including proteins, RNAs, and select lipids that can be taken up by recipient cells. The present studies tested the hypothesis that EVs may affect conceptus development and mediate embryonic-maternal molecular crosstalk during conceptus elongation in sheep. Size exclusion chromatography and nanoparticle tracking analysis (NTA) found that total EV number in the uterine lumen increased from day 10 to 14 in cyclic (C) ewes and was lower in day 12 and 14 pregnant (P) ewes. Intrauterine infusions of IFNT did not affect total EV number in the uterine lumen. Next, quantitative mass spectrometric analyses defined proteins and lipids in EVs isolated from the uterine lumen of day 14 C and P sheep. In total, there were 117 proteins that were differentially abundant between EVs from C and P ewes, with an enrichment for proteins involved in protein translation and localization in EVs from P ewes. Lipidomic analysis revealed that there are patterns in EV lipid profiles that separate by pregnancy status. Notably, phosphatidylethanolamine phospholipids and ceramides separated by PCA plot and clustered together by heatmap analysis. In vitro exposure of ovine trophectoderm cells to uterine EVs decreased their proliferation and increased their production of IFNT, although not at the level of gene expression. These and other studies support the idea that EVs mediate conceptus-endometrial interactions and modulate peri-implantation conceptus growth and elongation by providing a source of lipids for trophectoderm cell growth and modulating their proliferation. Supported by AFRI 2015-67015-23678 and 2016-67015-24741 from the USDA National Institute of Food and Agriculture.

28. PLAC1 Regulation of Hemochorial Placenta Development

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The hemochorial placenta possesses a diverse set of functions ensuring survival and development of the fetus within the female reproductive tract. Execution of these functions requires synchronized temporal and spatial differentiation of progenitor cells into specialized trophoblast cell types and their organization into a hemochorial placenta. Placental development requires the activation of specific genetic regulatory programs. Placenta Enriched 1 (PLAC1), an X-linked gene, has been implicated in the regulation of mouse and human placental development. In vivo mouse mutagenesis demonstrated that PLAC1 restrains placental growth. PLAC1 has also been shown to regulate human invasive/extravillous trophoblast development. The mouse is a powerful model for biomedical research but has some limitations in placenta research. Alternatively, the rat has proven to be an effective model for investigating hemochorial placentation associated with deep intrauterine trophoblast invasion, as is also observed in the human. In this study, we sought to establish a role(s) for PLAC1 in rat placentation. *Plac1* transcripts were prominently expressed in the junctional zone of the rat placenta, a structure analogous to the extravillous trophoblast column of the human placenta, and in trophoblast cells invading into the uterus. A PLAC1 mutant rat model was generated using Crispr/Cas9 genome editing and its impact on placentation investigated. Exon 3 of the *Plac1* locus was targeted resulting in a 469 bp deletion, corresponding to nucleotides coding for 95% of the PLAC1 protein. Placentation sites and fetal development were assessed during various stages of gestation in pregnancies generated from *Plac1*$^{(+/-)}$ x *Plac1*$^{(+/-)}$, *Plac1*$^{(+/-)}$ female x wild type male, and wild type female x *Plac1*$^{(+/-)}$ male breeding combinations. *Plac1* homozygous or hemizygous nulls and *Plac1* maternally-inherited heterozygotes exhibited placentomegaly. Specifically, the enlarged placenta was characterized by an expanded junctional zone and an irregular junctional zone-labyrinth zone boundary. These findings implicate PLAC1 as an important regulator of hemochorial placentation and provides a new tool for evaluating the involvement of PLAC1 in regulating the

trophoblast-uterine interface and deep placentation. (Supported by an ADA fellowship to JN, AHA fellowships to MM and KK, NIH grants HD020676, HD079363, and HD099638, and the Sosland Foundation)

29. Pancreatic Ductal Adenocarcinoma Highly Expresses Inhibin βA Subunit

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Cancer cachexia occurs in approximately 50% of all cancer patients and 80% of patients with advanced cancers. Several factors have been proposed to induce cachectic symptoms in human patients, including inhibin subunit βA (also known as activin A). We hypothesize that there is a marked increase in the production of activin A, causing the uncontrolled growth of cancer cells and the irreversible cachectic condition. Thus, we examined the expression and secretion of activin A in pancreatic ductal adenocarcinoma (PDAC) cell lines and tissue in human and mouse in comparison to non-cancerous pancreatic ductal epithelium, as well as the amount of circulating activin present in the serum of healthy donors compared to serum samples of PDAC patients through the Nebraska Biobank and the Rapid Autopsy Program (RAP) for Pancreas and RAP Patient-Derived Models Repository at UNMC. We detected increased amounts of activin A protein in KPC mouse pancreatic tissue using immunoblotting and immunocytochemistry assays. Additionally, we observed the expression of activin A in human PDAC cell lines. The average amount of circulating activin A in the serum of PDAC patients was over five-fold higher than the average of that is in the serum of normal patients based on our enzyme-linked immunosorbent assay data. This data strongly supports our hypothesis that the production of inhibin subunit βA is uncontrolled at the transcriptional, translational or posttranslational levels, resulting in the development and progression of cancer cachexia in several types of cancer, in addition to ovarian granulosa cell tumors. Research supported by KIM NRI COLLAB SEED 3132051012 and Dr. Kim's Startup Package.

30. Aryl Hydocarbon Receptor Signaling in Trophoblast Development

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The primary interface between mother and fetus, the placenta, plays numerous functions, including transport of nutrients and waste products, hormone secretion, and immunoprotection of the genetically distinct fetus. Our environment is a source of chemicals and toxicants that can affect cellular and molecular processes, including those controlling the function and development of the hemochorial placenta. Timing of environmental exposures are likely critical in determining their effects on placentation and postnatal health. The aryl hydrocarbon receptor (AHR) is a member of the PAS family of transcription factors and the only member of the PAS family known to be activated by endogenous ligands and ligands present in our environment. AHR is a key component of a molecular pathway sensitive to a wide range of xenobiotic exposures. AHR interacts with another member of the PAS family termed AHR nuclear translocator (ARNT) to regulate transcription of an expansive cadre of genes encoding a range of regulatory proteins, including enzymes and transporters important in the biotransformation, metabolism, and detoxification of environmental pollutants. The AHR repressor (AHRR) is a third member of the PAS family that modulates AHR:ARNT signaling. AHRR:ARNT complexes can compete with AHR:ARNT for binding to the xenobiotic response element (XRE) on target genes such as cytochrome P4501A1 (CYP1A1). The goal of this research project is to dissect the involvement of AHR signaling in hemochorial placenta development. We utilize trophoblast stem (TS) cells as in vitro models and have generated ARNT and AHRR mutant rat models using CRISPR/Cas9-mediated genome editing. Human TS cells express components of the AHR signaling pathway (AHR, ARNT, AHRR, CYP1A1, CYP1B1) and also enzymes contributing to the biosynthesis of endogenous AHR ligands (IDO1, IDO2, TDO2). Furthermore, 2,3,7,8-tetrachlorodibenzodioxin (TCDD), a classic AHR ligand, activates expression of CYP1A1 and CYP1B1 in human TS cells maintained in the stem cell state or induced to differentiate into extravillous trophoblast cells or syncytiotrophoblast. Activation of AHR signaling was dependent on the concentration of TCDD. In contrast, TCDD is not effective in activating AHR-mediated CYP1A1 or CYP1B1 expression in rat TS cells, which prompted a survey of responses to TCDD in trophoblast cells derived from a range of species, including pig, sheep, monkey, etc. ARNT and AHRR mutant rat models were successfully established. ARNT nulls die in utero, whereas AHRR nulls survive pregnancy. Characterization of the mutant rat strains is underway. In conclusion, the results of this study expand our understanding of the functions of AHR signaling in trophoblast development and provide new tools for examining elements of this complex regulatory network in vivo. (Supported by NIH grants HD020676, ES029280, and the Sosland Foundation)

31. Entinostat Induces PARPi Sensitivity Across Three Different Ovarian Cancer Models via Alteration of Homologous Recombination Pathway

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Ovarian cancer is a leading cause of gynecologic cancer death, in the United States and remains an inherently fatal disease due to its stealth development, making it life-threatening, in spite of being rare. Poly ADP ribose polymerase inhibitors (PARPi) are promising drugs, most effective in patients with tumors deficient in homologous recombination (HR) genes, mainly BRCA1/2. Our group has published that histone deacetylase inhibitors (HDACi) sensitized HR proficient *BRCA* wild-type ovarian cancer cells to PARPi, however the mechanism still remains elusive and the efficacy needed to be tested across multiple models. We recently tested Entinostat with and without Olaparib in three different ovarian cancer models, including human/mouse established cell lines, PDX derived primary cell lines and immune-competent/immune-compromised xenograft as well as PDX-derived preclinical mouse models to delineate the efficacy of Entinostat to sensitize ovarian tumors to Olaparib and determine the underlying mechanism. HR proficient BRCA wild-type ID8/SKOV3 and PDX derived primary cell lines were treated with Entinostat and Olaparib, alone or in combination and analyzed for cell proliferation. DNA damage was studied using Comet assay. Expression of cell proliferation, DNA damage and repair protein were done using Western blot analysis and immunofluorescence. Further, ID8-treated immune-competent mouse models, SKOV3-treated immune-compromised mouse model and HGSOC patient derived PDX mouse model generated in our lab were treated with vehicle, Entinostat, Olaparib, or the combination. The mice were monitored for toxicity and body weight measured twice weekly, till tissue harvest or survival. Cell proliferation was significantly decreased in Entinostat-Olaparib combination treated groups in all cell lines tested. Comet assay showed significantly longer comet tail length in combination treated cells, indicating DNA damage. Western blot and Immunofluorescence showed that combination treatment significantly decreased BRCA1, PCNA, RAD51 and increased cleaved PARP, yH2AX. Further, SKOV3-xenograft mouse model showed decreased tumor burden, ID8-xenograft mouse tumors showed decreased Ki67 and HGSOC derived PDX model showed longer survival when treated with Entinostat-Olaparib combination therapy. *In vitro* studies in ID8 cells is in progress. To conclude, Entinostat in combination with Olaparib decreased cell proliferation, increased DNA damage, induced HR deficiency *in vitro*, reduced tumor burden, decreased Ki67 in xenograft mouse model, and improved survival of HGSOC derived PDX mice, thereby potentially sensitizing homologous recombination proficient ovarian cancer to PARPi across multiple models.

32. Impact of High Fat Diet-Induced Obesity on Ovarian DNA Damage Repair Proteins in Rats

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Obesity is correlated with a heightened ovarian cancer risk and reproductive dysfunction. Upon DNA damage, cellular repair proteins, including Ataxia telangiectasia mutated (ATM), are induced and histone 2AX is phosphorylated (γH2AX) at the site of the DNA break. Previously we determined that hyperphagia-induced obesity alters the ovarian response to DNA damaging chemicals in mice. This study tested the hypothesis that high fat diet-induced obesity would also alter ovarian DNA damage protein abundance in rats. Female Wistar rats were fed a high fat diet (HFD; 60% Kcal) from 4 to 22 weeks of age, at which point their body weight differed from the control (CT) counterparts. Ovarian protein was isolated and targeted western blotting performed to quantify abundance of γH2AX, breast cancer type 1 susceptibility protein homolog (BRCA1), RAC-alpha serine/threonine-protein kinase (AKT1), DNA (cytosine-5)-methyltransferase 1 (DNMT1), histone deacetylase 1 (HDAC1), histone H3 [trimethyl Lys 9] (H3K9me3) and superoxide dismutase [Cu-Zn] (SOD1). Surprisingly, there was no effect of HFD-induced obesity on protein abundance of γH2AX, AKT1, BRCA1, HDAC1, H3K9me3, DNMT1 or SOD1 ($P > 0.05$). Using an untargeted LC-MS/MS approach, 17 and 19 proteins were identified to be decreased and increased ($P < 0.1$), respectively, in the ovaries of HFD relative to CT rats. Twelve of these altered proteins have roles in DNA damage repair (5 decreased; 7 increased). These data add further support to the tenet that obesity alters the ovarian capacity to repair DNA damage. Supported by funding from the Iowa State University Bailey Career Development Award to AFK, the Fulbright Foreign Student Program to EGA and the University of Missouri F21C program funding to PS.

33. Ovarian Influences on Postnatal Mouse Uterine Development

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Postnatal uterine development involves differentiation and development of the endometrial glandular epithelium (GE) and luminal epithelium (LE) as well as development of the mesenchyme into the endometrial stroma and myometrium. This period of development is critical, because it influences the embryotrophic capacity of the adult uterus. In particular, uterine glands and, by inference, their products and secretions are essential for embryo implantation and influence stromal cell decidualization and placental development. In mice and sheep, the ovary influences growth and development of the uterus, but effects on uterine gland development are not clear in mice. Uterine gland genesis begins around postnatal day (PD) 9 and continues through weaning (PD21) to puberty (4-5 weeks). The overall hypothesis is that factors produced by the ovary, including estrogen, regulate development of glands in the prepubertal mouse uterus. Here, C57BL/6J and CD-1 mice were ovariectomized (Ovx) on PD15. Intact and Ovx mice from each strain were analyzed on PD 20, 30, 40 and 60 (n=5 per PD/treatment). Uterine weight was not different ($P>0.10$) on PD20, but was substantially lower ($P<0.05$) in Ovx mice after PD20. Although the uteri of ovx mice were hypoplastic, they were histologically similar to intact uteri at each time point regardless of strain. No differences in gland development were observed in Ovx mice as determined by immunofluorescence analysis of forkhead box A2 (Foxa2), a transcription factor uniquely expressed in the GE of the uterus. Paradoxically, Foxa2 mRNA levels were higher in uterus of Ovx mice regardless of strain. These data support the hypothesis that the ovary and, by inference, its products influence postnatal uterine growth but does not negatively impact differentiation and development of uterine glands. Supported by NIH R01 HD096266.

34. AKT1 Regulates Fetal and Placental Development and Postnatal Growth

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The phosphatidylinositol 3-kinase (PI3K)/AKT pathway is involved in many biological processes including cell proliferation, differentiation, migration, and invasion. AKT is a family of three serine/threonine kinases (AKT1, AKT2, and AKT3). AKT1 has been implicated in fetal, placental, and postnatal growth. Fetal growth restriction is associated with deficits in intrauterine trophoblast invasion and uterine spiral artery remodeling. However, little is known about a role for AKT1 in intrauterine trophoblast invasion and trophoblast-guided uterine spiral artery remodeling. The rat represents an excellent model for investigating the regulation of intrauterine trophoblast cell invasion and deep placentation, features shared with human placentation. To begin to address the role for AKT1 in deep placentation, we generated a germline mutant *Akt1* rat model using CRISPR/Cas9 genome editing. A 1332 bp deletion spanning Exons 4 to 7 was generated resulting in a frameshift, a premature stop codon, and disruption of the entire kinase domain of the AKT1 protein. Mating of heterozygotes produced the expected Mendelian ratio. AKT1 protein was not detected and total AKT and phosphorylated AKT (Ser473) proteins were prominently decreased in mutant homozygotes as determined by western blotting. *Akt1* null fetuses and placentas were significantly smaller than those of wild-type littermates at gestation day 18.5. Furthermore, the chorioallantoic placenta was separated into two compartments: junctional zone and labyrinth zone. Both placental compartments were significantly smaller in *Akt1* nulls than in wild-type littermates. *Akt1* null male and female progeny also showed a significant deficit in postnatal growth. Our results indicate that AKT1 is required for fetal and placental development and postnatal growth in the rat. AKT1 critically serves as a regulator of junctional zone development, the site of invasive trophoblast progenitor cells. Future research will examine the involvement of AKT1 signaling in the modulation of intrauterine trophoblast invasion and trophoblast-guided uterine spiral artery remodeling. (Supported by AHA fellowships to KK and MM, NIH grants HD020676; HD079363, HD099638, and the Sosland Foundation)

35. TRAINEE ORAL PRESENTATION AND POSTER

Oxidative Stress Alters the Expression Profile of *Dppa3* in Oocytes and Decreases Di-Methylation of Histone H3K9 in the Pre-Implantation Embryo

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Increases in obesity rates are correlated to poor fertility in women. To mimic human obesity, female mice are fed a high fat and/or high sucrose diet which causes ovarian inflammation and oxidative stress. These obesity

phenotypes lead to reduced oocyte quality. Data from our lab showed altered expression of the maternal effect gene *Dppa3* in oocytes from obese mice. We hypothesized that oxidative stress dependent changes in the expression and/or localization of *Dppa3* transcripts alters DPPA3 protein expression and methylation profiles in embryos, which could have long-term effects on embryonic and fetal development. To test this hypothesis, murine cumulus oocyte complexes (COCs) were *in vitro* matured (MII) in the absence or presence of 100μM hydrogen peroxide (H_2O_2). Overall *Dppa3* mRNA abundance was significantly decreased in H_2O_2 exposed compared to control MII oocytes. However, localization of *Dppa3* mRNAs, measured by fluorescence in situ hybridization (FISH), was significantly increased in the sub-cortical maternal complex region of the H_2O_2 exposed oocytes. Both control and H_2O_2-matured oocytes were subsequently *in vitro* fertilized and cultured under normal conditions. There was no difference in *Dppa3* abundance in 2-cell or 4-cell embryos between the experimental groups. However, DPPA3 protein was significantly increased in 2-cell embryos from the H_2O_2 matured oocytes (i.e. H_2O_2 embryos). Importantly, 4- and 8-cell H_2O_2 embryos tended to have decreased levels of dimethylated H3K9. These data indicate that exposure of oocytes to oxidative stress during maturation alters the expression of *Dppa3* mRNA and DPPA3 protein, which in turn decreases methylation of H3K9. This epigenetic change may shift the timing of embryonic genome activation and have long term effects on the embryo that could contribute to poor fertility rates in obese women.

36. Codon Identity in Human Oocytes Reveals Age-Associated Defects in mRNA Decay

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Codon composition of mRNA is an emerging factor that affects both translational efficiency and mRNA stability. Codons that facilitate rapid translation promote mRNA stability and are considered optimal, while codons that slow translational efficiency destabilize mRNA, and considered non-optimal. We assessed the codon composition of mRNA in human germinal vesicle (GV) oocytes and metaphase II (MII) eggs from women of young (YNG, <30 yrs) and advanced maternal age (AMA, ≥40 yrs) to examine the relationship between codon composition and mRNA stability. We observed that non-optimal codons are enriched at the 5' end of the coding region in human oocyte and egg transcripts. In AMA samples, we observed a global increase of codon stability during the GV-to-MII transition. Among the transcripts that were commonly expressed in YNG and AMA, transcripts with non-optimal codons were retained in AMA oocytes, but degraded in YNG oocytes. Furthermore, an analysis of protein mass spec data during the human GV-to-MII transition of YNG women revealed that transcripts enriched in non-optimal codons resulted in early peptide truncations. Our data indicates that maternal aging causes defects in translation, which result in inefficient translational efficiency and the retention of maternal mRNA that are degraded in YNG oocytes. These results are important because they show that analyzing the relationship of codon composition to mRNA stability can illuminate the quality of the translational program in cells. In the case of oocytes, defects in translation can alter the RNA decay pathways and result in incorrect maternal mRNA dosage, which may negatively impact embryonic development.

37. University of Na, K-ATPase α4 Controls Glucose Uptake in Sperm via the Sodium Glucose Transporter

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Infertility is a global medical issue, affecting 1 out of every 6 couples. Male factor infertility accounts for ~50% of these cases, and of these, one third are idiopathic or of unknown cause. Understanding the role of proteins that are essential for sperm function is crucial to reducing male factor infertility. Our lab has focused on Na,K-Atpase α4 (ATP1A4), a male germ cell protein that exchanges Na^+ and K^+ across the sperm flagellar membrane. It is required for sperm motility, capacitation, and male fertility; its deletion in mice results in complete infertility. In addition, sperm from ATP1A4 knockout mice have reduced glucose uptake and decreased ATP levels. Here, we further investigated the mechanisms by which ATP1A4 is involved in these effects. By using PCR and immunoblot analysis, we found that mouse sperm express isoform 1 of the sodium glucose transporter (SGLT1); and that inhibition of SGLT1 with phloretin reduced sperm glucose uptake and total sperm motility. Altogether, these results suggest that by maintaining the transmembrane Na^+ gradient, ATP1A4 controls sperm glucose uptake via a Na^+-dependent mechanism that is mediated by SGLT1. Since sperm highly depend on glucose metabolism for the generation of ATP, our findings support that ATP1A4 is a regulator of sperm energetics. These findings uncover a novel mechanism for ATP1A4, as an ion transport system that supports sperm physiology and fertility. [Supported by NIH R01 HD080423]

38. Pluripotent Stem Cell Models in the KUMC Transgenic Facility

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

39. TRAINEE ORAL PRESENTATION ONLY (NO POSTER)

Loss of REST in Uterine Leiomyoma leads to an Altered Progesterone Response

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Uterine Leiomyoma (UL) are benign tumors that arise in the myometrial smooth muscle layer of the uterus. UL are present in over 75% of women, often causing heavy bleeding, severe pain, and reproductive dysfunction. Despite their prevalence, there is no long-term pharmaceutical treatment for UL, due to the lack of understanding about the molecular pathogenesis of the disease. Extensive evidence has indicated an aberrant response to the steroid hormones, estrogen and progesterone, which play a critical role in the pathogenesis of UL. We have shown that REST (RE1 Silencing Transcription factor) is a tumor suppressor, and when lost in UL, it leads to de-repression of its target genes. We report here a critical novel link between loss of REST and an altered response to progesterone in UL. We found that a large number of REST target genes are also targets of progesterone receptor (PGR). Analysis of ChIP-sequencing data shows conserved REST binding sites within 100 base pairs of PGR binding sites on approximately 200 target genes. Additionally, we generated a uterus specific conditional knockout mouse (cKO) model of REST. When REST is lost in our cKO mouse (*Rest* $^{f/f}$ *Amhr2* $^{+/Cre}$), we see a UL phenotype and an altered response to progesterone in the uterus. This phenotype consists of hyperproliferation in the uterus throughout the estrus cycle despite normal estrogen and progesterone levels. Furthermore, we identify a direct interaction between REST and PGR in the healthy myometrium. This interaction is disrupted in leiomyoma leading to aberrant regulation of progesterone receptor target genes. Collectively, our results identify a novel link between progesterone receptor and REST-regulated tumorigenic pathways in UL. Furthermore, we provide two important preclinical mouse models, which show loss of REST leads to a UL phenotype. This research was supported by NIH Grants 1R01HD076450 and R01 HD094373.

40. Zika Virus Infection Induces Endoplasmic Reticulum Stress and Apoptosis in Placental Trophoblasts

Philma Glora Muthuraj, Aryamav Pattnaik, 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 woman can be vertically transmitted to the fetus via the placenta leading to Congenital Zika syndrome (CZS). CZS is characterized by microcephaly, retinal defects and intrauterine growth retardation. ZIKV induces placental trophoblast apoptosis leading to severe compromise in the growth and development of the fetus. Further, the molecular mechanism behind ZIKV-induced apoptosis in placental trophoblasts is unknown. We hypothesize that accumulation of viral proteins in the endoplasmic reticulum could lead to sustained endoplasmic reticulum stress (ER stress) and trigger apoptotic events. Methods: HTR-8, a human normal immortalized trophoblast cell and human choriocarcinoma derived cell lines (JEG-3 and JAR) were infected with 0.1-1MOI ZIKV. Apoptosis was assessed by characteristic nuclear morphology staining with DAPI and caspase 3/7 activity. Results: We observed an increase in the mRNA levels of CHOP

and the spliced form of XBP1 gene, 16-24h post infection in trophoblast. We also observed an increase in the levels of ER stress markers such as p-IRE1α, p-eif2α, and activation of c-Jun N-terminal Kinase (JNK) and p38 mitogen- activated protein kinase (MAPK) after 16-24h of ZIKV infection in trophoblast . As prolonged ER stress can cause apoptosis, we observed a dramatic increase in trophoblast apoptosis 48h post infection. Mechanistically, inhibition of JNK by SP600125 or pan caspase by Z-VAD-FMK significantly blocked ZIKV-induced apoptosis in trophoblast. In conclusion, the mechanism of ZIKV-induced placental trophoblast apoptosis involves the activation of ER stress and MAPK activation.

41. Women's Attitudes Toward Vaccination During Preconception Care

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In 2019, the United States CDC reported the highest number of confirmed Measles cases since 1992. Pervasive anti-vaccine beliefs, in combination with the potentially fatal consequences of Rubella or Varicella infection during pregnancy, makes it increasingly important to clinically assess barriers to MMR and Varicella vaccination during preconception counseling. The primary outcome of this study was prevalence of non-immune status for Rubella and Varicella. Secondary measures were obtained from those with a negative immunity titer: self-reported attitudes, self-reported incidence of follow-up, recency of vaccine counseling, and knowledge of CDC vaccination recommendations. Cross-sectional surveys were administered via REDCap to all KU Advanced Reproductive Care clinic patients from January 2017 through June 2019 with negative Rubella or Varicella titer results. 1,767 patient records were reviewed. 11.3% (n=200) showed non-immune status to either Rubella and/or Varicella. 7.2% (n=124) and 4.5% (n=79) of records showed non-immune status to only Rubella or Varicella, respectively. Surveys administered to all non-immune patients achieved a 32.5% (n=65) response rate. 23.1% (n=15) of survey participants self-reported not receiving recommended vaccines following a negative titer result, the majority of which provided rationale of not wishing to further delay fertility treatment (53.3%, n=8). On average, respondents underestimated their knowledge of MMR and Varicella CDC vaccine recommendations. 67.7% of respondents stated that they would be open to further vaccine education from their providers. The prevalence of non-immune persons in the study population fell within the range for sufficient herd immunity against Rubella (<13-15%). Our study results indicate most patients would respond positively to further vaccine education from their clinicians during pre-conception counseling. The risk/benefit analysis of postponing fertility treatment to achieve adequate levels of immunity should be a focused discussion with patients in the setting of advanced reproductive care.

42. Early Reduced Growth Rates Predict Delayed or Altered Puberty and May Adversely Affect Reproductive Longevity in Beef Heifers

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A population of cows that have excess androstenedione (A4; High A4) in follicular fluid of dominant follicles and secreted from ovarian cortex media (30-fold>controls) has been identified. High A4 cows have similar theca molecular phenotypes to women with polycystic ovary syndrome (PCOS) including: irregular estrous cycles, increased ovarian inflammation, and reduced fertility. Because PCOS is identified at puberty, the manner heifers attain puberty was investigated. Heifers were classified using progesterone (P4) concentrations ≥ 1ng/ml to initiate puberty and continued cyclicity: 1) Typical- 378±2 day of age (DOA) (n=279); 2) Early-317±4 DOA (n=143); 3) Start-Stop- P4 ≥1ng/ml at 265±4 but discontinued cyclicity (n=91); 4) Non-Cycling heifers- no occurrence of P4 ≥ 1ng/ml during sampling period (n=98). Start-Stop and Non-Cycling heifers also had excess A4 secretion from ovarian cortex cultures similar to High A4 cows. Thus, our hypothesis was that early growth traits may be adversely altered in Non-Cycling and Start-Stop heifers leading to reduced reproductive maturation and performance compared to Early/Typical heifers. Weaning weight ($p=0.017$) was reduced in Start-Stop heifers and yearling weights ($p=0.0074$) was reduced in Start-Stop and Non-Cycling compared to Typical/Early heifers. Non-Cycling heifers had the greatest Antral Follicle Counts ($p<0.0001$) with reduced uterine horn diameter ($p=0.0053$) compared to Typical (Control, $p<0.0001$) heifers. There was a lower proportion of Start-Stop and Non-Cycling heifers with a reproductive tract score of 5 compared with Typical/Early heifers, and reduced response to prostaglandin synchronization resulting in fewer calves in the first 21 days of the breeding season in the Non-Cycling group. Interestingly, heifers in the Start-Stop group that do not regain cyclicity have similar growth and reproductive traits as the Non-Cycling heifers. Taken together, reduced growth and maturation observed in the Start-Stop and Non-Cycling heifers is initiated early in development and adversely affects timing of reproductive maturity and longevity in these heifers.

43. TRAINEE ORAL PRESENTATION ONLY (NO POSTER)
Atypical Protein Kinase C iota (PKCiota) is Essential for the Establishment of the Maternal-Fetal Exchange Interface during Mammalian Development
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In-utero mammalian development relies on the establishment of the maternal–fetal exchange interface, which ensures transportation of nutrients and gases between the mother and the fetus. This exchange interface is established via development of multinucleated syncytiotrophoblast cells (**SynTs**) during placentation. In mouse, SynTs develop via differentiation of the trophoblast progenitor cells (**TSPCs**) of the placenta primordium and in human; SynTs are developed via differentiation of villous cytotrophoblast progenitors (**CTBs**). Despite the critical need in pregnancy progression, conserved signaling mechanisms that ensure SynT development are poorly understood. Herein, we show that Atypical Protein Kinase C iota (**PKCiota**) plays an essential role in establishing the SynT differentiation program in trophoblast progenitors. Loss of PKCiota in mouse TSPCs abrogates SynT development leading to embryonic death at ~E9.0. We also show that PKCiota-mediated priming of trophoblast progenitors for SynT differentiation is a conserved event during human placentation. PKCiota is selectively expressed in the first-trimester CTBs of a developing human placenta. Furthermore, loss of PKCiota in CTB-derived human trophoblast stem cells (**Human TSCs**) impairs their SynT differentiation potential both *in vitro* and after transplantation in immunocompromised mice. Our mechanistic analyses indicate that PKCiota signaling maintains expression of GCM1, GATA2, and PPARG, which are key transcription factors to instigate SynT differentiation programs in both mouse and human trophoblast progenitors. Our study uncovers a conserved molecular mechanism, in which PKCiota signaling regulates establishment of the maternal-fetal exchange surface by promoting trophoblast progenitor to SynT transition during placentation.

44. The Function of ACTC1 in an in vitro Model of Human Placentation
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Early human placentation, from implantation to primary villous formation, is a difficult time period to study, as this is an inaccessible time point of pregnancy. The BAP model (**B**MP4+**A**83-01+**P**D173074), in which human embryonic stem cells (hESC) are differentiated to trophoblast, exhibits many features of placental trophoblasts at this early time point. One common feature we have discovered is the expression of a cardiac actin gene, *ACTC1*. *ACTC1* is expressed in cardiac muscle and vascular endothelium, as well as skeletal muscle cells undergoing fusion. The function of ACTC1 in trophoblast cells is unknown. Using CRISPR Cas9 technology, we knocked down *ACTC1* in hESC cell line H1 and treated H1 control and knockdown cells with BAP to determine the role of ACTC1 in trophoblast differentiation. Preliminary results show dramatic knock down of ACTC1 by western blot analysis. Gross morphology of the colonies on days 6 and 8 of BAP treatment reveals defective syncytialization and an expansion of cytotrophoblast numbers compared to non-transfected H1 controls. In control H1, expression of CDH1 declines over time in both Western blot and immunofluorescent analyses, indicating syncytialization. In ACTC1 knockdown cells, a pilot experiment showed that CDH1 levels at 6 days of BAP differentiation are 2.5 fold higher in *ACTC1* knockdown #2 (the most robust knock-down of ACTC1) than in unaltered H1 controls analyzed via western blot. Secreted CGB levels are significantly decreased in all *ACTC1* altered cell lines after 6 days BAP treatment compared to unaltered, H1 controls (2,050-2,700 mIU/ug DNA vs. 24,200 mIU/ug DNA; $p < .0002$). We conclude from these preliminary results that *ACTC1* may be required for the fusion of cytotrophoblast to syncytiotrophoblast and its misexpression could have implications for early trophoblast development in humans.

45. Single Cell Interrogation of the Maternal-Placental Interface
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The hemochorial placenta is a site of dynamic interplay between maternal cells and trophoblast cells. These cells cooperate to establish an interface required for nutrient delivery to promote normal fetal growth. The rat possesses a hemochorial placenta with deep trophoblast cell invasion into the uterus, similar to the human. Trophoblast cell invasion facilitates uterine spiral artery remodeling necessary for adequate blood supply to the fetus. Insufficient trophoblast cell invasion can lead to pregnancy complications such as early

pregnancy loss, intrauterine growth restriction, preeclampsia and preterm birth. In this study, we use single cell RNA sequencing (scRNA-seq) and single cell assay for transposase accessible chromatin sequencing (scATAC-seq) to characterize the transcriptome of the invasive trophoblast cell lineage, as well as other cell populations at the maternal-placental interface, a structure termed the metrial gland in the rat. We identified a robust set of transcripts that define invasive trophoblast cells (e.g. *Prl5a1, Prl7b1, Tpbpa, Plac1, Tfap2c, Igf2, Cdkn1c, Tfpi*), as well as transcripts that uniquely identify endothelial (e.g. *Cdh5, Egfl7, Adgrl4, Rasip1*), vascular smooth muscle (e.g. *Acta2, Myl9, Tagln, Myh11*), natural killer (e.g. *Nkg7*, *Prf1, Gzmb, Gzmm*), and monocyte/macrophage (e.g. *Fcgr3a*, *Lyz2, Aif1, Tyrobp, Cybb*) cell clusters. Expression of a prominent subset of rat invasive trophoblast cell transcripts is conserved in the invasive extravillous trophoblast cell lineage of the first trimester human placenta (e.g. *Fstl3, Igf2, Cdkn1c, Tfpi, Ascl2, Mmp12, Cited2, C1qtnf6*). We also identified accessible regions of chromatin and DNA binding motifs uniquely associated with each of the cellular constituents of the metrial gland. ASCL2, AP1, TFAP2C, and ATF1 DNA binding motifs are prevalent in accessible regions of the invasive trophoblast cell clusters. These findings provide a foundational dataset to identify and interrogate key conserved regulatory mechanisms essential for development and function of an important compartment within the hemochorial placentation site that is essential for a healthy pregnancy. (Supported by HD020676, HD079363, HD099638; Sosland Foundation)

46. Impact of High Fat Diet-Induced Obesity on Ovarian Chemical Metabolism Proteins in Rats

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In the United States, obesity affects 20% of girls and 40% of women, with higher rates in some minority populations. Obesity causes negative female reproductive effects, including poor oocyte quality, infertility, miscarriage, and offspring birth defects. Chemicals and their metabolites may affect ovarian function. Our previous work has demonstrated that hyperphagia-induced obesity is involved in the alteration of ovarian proteins related to chemical metabolism in mice. We hypothesized that ovarian chemical metabolism protein abundance would be altered by obesity induced by a high-fat diet in rats. Female Wistar rats from 4 to 22 weeks of age were fed a control diet (CT) or a 60% Kcal high-fat diet (HFD) and body weight was greater in the HFD-diet fed rats. Western blotting was performed to quantify ovarian protein abundance of insulin receptor (INSR), glutathione S-transferase Pi (GSTP1), cytochrome P450 2E1 (CYP2E1), and microsomal epoxide hydrolase 1 (EPHX1). Image J software was used to performed densitometric analysis. HFD-induced obesity did not affect ovarian abundance of INSR, GSTP1, or CYP2E1 ($P > 0.05$). However, EPHX1 was modestly increased ($P < 0.05$) in the ovaries of the HFD-fed compared to the CT-fed rats. A non-targeted approach used LC-MS/MS and 12 proteins involved in chemical metabolism were altered by HFD-induced obesity (decreased: ORM1, CES1C, YBX1, NAMPT, and S100A10; increased: CYP5A, DPEP1, YWHAZ, HADH, EPHX1, APOA1, and P4HB). We have previously demonstrated chemical detoxification or bioactivation in a chemical-specific manner by ovarian EPHX1. Increased ovarian EPHX1 protein induced by obesity in this and other obesity models support the hypothesis that obesity causes negative reproductive female effects by altering ovarian chemical metabolism. Supported by funding from the Iowa State University Bailey Career Development Award to AFK, the Fulbright Foreign Student Program to EGA and the University of Missouri F21C program funding to PS.

47. Increased Circulation of Pro-Inflammatory Cytokines Alters Steroidogenesis in Ovarian Somatic Cells in Beef Cows

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Systemic metabolic stress may lead to lipopolysaccharide (LPS) leak from the gut which subsequently induces expression of pro-inflammatory cytokines through activation of the toll-like receptor 4 (TLR4). Systemic inflammation may contribute to ovarian inflammation, and result in altered steroid production and decreased oocyte competency. Previous *in vitro* studies demonstrated that LPS suppresses androgen production in bovine theca cells. Our hypothesis is that cows with increased circulating pro-inflammatory cytokines will have altered steroidogenesis in ovarian somatic cells. To test this hypothesis, estrous cycles of multiparious Red Angus beef cows (n = 8) were synchronized with two injections of prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) 14 days apart. Cows were ovariectomized and blood collected via coccygeal venipuncture and plasma used for cytokine and LPS analysis. Follicular fluid (FF) was aspirated from follicles measured ≥ 7 mm and flash frozen for subsequent cytokine and steroid hormone analysis. Theca cells from large follicles were micro-dissected, flash frozen, and RNA extracted. We identified a population of cows with increased circulating TNFα (≥1000 pg/mL; High TNFα, 5748.6 ± 2810.6 pg/mL, n = 4; Control, 534.1 ± 153.2 pg/mL, n = 4). High TNFα cows also had a

significant increase in other circulating pro- and anti-inflammatory cytokines, including IL-1α ($P < 0.032$), IL-F5 ($P < 0.027$), IL-13 ($P<0.040$), and IL-21 ($P<0.063$). Interestingly, there were no significant differences between pro- and anti-inflammatory cytokines in the FF of High TNFα and Control cows. There were no differences in LPS concentrations in the plasma and FF of High TNFα and Control cows. In the FF of High TNFα cows, estradiol (E2) and progesterone (P4), were significantly increased. Conversely, androstenedione (A4), the predominant androgen produced in bovine species, was significantly decreased in High TNFα cows compared to Control cows ($P < 0.02$). There were no significant differences in the expression of steroidogenic enzymes (CYP17, CYP11, HSD3B, HSD17B) in the theca cells of High TNFα and Control cows. Collectively, our data suggests that increased circulating pro-inflammatory cytokines, in an LPS-independent mechanism, positively regulates E2 and P4 synthesis in granulosa cells. Conversely A4 synthesis by theca cells is inhibited which may be due to reduced luteinizing hormone (LH) signaling.

48. Na,K-ATPase α4 Undergoes Phosphorylation During Sperm Capacitation

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Na,K-ATPase α4 (ATP1A4) is an integral plasma membrane protein responsible for the exchange of Na^+ and K^+ between the cell and its environment. ATP1A4 is only found in male germ cells of the testes and spermatozoa, where it is necessary for sperm motility and sperm capacitation. Our previous data revealed that ATP1A4 membrane levels, as well as its activity, increase when sperm undergo capacitation *in vitro*, suggesting that regulatory mechanisms are operating to adjust ATP1A4 to the functional needs of the male gamete. Sperm cells are believed to be transcriptionally silent and they use posttranslational phosphorylation to regulate their activity and function. Here, we explored the phosphorylation of ATP1A4 both at serine/threonine and tyrosine residues in rat sperm. Using immunoprecipitation and western blot analysis, we found that ATP1A4 is phosphorylated under non-capacitating and capacitating conditions. However, we found specific differences in the levels and the pattern of protein phosphorylation between both conditions. Specifically, ATP1A4 phosphorylation of tyrosine residues increased and threonine phosphorylation remained constant, when non-capacitated and capacitated samples were compared. These results agreed with tandem mass spectroscopy (MS/MS), which identified unique phosphorylation sites in non-capacitated (T169, T450 and T645) and capacitated (S222, S223, T225, S228, Y427, T492, T602 and T609) sperm. These data show that ATP1A4 is post-translationally modified by phosphate addition and that the protein is subjected to a complex pattern of phosphorylation that depends on the state of the cells. Further experiments are underway to establish the functional relevance of ATP1A4 phosphorylation, concerning both the activity of the pump and its role during sperm capacitation. [Supported by NIH R01 HD080423]

49. Development of Novel Mouse Models Using CRISPR Genome Editing Approaches

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

50. Effects of GnRH-II on Spermatogenic Function of Swine

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The second mammalian form of GnRH (GnRH-II) and its cognate receptor (GnRHR-II) are produced in only one livestock species, the pig. Paradoxically, however, the interaction of GnRH-II with its receptor does not stimulate gonadotropin secretion. Instead, both are abundantly produced within the porcine testis, suggesting an autocrine/paracrine interaction. Our laboratory previously detected GnRH-II within porcine seminal plasma and GnRHR-II on the connecting piece of ejaculated spermatozoa, a region associated with motility, hyperactivation and fertilization. The objective of this study was to examine the effect of GnRH-II on porcine sperm function. In a pilot study (Exp. 1), ejaculates were collected weekly from mature, crossbred boars (n = 2–3) for 5 weeks. Semen samples were diluted in commercial extender (37.5 x 10^6 sperm/mL), treated with either phosphate-buffered saline (PBS; control) or D-ala^6 GnRH-II (1 µM) and stored at 17ºC for 6 days post-collection. Sperm were analyzed prior to treatment (Day 0) as well as on Day 3 and Day 6 post-collection. Sperm motility parameters (total and progressive) were assessed via computer-assisted sperm analysis (CASA); sperm morphology was evaluated via phase contrast microscope. Main effects of treatment were detected; treatment with GnRH-II tended to affect total and progressive motility of porcine spermatozoa ($P < 0.10$). The percentage of progressively motile sperm was enhanced in samples treated with GnRH-II compared with control samples (64.2 ± 1.7% vs. 62.1 ± 1.5%; $P = 0.062$). Likewise, total motility was greater in GnRH-II treated sperm samples compared with PBS-treated samples (81.5 ± 2.1% vs. 80.4 ± 2.1; $P = 0.0910$). No differences in sperm morphology were evident between treatment groups ($P > 0.10$). In Exp. 2, ejaculates from white crossbred boars (n = 3) were diluted in a commercial semen extender (37.5 x 10^6 sperm/mL), treated with increasing concentrations (0.0001, 0.001, 0.01, 0.1, 1 and 10 µM) of a GnRH antagonist that inhibits both the classical GnRH-I receptor (GnRHR-I) and GnRHR-II (SB-75, cetrorelix), and stored at 17ºC until CASA on Day 6 and 8 post-collection. Saline-treated samples were employed as a control. In this experiment, CASA was utilized to determine measures of sperm motion (total motility, progressive motility, slow and static), morphology [normal morphology (NM), bent tail, coiled tail, distal droplet, proximal droplet (PD), distal midpiece reflex, elongation and area], and kinematics [length of average path (DAP), length of straight line path, length of curvilinear path (DCL), average path velocity (VAP), straight line velocity, curvilinear velocity (VCL), straightness (STR), linearity (LIN), amplitude of lateral head displacement (ALH), beat cross frequency and wobble (WOB)]. On Day 6, sperm characteristics in samples treated with 10 µM SB-75 were significantly reduced (NM, DAP, DCL, VAP, VCL, ALH) or elevated (PD, WOB and area) compared with control samples. The same differences (except ALH; $P < 0.10$) for the 10 µM SB-75 treatment were detected on Day 8; however, total motility, slow, static, STR and LIN were also reduced in SB-75 treated samples ($P < 0.05$). Together, these data suggest that GnRH-II within seminal plasma mediates spermatogenic function in swine, likely via interaction with its receptor on the connecting piece. Supported by USDA/NIFA AFRI funds (2017-67015-26508; BRW).

51. Cigarette Smoke Exposure Activated Aryl Hydrocarbon Receptor Signaling in Human Trophoblasts and Altered Markers of Growth and Differentiation

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Although the association of cigarette smoke with increased risk of poor birth outcomes such as low birth weight and neonatal mortality is well-established, we still do not understand the exact mechanism of these outcomes. Cigarette smoke contains thousands of chemical compounds that are known or suspected to cause disease. The placenta is an essential organ for fetal development. Hemochorial placentation is characterized by the differentiation of trophoblast cells specialized to interact with uterine and fetal vascular beds. Human trophoblast stem (TS) cells provide a new *in vitro* model for testing the effects of environmental toxins such as cigarette smoke condensate (CSC) on differentiation and function. In this study, we utilized RNA-Seq analysis to examine changes in gene expression in human TS cells following exposure to CSC. In total, we identified about 900 transcripts that were reported to be significantly ($p_{adj} < 0.05$) altered. *CYP1A1* and *CYP1B1* were among the top induced transcripts indicative of functional aryl hydrocarbon receptor (AhR) signaling in human TS cells. The top affected associated network includes genes mapping to cellular assembly and organization, DNA replication, repair, and cellular development. Relevant transcripts that were significantly downregulated by CSC include transgelin (*TAGLN*) which is a marker of smooth muscle differentiation; actin alpha 1 (*ACTA1)* which plays a role in cell motility, structure and integrity; heart and neural crest derivatives expressed 1(HAND1) which is an essential transcription factor for trophoblast cell differentiation; and tissue factor pathway inhibitor (*TFPI2)*. Significant increases in transcripts such as APC membrane recruitment

protein 2 (*AMER2)*, a negative regulator of canonical Wnt signaling; inhibitor of DNA binding 2 (*ID2*), which antagonizes the activities of basic helix-loop-helix transcription factors, and glial cell missing 1 (*GCM1),* which is involved in the control of placenta-specific gene expression, could affect human TS cell differentiation. More noticeable was the significant decrease in achaete-scute family bHLH transcription factor 2 *(ASCL2)* which is essential for the differentiation of progenitor cell populations into specialized trophoblast cell types. Taken together, these data suggest that gene expression in human TS cells is significantly altered by cigarette smoke exposure including AhR pathway and genes encoding proteins implicated in the regulation of trophoblast cell differentiation and function. These alterations may impair proper development and function of the placenta and pregnancy outcome. Ongoing studies are assessing the specific role of AhR signaling in trophoblast differentiation and function. Supported by the Cross Family Foundation CPGM Pilot Award and NIH R01ES029280.

52. A Subcompartment Analysis of Oxidative Stress in Ovarian Reproductive Aging

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Environmental toxicants cause tissue damage, in part through reactive oxygen species (ROS) formation. ROS also contributes to aging. Previous work from our group revealed an increase in ovarian fibrosis in old mice compared to young mice and this is associated with a significant decrease in total ovarian hyaluronan. Hyaluronan (HA) is a large (>2 MDa) extracellular matrix (ECM) glycosaminoglycan that helps to maintain tissue homeostasis and is abundantly expressed in the ovary. In extra-ovarian tissues, HA depolymerization to low molecular weight fragments (<250kDa) by hyaluronidases and ROS can aid in tissue repair or, if persistent, can promote inflammation and fibrosis, both of which are hallmarks of ovarian aging. We hypothesized that ovarian ROS would be associated with HA loss in an age- and compartment-specific manner. To test this hypothesis, oxidative stress and antioxidant gene expression in whole ovaries or isolated ovarian stromal tissue from reproductively young (6-12 weeks) and old (14-17 months) mice were analyzed using a pathway targeted QPCR array, followed by QPCR-based gene expression validation. 4-hydroxynonenal (4-HNE) immunohistochemistry was used to detect ROS-mediated ovarian lipid peroxidation. HA was localized in ovaries from young and old mice followed by subcompartment quantification of HA-positive staining. In whole ovaries, the oxidant production related genes Ncf1 and Ncf2 were not different between reproductively old and reproductively young mice. The antioxidant genes Txn1 and Gpx6 were unchanged between age cohorts, but another antioxidant gene Hmox1 was significantly increased in ovaries from reproductively old vs young mice. In contrast to whole ovaries, the ovarian stroma from reproductively old mice had a significant increase in Ncf1 and Ncf2 compared to ovarian stroma from young mice. In addition, Txn1 and Hmox1 were significantly increased, while Gpx6 was significantly decreased in ovarian stroma of reproductively old mice when compared to reproductively young mice. 4-HNE adducts were localized to the stroma, follicles, corpora lutea, and theca cells in both age cohorts; only theca-associated 4-HNE was greater in reproductively old mice. This finding was intriguing since we also observed a significant HA decrease in the theca layer in old mice vs young mice. Collectively, these data suggest that increased theca cell oxidative stress could contribute to HA loss in this ovarian subcompartment, but not in the non-theca stromal cell compartment, with advanced reproductive age. In conclusion, our findings indicate that ROS could be a potential mechanism by which HA is degraded in ovarian reproductive aging. This work was supported by: R01HD093726, P20GM103549 and P30GM118247

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NOTES

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