PROGRAM BOOKLET

ASPEN PERINATAL BIOLOGY SYMPOSIUM

St. Regis Aspen Resort | Aspen, CO | August 28-31, 2022

Developmental Programming – Putting the Pieces Together

SAFETY STATEMENT

The Aspen Perinatal Biology symposium is committed to providing a safe, productive, and welcoming environment for all conference participants and staff. All participants, including, but not limited to, attendees, speakers, volunteers, NABT staff, service providers, and others are expected to abide by the following:

No Unacceptable behavior as defined by:

- Harassment, intimidation, or discrimination in any form.
- Physical or verbal abuse of any attendee, speaker, volunteer, exhibitor, staff member, service provider, or other meeting guest.
- Examples of unacceptable behavior include, but are not limited to, verbal comments related to gender, sexual orientation, disability, physical appearance, body size, race, religion, national origin, inappropriate use of nudity and/or sexual images in public spaces or in presentations, or threatening or stalking any attendee, speaker, staff member, service provider, or other meeting guest.
- Disruption of presentations at sessions, or at other events organized by the Perinatal Biology Symposium at the meeting venue, hotels, or other Perinatal Biology Symposium -associated facilities. The Perinatal Biology Symposium has zero-tolerance for any form of discrimination or harassment, including but not limited to sexual harassment by participants or our staff at our meetings.

The Perinatal Biology Symposium has zero-tolerance for any form of discrimination or harassment by participants or our staff at our events. This includes but is not limited to sexual harassment or unwelcome conduct based on race, color, religion, sex (including pregnancy), gender identity, nationality, age, disability, or genetic information.

If you experience harassment or hear of any incidents of unacceptable behavior, The Perinatal Biology Symposium asks that you inform the conference organizers-Drs. Kristen Govoni, (**kristen.govoni@uconn.edu**) Michelle Bacck (**Michelle.Baack@sanfordhealth.org**), Rebecca Simmons (**rsimmons@pennmedicine.upenn.edu**) so that appropriate action can be taken. We reserve the right to take any action deemed necessary and appropriate, including immediate removal from the meeting without warning or refund, in response to any incident of unacceptable behavior, and The Perinatal Biology Symposium reserves the right to prohibit attendance at any future meeting. have questions, concerns or complaints related to harassment are also encouraged to contact the conference organizers or the HHS Office for Civil Rights (OCR). Information about how to file a complaint with HHS OCR is at OCR's webpage, (**Filing a Civil Rights Complaint**). filing a complaint with the conference organizer is not required before filing a complaint of discrimination with HHS OCR, and that seeking assistance from the conference organizer in no way prohibits filing complaints with HHS OCR.

Filing a complaint with the conference organizers is not required before filing a complaint of discrimination with HHS OCR, and that seeking assistance from the conference organizer in no way prohibits filing complaints with HHS OCR. Individuals can notify NIH about concerns of harassment, including sexual harassment, discrimination, and other forms of inappropriate conduct at NIH-supported conferences (see NIH's **Find Help webpage**).

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ABOUT THE MEETING

Understanding the complex and interactive nature of environmental and genomic influences on reproduction and development across the lifespan necessitates interdisciplinary research including meetings that brings together clinicians, as well as applied and basic scientists in various disciplines, from agricultural to biomedical and related fields.

The theme of the 2022 Aspen Perinatal Biology Symposium, which is the 9th in a series, is "Developmental Programming – Putting the Pieces Together". The meeting will not only highlight regulators of healthy development, but also common mechanisms that determine the long-term consequences in offspring with compromised development. This Symposium will bring together clinicians and scientists, and established senior and junior investigators, from clinical medicine, basic research and applied livestock production, from around the world to report and discuss their findings in an atmosphere conducive to frank yet amicable exchange. Scientific exchange will occur across all levels via plenary sessions, poster sessions, trainee workshops, and informal discussions, with time also dedicated to presentations by and recognition of trainees and early career investigators.

The Program is designed very much like the successful past meetings, with a Keynote Lecture, the 3rd DJP Barker Memorial Lecture, 8 plenary sessions, as well as Career Development workshops each morning, and evening poster sessions. The plenary sessions will be in the morning and evening, leaving a large block of time in the afternoon and early evening for networking and informal discussions.

This year the meeting has moved back to Aspen, Colorado and the venue for the meeting is The St. Regis Aspen Resort. Importantly, this change in venue from the past 3 meetings allowed for accommodations to meet Covid-19 polices to provide a safe environment for attendees to interact and network during the entire meeting. Aspen and the surrounding area have a host of summertime activities such as incredible dining, shopping, live music, and outdoor activities including hiking, biking, rock climbing, picnics, paragliding, balloon rides, and day trips to Maroon Bells, Roaring Fork River, the John Denver Sanctuary or nightlife at Belly Up. Information about Aspen in the summer is found here: https://www.colorado.com/articles/10-awesome-ways-experience-aspen-summer

We are very pleased you chose to attend this unique meeting and hope your experience in Aspen is as exciting as we have found it to be!

The Organizing Committee

ORGANIZING AND SCIENTIFIC COMMITTEES

ORGANIZING COMMITTEE

- **Kristen E. Govoni**, Co-Chair (kristen.govoni@uconn.edu) – Associate Dean of Academic Program in the College of Agriculture, Health, and Natural Resources, Associate Professor in the Department of Animal Science at the University of Connecticut and member of the Fetal Programming Group at UConn. Dr. Govoni attended the 2016 Perinatal Biology Symposium as a presenting author on a poster and served on the Scientific Planning Committee of the 2019 Perinatal Meetings. Dr. Govoni has served on the planning committee for the American Society of Animal Science (ASAS) Cell Biology Symposium for the past 5 years, organized the Northeast Graduate Student paper competition for over 5 years, and served as the Northeast Director for the ASAS and Chair of the Publications Committee for the ASAS. Dr. Govoni has secured over $2 million in funding, published 44 peer-reviewed papers, and mentored 14 graduate as primary advisor and 15 as associate advisor. She has received numerous awards recognizing her teaching, mentoring, and service to the field of Animal Science.
- **Rebecca Simmons**, Co-Chair (rsimmons@pennmedicine.upenn.edu) – Hallam Hurt Professor in Neonatology, Center for Research on Reproduction and Women's Health at the Perelman School of Medicine, University of Pennsylvania. Her research program aims to understand the underlying molecular mechanisms that link fetal growth restriction to the later development of obesity and type 2 diabetes in adulthood. She has been actively involved in the Perinatal Biology Meeting since 2007 and was on the Scientific advisory committee for the 2019 meetings. Dr. Simmons has extensive experience organizing national meetings including the Perinatal Research Society, the American Diabetes Association, the U.S. and the International DOHaD Societies. In addition, she has organized multiple local symposia at the University of Pennsylvania.
- **Michelle Baack**, Co-Chair (michelle.baack@sanfordhealth.org) – Professor and Chair of Pediatrics at the University of South Dakota Sanford School of Medicine and Associate Scientist, Environmental Influences on Health and Disease, Sanford Research. She served as the Division Chief of Research before her new appointment as the Chair of Pediatrics in 2021. As a neonatologist and Sanford Health's site PI for NICHD Neonatal Research Network studies, she leads both clinical and basic research. Her laboratory's goal is to understand the role of mitochondria and metabolism in the developmental origins of health and disease (DOHaD). She has been actively involved in DOHaD research since 2011 and serves as a peer reviewer in the field including as a member of the NIH Nutrition and Metabolism in Health and Disease (NMHD) study section. She is a full member of the Perinatal Research Society, Pediatric Academic Society and the Society of Neonatal and Perinatal Medicine (SONPM) within the American Academy of Pediatrics. Her trainees had opportunities to present their work at the 2019 Perinatal Biology Meeting and found the platform to be exceptional for scientific exchange, networking and career development.

SCIENTIFIC COMMITTEE

- **Laura Brown** – Associate Professor, Department of Pediatrics, Division of Neonatology, University of Colorado
- **Lisa Joss-Moore** – Professor, Department of Pediatrics, Division of Neonatalogy, University of Utah
- **Andrew Norris** – Professor, Department of Pediatrics, Division of Pediatric Endocrinology and Diabetes, Department of Biochemistry and Molecular Biology, University of Iowa
- **Jeff Segar** - Professor, Department of Pediatrics, Division of Neonatology, Medical College of Wisconsin – Milwuakee
- **Sarbattama Sen** - Assistant of Pediatrics, Harvard Medical School
- **Sara Pinney** – Pediatric Endocrinologiest, Division of Endocrinology and Diabetes, Children's Hospital of Philadelphia
- **Maria (Hoffman) Peterson** - Assistant Professor, Department of Fisheries, Veterinary, and Animal Science, University of Rhode Island– URI
- **Dustin Yates** – Assistant Professor, Department of Animal Science, University of Nebraska-Lincoln
- **Carl Dahlen** – Associate Professor, Department of Animal Sciences, North Dakota State University

SPONSORS

The 2022 Perinatal Biology Symposium is completely self-funded—
that is, the meeting is funded through grants and gifts from our Sponsors,
which we acknowledge with gratitude on the following pages:

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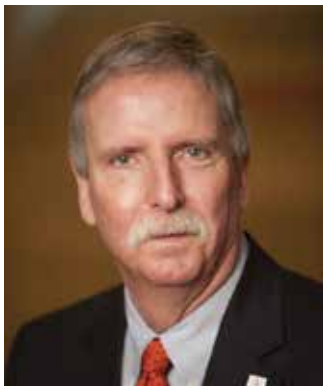
SPEAKER BIOS

DR. RYAN ASHLEY is a Professor of Reproductive Biology at New Mexico State University (NMSU) in the Department of Animal and Range Sciences. He grew up on a cattle ranch in eastern New Mexico where he was very active showing and judging livestock in 4H and FFA, while also playing basketball, baseball, and track. He earned a BS and MS in Animal Science from NMSU and then went to Colorado State University (CSU) for his PhD training in Biomedical Sciences under Dr. Terry Nett. After his doctorate, Dr. Ashley joined the laboratory of Dr. Thomas (Tod) Hansen for a post-doctoral fellowship at CSU before joining the Animal Science faculty at NMSU in 2010. A primary focus of Dr. Ashley's research program is elucidating the roles of the CXCL12/CXCR4 chemokine signaling axis during placental development with the long-term goal of improving pregnancy outcomes in livestock and women. Impaired placental development is a major underlying cause of pregnancy complications including intrauterine growth restriction and preeclampsia, and a leading cause of maternal, fetal, and neonatal morbidity and mortality worldwide. Using sheep as a model, his research addresses gaps in knowledge relevant to agricultural production and human health with the goal of identifying novel targets for diagnosis and treatment of pathological pregnancies.



DR. FRANK F. (SKIP) BARTOL, a Professor in the Department of Anatomy, Physiology and Pharmacology in the College of Veterinary Medicine, joined the Auburn University (AU) faculty in 1983. A Virginia native, he received the BS degree from Virginia Tech, MS and PhD degrees from the University of Florida through the Interdisciplinary Reproductive Biology Program, and advanced training in molecular biology in the Center for Animal Biotechnology at Texas A&M University. He has served as Associate Dean for Research and Graduate Studies in the AU College of Veterinary Medicine since 2009. His research in reproductive physiology and developmental biology, leading to proposal of the *'lactocrine hypothesis'* for maternal programming of postnatal development, has been supported by competitive grants from the National Institute of Food and Agriculture, the National Science Foundation, and both private and international agencies. In 2005 and again in 2020, Dr. Bartol was named a Donald Henry Barron Lecturer by the University of Florida Perinatal Biology Research Program. He was named Alumni Professor at AU in 2009, and in 2017 he was recognized as a Distinguished Alumnus by the College of Agriculture and Life Sciences at Virginia Tech. He is a member of the American Association for the Advancement of Science, the American Society of Animal Science, the American Society for Reproductive Immunology, the Society for the Study of Reproduction, and the Society for Theriogenology. An advocate for the responsible use of animals in research and education, Bartol is a contributing author to the Guide for the Care and Use of Agricultural Animals in Research and Teaching (3rd and 4th Editions), has served as Chair of the Animal Ethics Subcommittee for the Society for the Study of Reproduction, and is currently a voting member of the FASEB Animals in Research and Education Subcommittee to the Science Policy committee (2022-2025).

DR. COLIN C. CONINE, PH.D., is an Assistant Professor of Genetics and Pediatrics at the University of Pennsylvania Perelman School of Medicine and Division of Neonatology at the Children's Hospital of Philadelphia. He is a faculty member of the Penn Epigenetics Institute, the Institute of Regenerative Medicine, and the Center for Research on Reproduction of Women's Health, as well as an Investigator of the Center of Excellence in Environmental Toxicology. Dr. Conine received his B.S. in Biochemistry from the University of Rochester and Ph.D. from the University of Massachusetts Medical School. During his Ph.D. in Craig Mello's lab he found that small non-coding RNAs in sperm can transmit epigenetically inherited phenotypes to offspring. During his postdoc in Oliver Rando's lab, at UMass Medical, he found that sperm small RNAs in mammals can also transmit non-genetically inherited information to offspring. Dr. Conine started his lab at UPenn and CHOP in 2020. His research focuses on how RNAs function in male fertility, inheritance, and development. He was named a 2021 Pew Biomedical Scholar.

DR. GEOFFREY E. DAHL is the Harriet B. Weeks Professor in the Department of Animal Sciences at the University of Florida, Gainesville. He previously served as Chair of the Department for 12 years, serving as liaison between the university, livestock producers, and allied industries in Florida.

Dr. Dahl conducts applied and basic research with direct impact on dairy production. Specific research interests include effects of photoperiod manipulation on production and health, the impact of frequent milking in early lactation on milk production, and heat stress abatement during the dry period on cow productivity and health. Those research efforts are disseminated through his Extension programming in the US and abroad. Indeed, Dr. Dahl has been invited to present his research findings in 20 countries and Geoff has active Extension program efforts in a variety of developing countries including Sri Lanka, Nepal, Rwanda and Ethiopia. Dr. Dahl has authored over 150 peer-reviewed papers and numerous symposium and popular press articles. He has trained 27 graduate students and post-doctoral fellows.

Dr. Dahl is a member of several professional and honorary societies including the American Dairy Science Association (ADSA), the American Society of Animal Science, the Society for the Study of Reproduction, American Association for the Advancement of Science (AAAS), and the Endocrine Society. He served as President of ADSA from 2018 to 2019. Geoff has received numerous awards including the *Award of Honor* from ADSA and is a *Fellow* in AAAS.

DR. CARL DAHLEN has been intimately involved in research efforts with a focus on reproduction, nutrition, and management of cattle and sheep since the year 2000. The emphasis of his current research program is to improve fertility in livestock species and to evaluate implications of nutrition and management strategies on reproductive and offspring outcomes. Dahlen joined the North Dakota State University faculty in 2010 as a Beef Cattle Extension Specialist where he engaged in integrated Extension and research efforts taking place on over 350 commercial beef operations. Dahlen was instrumental in developing innovative training methods that empower county, area, and state Extension personnel to better serve their beef-producing clientele. The unique mix of his research background and practical experience has led to several novel research techniques, data collection efforts, and training methodologies. Dahlen was an integral part of a team that developed and optimized a standing flank hysterectomy procedure that allows his group to achieve an exemplary combination of high-level science and fiscal responsibility. Publications using this model have been geared toward answering questions about developmental programming, focusing on implications of *maternal* nutritional management on offspring characteristics. In 2018 Dahlen transitioned to position that allowed him to dedicate more time to research, as well as teach undergraduate/graduate classes in reproductive physiology. A new facet of his research program has been dedicated to addressing whether *paternal* (i.e. sire) nutrition and management was not only impacting semen characteristics and molecular composition, but also implicit in offspring outcomes. Other recent efforts involve evaluating impacts of nutritional perturbations during gestation on offspring and transgenerational endpoints, and utilizing sheep as a biomedical model for women's vaginal health. Dahlen's efforts are supported by his wife Roberta and their sons, Arthur and Lyle.

DR. ELLEN DEMERATH received her PhD. in Biological Anthropology from the University of Pennsylvania and is Professor of Epidemiology and Community Health at the University of Minnesota, School of Public Health. Her research is at the interface of nutrition, human biology, and child development, and seeks to understand how maternal and early-life nutritional factors alter health trajectories across the life course. Her current studies focus on maternal nutrition and gestational diabetes in shaping human breast milk composition, and identifying nutritional indicators of preterm infant growth that predict neurodevelopmental outcomes. Dr. Demerath has published over 200 peer-reviewed articles and book chapters on human growth, nutrition, and obesity, and her research has been continuously funded by NIH since 2005. She has participated in expert panels on nutrition during pregnancy and infant adiposity sponsored by the National Institutes of Health and the National Academy of Sciences. Since 2013, she has directed the University of Minnesota Driven to Discover Research Facility, an innovative community outreach program that supports a wide range of human subjects research involving over 10,000 community participants per year.

DR. ANDREA EDLOW, MD, MSc is an Associate Professor of Obstetrics, Gynecology and Reproductive Biology at Harvard Medical School and a Maternal-Fetal Medicine specialist at Massachusetts General Hospital. Dr Edlow's laboratory focuses on the effects of maternal obesity and maternal immune activation on fetal brain development and offspring behavior, and how these effects are modified by fetal sex. Throughout the pandemic, Dr Edlow has investigated COVID-19 and the COVID-19 vaccines in pregnancy and lactation, including the effects of maternal SARS-CoV-2 infection on the maternal, placental and cord blood immune profile.

Lab website: https://massgeneral.link/AndreaEdlowLab
Twitter: @EdlowLab

DR. BRIGID GREGG, MD, is an Assistant Professor of Pediatrics in the Division of Endocrinology, Diabetes and Metabolism at Michigan Medicine.

Dr. Gregg received her MD degree from Case Western Reserve University and completed her pediatrics residency and pediatric endocrinology fellowship training at the University of Chicago and Kovler Diabetes Center. She then moved to the University of Michigan to pursue basic and translational metabolic disease research at the Caswell Diabetes Institute.

The Gregg lab is focused on characterizing early life events that predispose individuals to developing metabolic disease, with the ultimate aim of identifying interventions to improve metabolic outcomes in high risk individuals. The Gregg lab uses animal models along with biospecimens from a human mother infant cohort to study how nutritional influences in the neonatal/infancy period can have a long lasting impact on the risk of obesity, insulin resistance, pancreatic beta-cell dysfunction, diabetes, and NAFLD.

DR. FOLAMI IDERAABDULLAH, PhD completed her bachelor's degree in biology at The Pennsylvania State University. She earned her Ph.D. in Genetics & Molecular Biology at UNC Chapel Hill where she defined mouse strain genetic diversity and studied its role in parent of origin effects. She completed her postdoctoral training at the University of Pennsylvania in 2012 studying developmental epigenetics and the role of DNA regulatory elements in genomic imprinting. Her lab studies how gene-environment interactions in the fetal/developmental environment modulate the epigenome to program the trajectory of health & disease. Her lab's work has been instrumental in showing that early life exposure defines germ and somatic cell epigenetic profiles into adulthood. More importantly they show this effect is substantially modulated by parental genotype. This work supports the key tenets of DOHaD while highlighting the importance of considering the role of early exposures in Precision Medicine. Her research is supported by NIH grants through NIEHS & NIDDK. Her other roles include: Co-director - Developmental Disease group, UNC Center for Environmental Health and Susceptibility; Board of Directors - Genetics Society of America; and Primary Investigator - UNC training program, Educational Pathways to increase Diversity in Genomics.

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Website: https://www.med.unc.edu/genetics/directory/folami-ideraabdullah-phd/

DR. SONNET S. JONKER, PhD, is an Associate Professor at Oregon Health & Science University (OHSU), where she leads a lab studying the developing cardiovascular system in fetal and newborn sheep. She has published extensively on the proliferation and terminal differentiation of cardiac myocytes in the perinatal period, as well as coronary growth and function in the perinatal heart. The goal of her research is to discover how prenatal stress influences the structure and function of the heart for life, and to develop therapeutic approaches for infants with undergrown hearts and those with congenital defects.

DR. KYLIE KAVANAGH

DVM MS MPH FAAA, Associate Professor of Pathology, is a comparative physiologist whose research focus is the intersections between aging, nutrition and metabolism. She primarily uses nonhuman primate models with an emphasis on insulin resistance, diabetes, obesity, and the pro-inflammatory drivers that underpin these conditions. One unique model of accelerated aging and metabolic disease development is the radiation-survivor nonhuman primate which is a national resource held at Wake Forest School of Medicine. Senescence and microbial translocation are new directions in her geroscience program, and these sources of inflammaging are amendable to therapeutic interventions. She is the Director of the Nonhuman Primate program within the CTSI, is the PI of a T35 training program, and is on the executive committees for the Centers on Diabetes, Obesity and Metabolism, and the Vaccines at the Extremes of Aging. She holds funding from NIA, NHLBI, NIAID, NIDDK and DOD and engages with the industry partners to evaluate developing therapeutics for metabolic diseases. She has a wonderful team who deserve all the credit, all the time.

DR. HASAN KHATIB

is a professor of genetics in the Department of Animal and Dairy Sciences at the University of Wisconsin-Madison. His research focuses on understanding the contributions of epigenetics to production, reproduction, and health traits. More specifically, his research examines the transgenerational epigenetic effects of paternal and maternal nutrition on phenotypes of the next generations in livestock. His group recently demonstrated that DNA methylation patterns in the sperm were affected by a paternal diet and were transgenerationally inherited by subsequent generations in sheep. He is also interested in the identification of epigenetic markers as predictors of embryo development and fertility using non-invasive methods. Research methods used in his lab include embryo production, transcriptomics, whole-genome bisulfite sequencing, cell culture, gene editing, and epigenome editing. Dr. Khatib is the editor of the books "Livestock Epigenetics" and "Molecular and Quantitative Animal Genetics".

DR. CALEB LEMLEY is an Associate Professor in the Department of Animal and Dairy Sciences, Mississippi State University. He received a B.S. in Biochemistry in 2005 from West Virginia University. He received a M.S. in 2007 and a Ph.D. in 2010 in Reproductive Physiology from West Virginia University. Dr. Lemley was awarded the Lalor Foundation Postdoctoral Basic Research Fellowship followed by a USDA Postdoctoral Fellowship while investigating developmental programming in an ovine model at North Dakota State University from 2010 to 2012. Since joining the faculty at MSU in 2012, Dr. Lemley has secured approximately 7.2 million dollars in funding and published 62 peer-reviewed journal articles, 4 book chapters, and 125 conference abstracts. Recently he received the Excellence in Research faculty award from the Mississippi Agricultural and Forestry Experiment Station. His research at MSU focuses on reproductive endocrinology, developmental programming, and environmental influence on conceptus development.

DR. KRITHIKA LINGAPPAN MD MS PhD is Associate Professor at UPenn/CHOP in the department of Pediatrics, Division of Neonatology. Her unique niche is to elucidate the mechanisms sex-specific differences in neonatal hyperoxic lung injury with the goal to develop individualized therapeutic options to decrease morbidity in preterm babies. Sex-specific differences exist in various forms of organ injury in adults and children. Neonatal outcomes for males are worse than females for many diseases, including bronchopulmonary dysplasia (BPD). Dr.Lingappan has highlighted the critical role of sex as a biological variable in the outcomes in preterm babies and the molecular mechanisms underlying them.

DR. EMIN MALTEPE MD PHD. I am a pediatric physician-scientist at UCSF specializing in neonatology. My basic research lab has focused on the role of oxygen tension as a regulator of embryonic, fetal and placental development. I have sought to uncover mechanisms whereby hypoxia signaling pathways regulate normal development, contribute to the origins of pregnancy complications that drive ever growing numbers of preterm births, and drive disease processes such as pulmonary hypertension in newborn infants. As a practicing neonatologist, I have been driven by the challenges of translating research insights into patient care, especially in the uniquely challenging NICU environment. To address this important unmet need, I co-founded the Initiative for Pediatric Drug and Device Development (www.ipd3.org), a multi-institutional collaborative comprised of leaders in pediatrics and pharmaceutical sciences that functions as a "one-stop-shop" to advance drug and device development for pediatric indications. In this capacity, we have been working with non-profit and industry sponsors on multiple fronts, including neurotherapeutics for birth asphyxia, cardioprotective agents for infants undergoing repair of congenital heart defects, and oxygen delivery biotherapeutics for intrauterine hypoxic states.

DR. HANNAH MORGAN is currently a Research Fellow at the University of Nottingham, UK, working in the lab of Dr Adam Watkins. She obtained her BSc(Hons) in Physiology from the University of Newcastle in 2012 and started down the track of reproductive physiology research. She obtained a Masters in Maternal and Fetal Health at the University of Manchester in 2014 and established an interest in placental and embryo development. She received a PhD from the University of Glasgow in 2018, studying placental development and uterine vascular remodelling in a rat model of gestational hypertension. Her current work focuses on examining the impact paternal nutrition on pre-implantation embryo development, the formation of the placenta and growth of the fetus in *utero* in mice.

DR. LESLIE MYATT, PhD FRCOG is Professor of Obstetrics and Gynecology, Director of Perinatal Research, Deputy Director and Endowed Professor in the Bob and Charlee Moore Institute of Nutrition and Wellness at the Oregon Health & Science University, Portland. He has directed NIH-funded Physician Scientist Training (MD/PhD) and Women's Reproductive Health Research Scholars programs. Dr Myatt has served as North American Editor of the journal Placenta, and as President of the Perinatal Research Society, the International Federation of Placenta Associations and the Society for Gynecologic Investigation. He is currently the Principal Investigator of the Global Pregnancy Collaboration (CoLab), a consortium of over 40 international investigators and groups addressing adverse pregnancy outcomes in underserved populations mainly by facilitating sharing of clinical data and bio-specimens. His primary research interests are 1. The effects of maternal obesity, gestational diabetes and sexual dimorphism on mitochondrial respiration in the placenta and their relationship to epigenetic regulation of placental function and fetal programming and 2. Autocrine/paracrine mechanisms in fetal membranes involved in parturition. He has published over 300 papers and 375 abstracts and has served on many review panels and study sections for the National Institutes of Health, Canadian Institutes of Health Research and other international grant giving bodies. He was presented with the Naftolin Award for Mentorship in 2014 and the Distinguished Scientist Award in 2017 by the Society for Reproductive Investigation.

DR. DEAN MYERS earned his MS and PhD in reproduction at the University of Wyoming. Dr. Myers did his post-doctoral training with Dr. Peter Nathanielsz in the Laboratory for Pregnancy and Newborn Research at Cornell University, Ithaca, NY. He stayed at Cornell for a short period as an Assistant Professor in Physiology before relocating to the Oklahoma University Health Sciences Center, Oklahoma City where he is now the John W. Records Chair and Professor in Maternal-Fetal Medicine, Department of Obstetrics and Gynecology. He is also Associate Vice President for Research at the Oklahoma University Health Sciences Center. He served as a regular member of the Pregnancy and Neonatology NIH study section and continues to regularly ad hoc review for NIH. Dr. Myers' prior research focused on development of the fetal hypothalamo-pituitary-adrenal axis as well as fetal adipose tissue and the mechanisms via which gestational hypoxia impacts these critical fetal systems using the timed pregnant sheep model. More recently, his NIH funded research has expanded to include the deciphering the mechanisms of vertical transfer of Zika virus and how Zika virus targets and impacts the non-human primate fetal brain. His current research also focuses on the mechanisms by which maternal obesity and diet impact the developing non-human primate fetus, including the role of the placenta as a mediator of vertical transfer of the maternal physiological environment and the impact of maternal diet and obesity on the developing brain. Dr. Myers presently uses the Olive baboon as a non-human primate model for his research.

DR. PERRIE O'TIERNEY-GINN, PhD is a Research Associate Professor of Obstetrics & Gynecology at Tufts University and Interim Executive Director of the Mother Infant Research Institute (MIRI) at Tufts Medical Center in Boston, Massachusetts.
Her overall interest is to understand the effect of the maternal nutritional environment on placental function, and fetal nutrient delivery and growth. A self-described "Perinatal Ecologist," Dr. O'Tierney-Ginn is fascinated by the interaction between the mother, baby and placenta and their environment. Dr. O'Tierney-Ginn's work is funded by the Eunice Kennedy Shriver National Institute of Child Health and Human Development.

You can find out more about her work at www.placentascience.com.
Twitter: @PlacentaSci and @PerrieO

DR. MARY-ELIZABETH PATTI, MD is an Investigator at Joslin Diabetes Center, Adult Endocrinologist and Director of the Hypoglycemia Clinic, Co-Director of the Molecular Phenotyping Core, and Associate Professor of Medicine at Harvard Medical School. Dr. Patti's NIH-funded laboratory studies are focused on identification of molecular and epigenetic mechanisms by which environmental/nutritional risk factors during early life confer risk for diabetes. Her laboratory utilizes cellular and animal models to study how parental and early-life exposures impact the epigenome and impact diabetes risk in subsequent generations. Clinical/translational studies are focused on the role of the intestine as a mediator of systemic glucose metabolism and its alterations after bariatric surgery, and the development of novel approaches to treatment of post-bariatric hypoglycemia.

Dr. Patti received her MD from Jefferson Medical College magna cum laude. She completed internal medicine residency at the University of Pittsburgh and endocrinology fellowship at Harvard Medical School (Longwood Area Endocrinology Training Program). Dr. Patti has held numerous leadership roles in the diabetes scientific community, including service as organizer of a diabetes-focused Keystone Symposium and chair of the American Diabetes Association Scientific Sessions Planning Committee. She was elected to the American Society of Clinical Investigation in 2009, Association of American Physicians in 2022, and to Fellowship in both the American College of Physicians and Obesity Society in 2014.

DR. CETEWAYO S. RASHID earned his PhD in Nutritional Sciences at the University of Kentucky in 2014. His graduate work explored the effects of perinatal exposure to polychlorinated biphenyls on obesity and glucose homeostasis. Dr. Rashid completed postdoctoral studies at the University of Pennsylvania investigating the metabolic health consequences of parental exposure to the ubiquitous contaminant, bisphenol A. Dr. Rashid is currently an Assistant Professor of Pharmacology and Nutritional Sciences at the University of Kentucky where he continues to study the effects of environmental chemical exposure on metabolic health. Specifically, Dr. Rashid's research aims to determine how exposure to organophosphate flame retardants, such as tris(1,3-dichloro-2-propyl) phosphate, increase risk for metabolic syndrome.

DR. KEVIN SINCLAIR is Professor of Developmental Biology and Head of the Division of Animal Science within the School of Biosciences at the University of Nottingham. His research interests lie in metabolic programming during early development, where epigenetic outcomes are determined in embryonic cells and tissues, and long-term developmental consequences assessed in offspring. His group were the first to discover that developmental anomalies following embryo culture were due to errors in genomic imprinting. Also, first to demonstrate that reductions in folate and vitamin B12 in maternal diets lead to epigenetic modifications to DNA methylation associated with hypertensive and insulin resistant offspring. Subsequently demonstrated that paternal malnutrition epigenetically modifies DNA methylation and adversely affects cardio-metabolic health in offspring. Published the first detailed reports of cardio-metabolic and musculo-skeletal health in aged cloned offspring, and provided details of concordant DNA methylation in embryonic and somatic-cell lineages. Ongoing work is assessing the nature and extent of aneuploidy and epigenetic dysregulation following mammalian embryo culture.

DR. EMILY J SU, MD, MSCI is a Professor in the Division of Reproductive Sciences and the Division of Maternal-Fetal Medicine within the Department of Obstetrics and Gynecology at the University of Colorado School of Medicine. A native Midwesterner, she completed her Ob/Gyn residency and Maternal-Fetal Medicine fellowship at Northwestern University in Chicago. She stayed at Northwestern as faculty for several years before moving to Colorado about 7 years ago. She has been grant-funded since completion of her fellowship, including an AAOGF/SMFM Career Development Award and an NIH K08 Mentored Clinical Scientist Research Career Development Award that ultimately transitioned into an R01 award that is now in its eighth year. Her research primarily focuses on mechanisms of impaired placental angiogenesis in severe fetal growth restriction. She was a 2015 recipient of the Society for Reproductive Investigation (SRI) President's Achievement Award and is also the Secretary-Treasurer Elect for the society, and she will be inducted as a fellow of the American Gynecological and Obstetrical Society (AGOS) this fall.

DR. ALISON WARD grew up in Saskatoon, Saskatchewan where she obtained her B.S. in Animal Science in 2006, M.S. in 2008, and Ph.D. in 2011 from the University of Saskatchewan and completed a postdoctoral fellowship with the Saskatchewan Cancer Agency in 2015. Dr. Ward began as an Assistant Professor in 2015 at North Dakota State University and was promoted to Associate Professor in 2021. Her research focuses on nutritional epigenetics, particularly the impact of maternal nutrition in early gestation on fetal programming in beef cattle. Dr. Ward has been awarded over $1.8 million in funding as PI or Co-PI, with over $1.4 million directly to her program. She has 36 peer-reviewed publications and has mentored 9 graduate students and 2 postdoctoral fellows.

PROGRAM

Aspen Perinatal Biology Symposium

"Developmental Programming – Putting the Pieces Together"

https://www.asas.org/meetings/perinatal-biology-symposium-2022

SUNDAY, AUGUST 28

5:00–7:45 pm	**Registration**
5:30–6:30 pm	**Opening reception**
6:30–6:45 pm	**Welcome and opening remarks** Kristen Govoni, Organizing Co-Chair
6:45–7:45 pm	**Video Presentation of Keynote Address** Kevin D. Sinclair, Professor Developmental Biology, University of Nottingham ***Maternal nutritional effects in developing oocytes and embryo***
7:45 pm	**Networking** (on your own)

MONDAY, AUGUST 29

6:45–8:15 am	**Continental Breakfast**
7:00–8:00 am	**TRAINEE WORKSHOP 1:** ***Collaborating in Perinatal Biology*** Chair: Kristen Govoni, University of Connecticut Panelists: Teresa Davis, Baylor College of Medicine Caitlin Vonderohe, Baylor College of Medicine Ryan Ashely, New Mexico State University

SESSION I – ***What Dad Can Do for You: Paternal Contributions to Offspring Health***
Chair: Kristen Govoni, University of Connecticut

8:15–8:45 am	Carl Dahlen, Associate Professor, Animal Sciences, North Dakota State University ***Overview: the paternal contribution to developmental programming***
8:45–9:15 am	Hasan Khatib, Professor of Genetics and Associate Chair, Department of Animal and Dairy Sciences, University of Wisconsin-Madison ***Effects of paternal nutrition on the epigenome and phenotypes of the offspring***
9:15–9:45 am	Colin Conine, Assistant Professor Pediatrics and Genetics, Perelman School of Medicine, University of Pennsylvania ***The transmission of epigenetic information to offspring by sperm RNAs***
9:45–10:15 am	Hannah Morgan, Post-Doctoral Research Fellow, Faculty of Medicine & Health Sciences, University of Nottingham ***Dads, diet and development: paternal influences on fetal growth***
10:15–10:45 am	Mary Elizabeth Patti, Associate Professor Medicine, Joslin Institute, Harvard University ***Reversibility of Paternal Contributions to Integenerational Inheritance–A New Approach to Metabolic Disease Prevention?***
10:45–11:00 am	**Break**

SESSION II – Male vs Female: is it ever close? Outcomes based on fetal sex
Chair: Sara Pinney, University of Pennsylvania

11:00–11:30 am	Krithika Lingappan, Associate Professor Pediatrics, Perelman School of Medicine University of Pennsylvania ***Sex as a vital biological variable in the newborn lung injury and repair***
11:30 am–12:00 pm	Perrie O-Tierney-Gin, Research Associate Professor, Mother Infant Research Unit, Tufts Medical Center ***Let's talk about sex–differences between male and female offspring in placental nutrient metabolism and delivery***
12:00–12:30 pm	Les Myatt, Professor Obstetrics and Gynecology, Oregon Health Sciences University ***Sexual dimorphism in placental adaptive responses to maternal metabolic disease***
12:30–12:45 pm	**Networking Details** Chairs: Rebecca Simmons and Michelle Baack
12:45–4:00 pm	**Optional Networking Event** Explore Aspen as part of Scavenger Hunt Team
4:00–6:00 pm	**Dinner on your own**

SESSION III – Maternal superpower–creating the perfect food: Maternal environment effects on lactation and offspring outcomes
Chair: Maria Hoffman, University of Rhode Island

6:00–6:30 pm	Geoff Dahl, Professor, Animal Sciences, University of Florida ***High Impact of high temperature; effect of in utero heat stress in the calf***
6:30–7:00 pm	Frank F. (Skip) Bartol, Alumni Professor & Associate Dean for Research and Graduate Studies, College of Veterinary Medicine, Auburn University ***Lactocrine hypothesis – postnatal programming***
7:00–7:30 pm	Brigid Gregg, MD, Assistant Professor of Pediatrics, Division of Pediatric Endocrinology, University of Michigan–Ann Arbor, Early Stage Investigator Speaker ***Lactational diet and DOHaD***
7:30–8:00 pm	Ellen Demerath, Professor of Epidemiology and Community Health, University of Minnesota School of Public Health ***Human milk composition as a link between maternal metabolic status and infant growth and body composition***
8:00–9:30 pm	**POSTER SESSION I**

TUESDAY, AUGUST 30

6:45–8:15 am	**Continental Breakfast**
7:00 –8:00 am	**TRAINEE WORKSHOP 2:** ***Tales and tips to help you blaze your own trail*** Panelists: Academic/MD Clinician Scientist & Moderator - Michelle Baack, M.D., Professor and Chair of Pediatrics, University of South Dakota-Sanford School of Medicine. Clinical and basic research Academic/PhD Guide in Animal Science - Kristen Govoni, Ph.D., Associate Dean of Academic Program in the College of Agriculture, Health, and Natural Resources, Associate Professor in the Department of Animal Science at the University of Connecticut Academic/PhD Guide in Medicine - Peter Vitiello, Ph.D., Associate Professor and Director of the Laboratory Research for Neonatal-Perinatal Medicine Division, Department of Pediatrics, The University of Oklahoma College of Medicine Academic/MD Clinician Scientist Guide–Rebecca Simmons, M.D., Hallam Hurt Professor in Neonatology, Center for Research on Reproduction and Women's Health at the Perelman School of Medicine, University of Pennsylvania Pharmaceutical Industry Guide–David Chapman, Ph.D., Director, Women's Health & Metabolism Internal Medicine North America Medical Affairs, Pfizer

SESSION IV – Immunity on the Playground: Inflammation and Immune modulation in the First 1,000 days
Chair: Lisa Joss-Moore, University of Utah

8:15–8:45 am — Andrea Edlow, Assistant Professor Harvard Medical School. Massachusetts General Hospital
Transplacental transfer of maternal immunity: durability and correlates of protection

8:45–9:15 am — Kylie Kavanagh, Associate Professor Pathology-Comparative Medicine, Wake Forest University
Maternal metabolic syndrome and offspring immune activation in old world nonhuman primates

9:15–9:45 am — Ryan Ashley, Professor, Department of Animal & Range Sciences, New Mexico State University
The role of the CXCL12/CXCR4 chemokine axis in placental development and fetal health

9:45–10:15 am — Dean Myers, Associate Vice President for Health Sciences Research, Professor and John W. Records Chair in Maternal Fetal Medicine, Vice Chair for Basic Research, Department of Obstetrics and Gynecology, University of Oklahoma Health Sciences Center
The Olive baboon, Western-style diet, maternal obesity and fetal/placental impact: what we are learning along the way about diet versus obesity in a non-human primate

10:45–11:00 am — **Break**

SESSION V – Novel Environmental Factors Programming the Offspring
Chair: Rebeccca Simmons, University of Pennsylvania

11:00–11:30 am — Alison Ward, Associate Professor, Department of Animal Sciences, North Dakota State University
Mitigating the effects of feed restriction on fetal developmental programming by strategic supplementation of one-carbon metabolites in beef cattle

11:30 am–12:00 pm — Cetewayo Rashid, Assistant Professor Pharmacology and Nutritional Sciences, School of Medicine University of Kentucky
Organophosphate flame retardants: metabolism disrupting chemicals in adults and offspring

12:00–12:30 pm — Folami Ideraabdullah, Associate Professor, Department of Genetics and the Department of Nutrition at the Gillings School of Global Public Health, University of North Carolina
Modeling interindividual effects of maternal vitamin D deficiency in the mouse

12:30–12:45 pm — Trainee talk–Nicole Tillquist, University of Connecticut
Effects of poor maternal nutrition during gestation on colostrum and milk composition in F0 ewes

12:45–1:00 pm — Trainee talk–Alexa Sassin, Baylor College of Medicine
Alterations of the Gastrointestinal Microbiome Associated with Western-Style Diet Feeding in a Primate Model of Testosterone Induced Polycystic Ovarian Syndrome May Modulate Reproductive Health

1:00–6:00 pm — **Free time and networking**

6:00–7:30 pm — **Conference Dinner and Presentation of Awards**

SESSION VI – DJP Barker Memorial Lecture

7:30–8:30 pm — Rebecca Simmons, Hallam Hurt Professor in Neonatology, Center for Research on Reproduction and Women's Health at the Perelman School of Medicine, University of Pennsylvania
The Yin and Yang of Developmental Programming

8:30–9:45 pm — **POSTER SESSION II**

WEDNESDAY, AUGUST 31

7:30–8:30 am **URiS Workshop and continental breakfast – From Unicorns to Thoroughbreds: How to thrive and propagate underrepresented scientist** (Breakfast included)
Chair: Rebecca Simmons, University of Pennsylvania
Panelists: Folami Ideraabdullah, University of North Carolina
Cetewayo Rashid, University of Kentucky.
Sponsored by NIH

SESSION VII – Heart-felt connections made early in life: Vascular Effects
Chair: Michelle Baack, University of South Dakota Sanford School of Medicine

8:45–9:15 am Emin Maltepe, Associate Professor, Department of Pediatrics, University of California–San Francisco
Effects of hypoxia on placental development and role of HIF1a

9:15–9:45 am Caleb O. Lemely, PhD. Associate Professor, Animal and Dairy Sciences, Mississippi State University
Placental rhythms and blood flow during compromised maternal nutritional status

9:45–10:15 am Emily Su, Associate Professor, Divisions of Maternal-Fetal Medicine & Reproductive Sciences, Department of Obstetrics and Gynecology, University of Colorado
Human placental villous stromal extracellular matrix regulates fetoplacental angiogenesis in severe fetal growth restriction

10:15 –10:45 am Sonnet S. Jonker, PhD. Associate Professor of Medicine, Center for Developmental Health, Knight Cardiovascular Institute, Oregon Health & Science University, Portland, OR
Transience of plasticity in the perinatal heart

10:45 –11:00 am **Break**

SESSION VIII – Trainee selected Presentations 15-minute presentations
Chair: Kristen Govoni, University of Connecticut

11:00–11:15 am Trainee talk–Rachel Gibbs, University of Nebraska–Lincoln
Manipulating β2 adrenergic activity in IUGR-born lambs with daily clenbuterol injections improved glucose-stimulated insulin secretion and oxidative metabolism at 60 days of age

11:15–11:30 am Trainee talk–Amelia Tanner, Colorado State University
Maternal hyperglycemia increases uteroplacental oxygen utilization but fails to restore fetal glucose uptake in chorionic somatomammotropin RNAi pregnancies

11:30–11:30 am Trainee talk–Rosa Icela Luna-Ramirez, University of Arizona
Single-cell transcriptomics identifies β-cell subpopulations in ovine FGR fetuses

11:30–11:45 am Trainee talk–Hannah Kyllo, University of Colorado, School of Medicine
Increased Fetal Pyruvate Output and Placental Pyruvate Utilization during Intrauterine Growth Restriction

11:45 am–12:15 pm **Conference Closure–final comments and election of next Organizing Committee**

ABSTRACTS

MONDAY, AUGUST 29, 2022

I-I Vitamin and mineral supplementation and rate of gain during the first trimester of gestation in heifers affect the fetal hepatic lipidome at d 83 of gestation

[1]M. Crouse, [2]K. McCarthy, [2]A. Ward, [2]P. Borowicz, [2]L. Reynolds, [3]J. Forcherio, [3]R. Scott, [2]J. Caton, and [2]C. Dahlen†. [1]*USDA, ARS, U.S. Meat Animal Research Center, Clay Center, NE 68933, USA,* [2]*Department of Animal Sciences, and Center for Nutrition and Pregnancy, North Dakota State University, Fargo, ND 58108, USA,* [3]*Purina Animal Nutrition LLC, Gray Summit, MO 63039, USA*

Objectives: *The objective of this study was to evaluate the effects of feeding heifers a vitamin and mineral supplement and targeting divergent rates of gain during early gestation on the fetal liver lipidome at d 83 of gestation.* **Methods:** *Seventy-two crossbred Angus heifers were randomly assigned in a 2 × 2 factorial arrangement to one of four treatments comprising the main effects of vitamin and mineral supplementation (***VTM** *or* **NOVTM***) and feeding to achieve different rates of gain (low gain [***LG***] 0.28 kg/d, vs. moderate gain [***MG***] 0.79 kg/d). To achieve the different rates of gain, MG heifers received a protein/energy supplement that contained fish oil as a component of the supplement. Thirty-five gestating heifers with female fetuses were ovariohysterectomized on d 83 of gestation, and fetal liver was collected and analyzed by Metabolon Inc.* **Results:** *Polyunsaturated fatty acids (***PUFA***) were increased (P < 0.05) in fetal liver of MG vs. LG heifers. The concentrations of nearly all acyl carnitines measured were decreased (P < 0.05) in fetal liver of VTM-LG and NoVTM-MG compared with NOVTM-LG and VTM-MG heifers; however, there were no differences in acetyl-CoA, ketones, or metabolites in the TCA cycle.* **Conclusions:** *These results demonstrate that bovine fetal livers accumulate PUFA which is consistent with prior research and has demonstrated positive growth responses in ruminants. Furthermore, acyl carnitines are differentially responsive to maternal vitamin/ mineral status and energy/protein intake; however, without a response in other markers of energy or fatty acid metabolism, these data suggest that energy balance of fetal livers across treatments remains relatively stable. USDA is an equal opportunity employer and provider. (Funding: NIFA #2018-67011-31708).*

I-II Fetal hypoglycemia induced by placental SLC2A3 RNA interference alters fetal pancreas development and function at mid-gestation

V.C. Kennedy[1], C.S. Lynch[1], A.R. Tanner[1], Q.A. Winger[1], P.J. Rozance[2], R.V. Anthony[1]. [1]*Colorado State University College of Veterinary Medicine, Fort Collins, CO, USA,* [2]*University of Colorado Anschutz Medical Campus, Aurora, CO, USA*

Objectives: Glucose, the primary energy substrate for fetal oxidative processes and growth, is transferred from maternal to fetal circulation down a concentration gradient by placental facilitative glucose transporters. In sheep, SLC2A1 and SLC2A3 are the primary transporters available in the placental epithelium, with SLC2A3 located on the maternal-facing apical trophoblast membrane and SLC2A1 located on the fetal-facing basolateral trophoblast membrane. Therefore, the objective of this study was to characterize consequences of diminished placental SLC2A3 glucose transport at mid-gestation (75 dGA) in sheep. **Methods:** Using *in vivo* lentiviral-mediated RNA interference (RNAi), we produced SLC2A3-RNAi (n=6) and non-targeting sequence control (NTS-RNAi; n=6) pregnancies, resulting in a 37% reduction (P≤0.05) in placental SLC2A3 concentration at 75 dGA. **Results:** SCL2A3-RNAi fetuses were hypoglycemic (umbilical vein; 1.96±0.13 vs. 1.14±0.12 mmol/L; P≤0.01) and the fetal pancreas was lighter (P≤0.05; 470.0 ±34.4 vs. 363.4±15.9 mg). Associated with the reductions in fetal glucose concentrations and pancreas weights, both umbilical artery concentrations of insulin (P=0.11; 0.85±0.14 vs. 0.47±0.12 ng/mL) and glucagon (P=0.06; 81.1±15.8 vs. 38.1±6.5 pg/mL) were reduced. By contrast, fetal liver weight (P=0.70) and umbilical artery IGF1 (P=0.82) were not impacted. These findings led us to recently subject RNA derived from SLC2A3-RNAi (n=6) and NTS-RNAi (n=6) fetal pancreases for transcriptomic analysis. RNA-sequencing was performed on the Illumina NovaSEQ6000 platform, and Differentially Expressed Gene (DEG) analysis is currently being conducted using the CLC Genomics Workbench. Functional analysis of DEG's will be performed using DAVID and IPA, to assay pathways impacted in SLC2A3-deficient pregnancies. **Conclusions:** Our results suggest that fetal hypoglycemia during the first-half of gestation, impacts fetal pancreas development and function, that is not limited to β cell function. Interestingly, fetal liver development and function did not appear to be impacted, suggesting a partitioning of the effect of fetal hypoglycemia during the first-half of gestation. (Supported by NIH HD094952, NIH HD093701 and USDA-NIFA 2021-67034-34969).

I-III Investigation of the impact of prenatal transportation stress on the hematological profile and growth of perinatal Brahman calves

[1,2]A.L. Earnhardt, [2]G.A. Perry, [2]C.R. Long, [2]R.D. Randel, and [1]T.H. Welsh. *Texas A&M AgriLife Research, [1]College Station and [2]Overton, TX, USA*

Objective: Assess whether prenatal transportation stress (PNS) affected the hemogram and if the hemogram was related to pre-weaning growth of Brahman calves. **Methods:** Brahman cows artificially inseminated in 2018 and 2020 were assigned as Control (n=35 and n=26, respectively; not transported) or PNS (n=37 and n=25, respectively; 2h of transportation at 60, 80, 100, 120, and 140±5 d of gestation). Hemograms were determined by automated complete blood count analysis of samples obtained from calves at 28±5 (2019: Control, n=25; PNS, n=29) and 40±5 days of age (2021: Control, n=24; PNS, n=23). Sex classification, birth weight (BWT), weaning weight (WWT), and average daily gain (ADG) were recorded. Data were analyzed using SAS' GLM and CORR procedures. **Results:** Neither PNS nor sex affected white blood cell number (WBC), absolute neutrophils (NEUT), absolute lymphocytes (LYMPH), and the neutrophil:lymphocyte ratio (RATIO) in the 28-day-old calves. Pre-weaning ADG was affected (P<0.01) by NEUT. The WWT was affected (P<0.05) by WBC, NEUT, and RATIO. For the 40-day-old calves WBC and NEUT were greater (P<0.05) in PNS than Control; RATIO tended (P<0.1) to be greater in PNS. Analysis of 2019 and 2021 pooled data determined that NEUT and RATIO were greater (P<0.05) in PNS than Control calves. An effect (P<0.05) of LYMPH on WWT and a positive correlation of LYMPH and WWT (r=0.26; P<0.05) were identified. **Conclusions:** Although granulocyte numbers increased in PNS calves the hemogram did not exceed the normal range. The associations of NEUT and LYMPH with ADG and WWT is reminiscent that serum immunoglobulin concentration of neonatal calves predicts pre- and post-weaning health (Wittum and Perino, *Am. J. Vet. Res.*, 56:1149−1154; 1995). The influence of PNS on functionality of innate and adaptive immune cell types of neonatal calves and phenotypic linkage to health and growth remain to be evaluated. (Supported by USDA-NIFA Grants 2018-67015-28131; 2019-67015-2957).

I-IV Liver mRNA expression is altered by sex, but not maternal diet in mature sheep

[1]N. Tillquist, [1]A. Reiter, [1]M. Kawaida, [1]B. Smith, [2]R. Gately, [2]A. Uden, [3]B. Thompson, [1]S. Reed, [1]S. Zinn, and [1]K. Govoni. *[1]Department of Animal Science, University of Connecticut, Storrs, CT, USA, [2]Cummings School of Veterinary Medicine, Tufts University, North Grafton, MA, USA, [3]School of Medicine Division of Medical Oncology, University of Colorado, Aurora, CO, USA*

Objectives: Poor maternal nutrition negatively impacts offspring growth and metabolism; however, the mechanisms contributing to persistent effects postnatally are not well-established. The objective was to determine the effects of poor maternal nutrition during gestation on offspring liver mRNA expression. We hypothesized that offspring of restricted- and over-fed ewes would exhibit changes in mRNA expression of genes involved in liver metabolism. **Methods:** Forty-six multiparous Dorset ewes pregnant with twins were fed 100% (CON), 60% (RES), or 140% (OVER) of National Research Council requirements from d 30 ± 0.02 of gestation until parturition. Offspring were raised on control diets, and liver biopsies were collected from a subset of offspring [CON (n=6 ewes; 8 rams), RES (n=9 ewes; 7 rams), and OVER (n=8 ewes; 8 rams)] at d 256 ± 1.26 of age and snap-frozen in liquid nitrogen. RNA was extracted and RNA-Seq performed using Illumina Sequencing: NovaSeq 6000 S1 v1.5. **Results:** We did not detect an effect of maternal diet on offspring liver mRNA expression ($P \geq 0.38$). An effect of sex was observed with 1921 differentially expressed genes (DEGs) in rams relative to ewes (931 up- and 990 down-regulated; $P \leq 0.05$). Gene ontology (GO) analysis (Panther 17.0) of DEGs revealed changes in genes involved in molecular function that were primarily categorized under binding (147 up-regulated;164 down-regulated) and catalytic activity (171 up-regulated;142 down-regulated). Additionally, GO analysis of biological processes showed that DEGs were categorized under cellular process (309 up-regulated;285 down-regulated), biological regulation (134 up-regulated;177 down-regulated), and metabolic process (227 up-regulated;152 down-regulated). **Conclusions:** At this time point, we did not detect an effect of maternal diet on offspring liver gene expression; however, sex has an important role in gene expression in the liver.

I-V Chronic Prenatal Cannabis Exposure Impacts Placental Perfusion and Fetal Oxygen Availability in a Rhesus Macaque Model

[1]K. Ryan, [2]M. Schabel, [2]V. Roberts, [2]JJ. Terrobias, [1,2]J. Lo. *[1]Department of Obstetrics and Gynecology, Oregon Health & Science University, Portland, OR, USA, [2]Division of Reproductive and Developmental Sciences, Oregon National Primate Research Center, Beaverton, OR, USA*

Objective: Prenatal cannabis use is associated with adverse perinatal outcomes and the placenta likely contributes to these detrimental outcomes. Our group has developed the use of Blood oxygen level dependent (BOLD-MRI) and Dynamic contrast-enhanced MRI (DCE-MRI) in the non-human primate (NHP) to evaluate changes in placental oxygenation and perfusion. Our objective was to evaluate the adverse effects of delta-9-tetrahydrocannabinol (THC, main psychoactive component of marijuana) exposure on placental vascular function and associated pathology. **Methods:** Rhesus macaques were divided into 2 groups, control (CON, n=5) and cannabis-exposed (THC, n=5). All animals were on a standard chow diet with the THC group receiving an additional THC edible daily. These animals were titrated to 2.5mg/7kg/day of THC (equivalent to a heavy medical cannabis dose) over ~4 months to model established medical cannabis acclimation guidelines. All animals underwent time-mated breeding with the THC group maintained at their THC dose throughout pregnancy. Animals underwent serial BOLD-MRI and DCE-MRI at gestational days 85 (G85), G110, G135, and G155 (term is ~G168) followed immediately by cesarean section delivery at G155 with placental tissue collection. **Results:** Placental blood flow and fetal oxygen transport capacity were decreased in the THC-exposed group relative to controls across gestation demonstrated by shorter *T2** values (mean ± standard deviation): 70.6±11.8 vs. 54.4±19.2 at G85, 57.6±11.2 vs. 44.9±15.0 at G110, 43.9±14.9 vs. 29.0±8.7 at G135, and 32.9±11.9 vs. 28.7±8.8 at G155. In correlation, we found increased syncytial knotting and microscopic infarctions in THC-exposed placentas which is consistent with aberrant maternal perfusion of the placental intervillous space. **Conclusion:** Chronic prenatal THC exposure diminishes placental perfusion and oxygen availability throughout pregnancy, associated with microscopic placental infarctions in the NHP. The longer-term consequences of these adverse placental findings are unknown, but may impact offspring development. (Supported by NIH R03 HD97116).

I-VI Late gestational nutrient restriction alters placental and fetal growth in the primiparous bovine dam

C.A. Redifer, K.J. Latimer, A.R. Rathert-Williams, and A.M. Meyer. *Division of Animal Sciences, University of Missouri, Columbia, Missouri, USA*

Objectives: Determine the effects of late gestational maternal nutrient restriction (NR) on uteroplacental blood flow, circulating maternal metabolites, placental size, and fetal growth. **Methods**: Primiparous fall-calving crossbred beef heifers (body weight; BW: 466 ± 30 [SD] kg) bred to a single sire were individually-fed either 100% (control; CON; n = 10) or 70% (NR; n = 12) of energy and protein requirements for maintenance, pregnancy, and growth from d 160 of gestation to parturition. Transrectal color Doppler ultrasonography of both uterine arteries and jugular blood samples were collected pre-treatment and every 21 d until calving. Post-calving, calf and expelled placenta size were measured. Treatment was a fixed effect, and treatment initiation date and calf sex (when $P < 0.25$) were covariates. Uterine blood flow and circulating metabolites included day and treatment x day (repeated measures). **Results**: Cross-sectional area and flow volume of both uterine arteries and total uterine blood flow were unaffected ($P \geq 0.23$) by NR. Nutrient restricted dams had decreased ($P < 0.01$) heart rate after treatment initiation. Nutrient restriction decreased ($P \leq 0.05$) maternal plasma glucose and triglycerides and tended to decrease ($P = 0.06$) serum urea nitrogen but increased ($P < 0.01$) non-esterified fatty acids. Total placental weight tended to be less ($P = 0.10$) for NR dams; however, ipsilateral, contralateral, cotyledonary, and intercotyledonary placental weights were unaffected ($P \geq 0.12$). Cotyledonary number was greater ($P = 0.03$) while cotyledonary size was less ($P = 0.04$) in NR dams. Calves born to NR dams had less ($P \leq 0.04$) birth BW and heart girth and tended to have less ($P \leq 0.09$) abdominal girth, cannon circumference, and longissimus muscle area. Ponderal index and gestation length were unaffected ($P \geq 0.30$). **Conclusions**: Late gestational nutrient restriction reduced fetal growth, likely through decreased placental size and circulating nutrients rather than a reduction in total blood flow supplying the uteroplacenta. (Supported by USDA-AFRI grant 2017-67015-26587). *Travel Award: Sponsored by United States Department of Agriculture, National Institute of Food and Agriculture*

I-VII Investigating the effects and inheritability of a maternal high fat diet on embryo health

[1]A. Klein, [2]T. Larsen, [2]C. T. Gandy, [1]K. Siemers, [1,2]M. Baack, MD. *[1]University of South Dakota – Sanford School of Medicine, Basic Biomedical Sciences, Vermillion, SD, [2]Environmental Influences on Health and Disease Group, Sanford Research, Sioux Falls, SD.*

Objective: This study builds upon past work which used a rat model to show how a maternal high fat (HF) diet incites mitochondrial dysfunction and cardiac disease in offspring across their lifespan. To understand whether these mitochondria-mediated consequences are maternally inherited or acquired during fetal exposure, we investigated HF diet effects on maternal ovaries, fertility, and early embryogenesis and tested potential mitigating effects of periconceptual supplementation with antioxidant, Coenzyme Q10. **Methods:** First generation (F0) female rats were fed a HF diet and bred with control males. After 28 days, half were switched to a CoQ10-supplemented diet before breeding. Serum, ovaries, and blastocysts were collected on embryonic day 4. Group comparisons were made by Student's T-test or one-way ANOVA with multiple group comparisons. Significance set at $p<0.05$. **Results:** Ovaries from F0 dams on HF diet are smaller ($p=0.01$, n=20/group) and have more oxidized and fragmented mitochondrial DNA ($p=0.18$, n=4/group and $p=0.04$, n=2-3/group, respectively) which was associated with increased breeding time before successful pregnancy ($p=0.02$, n=5-10/group). Dietary supplementation with CoQ10 increased ovarian mitochondrial CoQ levels and improved fertility in HF-fed dams. Gardner embryo grades were not different between control, HF diet-exposed, and CoQ10-supplemented embryos. Preliminary data from immunofluorescent staining of mitochondria and ROS suggests more mitochondrial signal in HF diet-exposed embryos compared to controls. Ongoing experiments will examine the effects of intervention on stillbirths, neonatal mortality, and cardiometabolic disease at birth, in adulthood and subsequent generations. **Conclusions:** While data so far shows that a HF diet incites oxidative stress in the maternal ovary that impacts fertility, no consequences are found at the preimplantation embryo level. This suggests that at least some offspring consequences are due to fetal exposure, and dietary interventions after pregnancy may mitigate *in utero* programming. Pinpointing critical windows of developmental risk will lead to well-timed translatable preventative strategies to improve the life-long health for generations to come. (NIH/NHLBI-1R01HL160980-01 & NIH/NIGMS-2P20GM103620-06) *Travel Award: Sponsored by National Institutes of Health*

I-VIII Differentially Expressed Long Non-Coding RNA transcripts in Islets from Growth Restricted Sheep Fetuses

M Varela, RI Luna-Ramirez, MJ Anderson, R Goyal, SW Limesand. *Animal and Comparative Biomedical Sciences, University of Arizona, Tucson AZ*

Objectives: Placental insufficiency-induced fetal growth restriction (FGR) increases the risk for metabolic diseases in adulthood, and the higher incidence of Type-2 Diabetes infers deficiencies that develop in pancreatic β-cells. In human and animal models of FGR, reductions in β-cell mass and insulin secretion capacity were apparent. Emerging evidence shows that long intergenic noncoding RNAs (lincRNA) play regulatory roles in cells, and several lincRNAs are known to affect the islet regulome. The objective of this study was to identify differentially expressed lincRNA transcripts associated with physiological adaptations in islets from FGR fetal sheep. **Methods:** Islets from FGR fetuses were collected at 0.9 of gestation following maternal hyperthermia-induced placental insufficiency and compared to islets isolated from control fetuses. Differentially expressed genes were identified with high-throughput sequencing of islet RNA (n = 4/group) that were mapped to the Oar_4.0 sheep genome. Our analysis included β-cell-specific lincRNA orthologs that were defined in humans and mice as well as conserved lincRNA genes annotated in the sheep genome. Differential expression in FGR islets was confirmed with quantitative PCR in an expanded cohort of control and FGR islets (n ≥ 8/group). **Results:** The FGR fetuses weighed less than the control fetuses (1.3 ± 0.03 vs 3.5 ± 0.2 kg; $P < 0.001$) at necropsy. Of the 4098 lincRNAs previously annotated in the sheep genome, 1606 lincRNA genes were expressed in fetal islets (> 1 FPKM), and 62 lincRNA genes were differentially expressed between FGR and control fetuses. Specifically, for the β-cell specific lincRNA transcripts, 1457 of the 1993 genes examined were expressed, and 28 genes differed significantly in the FGR islets compared to control. The H19, MALAT1, and PLUTO were evaluated with qPCR and increased 4.6-fold, 2.0-fold, and 2.5-fold in FGR islets, respectively. In ischemic islet cultures, MALAT1 expression increase 1.6-fold ($P<0.05$), indicating MALAT1 expression is stimulated during oxygen and glucose deprivation. **Conclusions:** High throughput RNA sequencing identified lincRNAs with physiologically relevant pathways that effect β-cell proliferation and maturation. These adaptations in lincRNA expression may define the increased susceptibility of patients to early adulthood dysfunction in insulin secretion. (NIH R01 DK084842) *Travel Award: Sponsored by United States Department of Agriculture, National Institute of Food and Agriculture*

I-IX Long-term leucine supplementation enhances lean growth by stimulating mTORC1-dependent translation initiation in a preterm piglet model

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Objectives: Extrauterine growth restriction is a common complication of preterm birth and is associated with reduced lean growth and long-term morbidities. Previously, we showed that intermittent pulses of leucine during continuous orogastric feeding increased mTORC1 signaling, increasing protein synthesis in skeletal muscle of neonatal pigs born at term. The objective of this study was to determine the extent to which leucine pulses during continuous feeding would promote lean growth by enhancing mTORC1 signaling in a preterm piglet model. **Methods:** Pigs delivered by cesarean section at 105 d gestation (approximately 10 days preterm) were continuously fed a protein- and energy-balanced milk-replacer diet (195 kcal ME and 13.5 g protein [kg body weight (BW)$^{-1}$·d^{-1}]). Pigs (n=11-12) were randomly assigned to Leucine (Leu) or Alanine (Ala, isonitrogenous control) groups and treatments were administered as a pulse (1.6 mmol·kg BW^{-1}·h^{-1}) for 1 h every 4 h for 21 d. Body composition was determined by DXA and indices of amino acid signaling, mTORC1 activation, and muscle protein synthesis were determined postprandially, 60 min after initiation of the final pulse. **Results:** Leu pigs had a 10% higher average daily gain (ADG) (P<0.05) than Ala pigs. Total lean mass tended to be higher (+13%; P<0.06) in Leu compared to Ala, and longissimus dorsi muscle weight was 17% heavier in Leu than Ala pigs (P=0.01). Indices of mTORC1 activation, i.e., phosphorylation of S6K1 and 4EBP1 and abundance of the eIF4E-eIF4G complex, were increased in longissimus dorsi and gastrocnemius muscle of Leu compared to Ala pigs (P<0.05). Skeletal muscle protein synthesis also increased in skeletal muscle tissue of Leu pigs compared to Ala pigs (P<0.05). **Conclusions:** These results show that leucine supplementation during continuous feeding enhances mTORC1-activated translation initiation in skeletal muscle leading to an increase in protein synthesis and subsequent increase in muscle mass and lean growth in a preterm piglet model. Research was supported by NIH and USDA. *Travel Award: Sponsored by United States Department of Agriculture, National Institute of Food and Agriculture*

I-X Differential fatty acid uptake in human trophoblast cells is ATP-dependent

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Objectives: Gestational diabetes causes placental lipid accumulation and essential long-chain polyunsaturated fatty acid (LCPUFA) deficiency in infants which signals poorer outcomes for both mother and baby. Physiologic LCPUFA biomagnification in the fetus suggests placental fatty acid transport occurs by both passive and active mechanisms. This study's objective was to determine whether differential fatty acid uptake in human trophoblasts is mitochondrial-mediated. **Methods:** Using MitoTracker fluorescent tagging of mitochondria and 4,4-difluoro-3a,4a-diaza-s-indacene, BODIPY, a fluorophore attached to fatty acids of variable lengths, we tracked live-cell uptake in BeWo and isolated cytotrophoblasts (CTB) from consenting mothers. Experiments were repeated in the presence of oligomycin (OM), which inhibits ATP-synthase, 2-deoxyglucose (2dG) which competitively inhibits glycolysis, etomoxir (Eto) which inhibits fatty acid oxidation, and carbonyl cyanide 4-(trifluoromethoxy) phenylhydrazone (FCCP) which uncouples respiration. Statistical analysis was conducted using Student's T-test per drug or 2-way ANOVA to determine fatty acid-specific, drug-based, and interaction effects. Significance was set at p<0.05. **Results:** Live-cell imaging shows rapid uptake of both BODIPY-C12, which mimics a 16-carbon saturated fatty acid like palmitate, and BODIPY-C16, which mimics a 20-carbon LCPUFA occurs in BeWo and CTB. The time to peak uptake was longer for BODIPY-C16 than BODIPY-C12 (p<0.0001). Intracellularly, both fatty acids colocalize with mitochondria. Interestingly, BODIPY-C16 stimulates visible cytoplasmic projections that facilitate peripheral uptake, followed by perinuclear accumulation. Treatment with 1uM OM, 50 mM 2dG, or 150 uM Eto significantly decreased ATP levels in BeWo while 0.3 uM FCCP did not (p=0.017, 0.002, 0.012, 0.458 respectively; n=3). ATP-inhibitors, slowed the rate of BODIPY-C16 uptake (p<0.0001 with 2dG and Eto; n=4). Conversely, 2dG and Eto increased the rate of BODIPY-C12 uptake (p=0.007, p=0.012 respectively; n=2). Primary cytotrophoblasts follow a similar trend for BODIPY-C12 and BODIPY-C16 uptake and response to ATP-inhibitors (n=2). **Conclusions:** Differential fatty acid uptake in human trophoblasts is ATP-dependent which may explain placental lipotoxicity and LCPUFA deficiency associated with poorer pregnancy outcomes. (NIH/NIGMS 2P20GM103620-06) *Travel Award: Sponsored by National Institutes of Health*

I-XI Effects of estrogen on the expression of estrogen receptors in the uterus and cervix in periparturient ewes

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Objectives: Estradiol induces parturition and fetal maturation in ewes, but mechanisms are unclear. The aim of this study was to evaluate if the estrogenic response of the uterus and cervix in periparturient Rambouillet ewes is affected by estradiol levels, by quantifying the expression of estrogen receptors (ER; ERα and ERβ). Our hypothesis was that estrogen levels would affect ER expression. **Methods:** We administered estradiol or the estrogen synthesis inhibitor letrozole, which inhibits aromatase. Pregnant ewes (n=27) were randomly assigned to a 2×2 factorial arrangement with main factors of estradiol implants (Control (C) or Estradiol (E) implants; 200 mg/ewe) and letrozole (Control (C) or 1 mg/kg Letrozole (L) in sesame oil 1:1 v/v 50 mg/ml final concentration), resulting in 4 E × L combinations: C+C (n=6), E+C (n=6), C+L (n=8), and E+L (n=7). Treatments began at d 139 to 142 of gestation and ewes were euthanized 26 hr later. Formalin-fixed cross-sections of uterus and cervix were immunofluorescently stained for ER along with DAPI for nuclear staining. One image of the entire cross-section of each tissue was generated to evaluate ER distribution and confocal imaging of individual uterine (glands, myometrium, endometrial epithelium) and cervical (cervical glands and stroma) compartments was generated for image analysis. Data were analyzed using the MIXED procedure of SAS. **Results:** ERα staining in myometrium was less in E+C compared with C+C ewes (5.42 vs 5.61 intensity units; P-value = 0.09), whereas in uterine glands, endometrial epithelium, and cervix ERα expression was not affected by treatment. Similarly, no effect of treatment was found for ERβ expression in any uterine compartments. ERβ expression in cervix was not evaluated. **Conclusions:** Results suggest that endometrial, uterine glands, and cervical estrogenic response is unaffected by estradiol levels in periparturient ewes, but myometrial ERα is down-regulated by estrogen treatment (Supported by USDA-NIFA-AFRI 2021-67015-34277). *Travel Award: Sponsored by United States Department of Agriculture, National Institute of Food and Agriculture*

I-XII Supplementing one-carbon metabolites to nutrient-restricted cows during early pregnancy affects placental vascularity

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Objectives: The objectives were to evaluate the effects of plane of nutrition and supplementation of one-carbon metabolites (OCM) on placental vascularity during early gestation. **Methods:** Thirty-two Angus-crossbred heifers were estrus-synchronized and bred to a single sire with female-sexed semen. The experimental design was a 2 × 2 factorial with two levels of weight gain: control (CON; 0.6 kg/d average daily gain) and restricted (RES; -0.23 kg/d); and OCM: supplementation (+OCM; fed ruminal-protected methionine (10 g/d) and choline (60 g/d) and weekly injections of 320 mg folate and 20 mg vitamin B_{12}) or no supplementation (-OCM; corn carrier and saline injections). Heifers were individually fed and randomly assigned to treatment at breeding (d 0). Placentas were collected on d 63 of gestation (full gestation approximately 280 d). Vascularity was assessed via intensity of CD34 and CD31 fluorescent staining. Images were analyzed for capillary area density (CAD) and capillary number density (CND). Areas evaluated included fetal cotyledon (COT), maternal caruncle (CAR), whole placentome (CAR+COT), fetal membranes (FM), endometrial stratum compactum (SCOM), and endometrial glands (EG). Data were analyzed with the GLM procedure in SAS, with heifer as experimental unit. **Results:** There was a gain × OCM interaction ($P < 0.03$) for CAD within CAR+COT and SCOM. Additionally, CAD within FM tended ($P = 0.10$) to be influenced by gain, while EG was influenced ($P = 0.01$) by OCM. For CND, there was a tendency ($P < 0.10$) for COT to be influenced by gain, and CAR and EG by OCM. The CAD was greater in CAR+COT regions of the CON-OCM compared with CON+OCM and RES-OCM ($P < 0.02$), but not different from RES+OCM. **Conclusions:** The results indicate that heifer rate of gain and OCM supplementation affected placental vascularization, which may impact placental function during early gestation. (Supported by USDA-NIFA-AFRI 2018-07055). USDA is an equal opportunity provider and employer.

I-XIII Replacement insulin during IGF-1 infusion increases growth in fetal sheep

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Objectives: Insulin-like growth factor-1 (IGF-1) is an essential fetal growth hormone that correlates with birth weight. IGF-1 is a potential therapeutic agent to mitigate intrauterine growth restriction. Infusion of IGF-1 to the normally grown sheep fetus increases fetal organ weight selectively and myoblast proliferation but does not consistently increase body or skeletal muscle weight. However, IGF-1 infusion decreases fetal plasma insulin concentrations. We hypothesized that during a one-week fetal infusion of IGF-1, euinsulinemia must be maintained to support fetal body, organ, and skeletal muscle growth. **Methods:** Catheterized late gestation sheep fetuses received a one-week intravenous infusion of either IGF-1 (IGF, n=3), IGF-1 with insulin and dextrose infusions to maintain euinsulinemia and euglycemia (IGF+INS, n=3), or saline (SAL, n=2). Final fetal blood gas, glucose, lactate, amino acid, and insulin concentrations were measured. Fetal body and organ weights were obtained. One-way ANOVA was performed to compare differences among groups with *post hoc* analysis by Tukey's test. *P*-values indicate *post hoc* test unless otherwise specified. **Results:** Fetal weight was 33% and 9% larger in IGF+INS compared to SAL and IGF, respectively (P=0.09, ANOVA). Liver weight was 78% and 39% larger in IGF+INS compared to SAL (P=0.02) and IGF (P=0.08), respectively. Adrenal gland weight was 77% and 72% larger in IGF+INS compared to SAL and IGF, respectively (P<0.1). Heart weight tended to be highest in IGF+INS (P=0.06, ANOVA). Insulin concentrations in IGF were ~40% lower than IGF+INS and SAL, but this was not statistically significant. Plasma glucose and amino acid concentrations were similar among groups. Lactate concentrations were 3-fold higher (P=0.06, ANOVA) and oxygen content was 62% lower (P<0.05) in IGF+INS compared to IGF or SAL. **Conclusions:** Maintaining euinsulinemia during fetal IGF-1 infusion tends to increase fetal body and organ growth compared to IGF-1 infusion alone; studies are ongoing to confirm this effect. We speculate that IGF-1 and insulin have independent effects in regulating fetal growth. (Funding: Colorado NORC P30-DK048520).

I-XIV The effect of one-carbon metabolite supplementation in combination with plane of nutrition during early gestation on maternal serum and fetal fluids

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Objectives: Our objective was to evaluate the effect of one-carbon metabolites (OCM; folate, vitamin B_{12}, choline, and methionine) supplementation in combination with plane of nutrition in early gestation on maternal serum glucose, BUN, and NEFA concentrations as well as fructose and glucose concentrations in allantoic and amniotic fluid. **Methods:** Thirty-two cross-bred Angus heifers were estrous synchronized and artificially inseminated with female-sexed semen. At breeding (day 0), heifers were assigned to treatments in a 2 × 2 factorial design. The first factor was gain: control (CON; 0.60 kg/day ADG) versus restricted (RES; -0.23 kg/day). The second factor was OCM: supplementation (+OCM; ruminal protected choline [0.60 g/day] and methionine [20 g/day] in a ground corn carrier, and weekly injections of 320 mg folate and 20mg vitamin B_{12}) or no supplementation (-OCM; corn carrier and saline injections). Blood samples were collected on day 0, 35 and 62. Allantoic and amniotic fluid were collected on day 63 relative to breeding. Data were analyzed using the MIXED procedure of SAS with day as repeated measure for glucose, BUN, and NEFA with significance at $P < 0.05$. **Results:** Serum glucose was greater in CON than RES (3.44 vs 3.21 ± 0.07 mM; $P = 0.03$). The gain by day interaction was significant for BUN and NEFA ($P < 0.05$), with BUN concentrations increasing and NEFA decreasing over time for CON but not for RES. Amniotic fructose concentration was greater in CON-OCM than CON+OCM and RES-OCM, with RES+OCM intermediate ($P = 0.005$). Allantoic glucose concentration tended to be greater ($P = 0.09$) for CON-OCM than CON+OCM. **Conclusions:** We conclude that supplementation of OCM in early gestation increases concentrations of energy metabolites glucose and fructose in fetal fluids of RES heifers. (Supported by USDA-NIFA-AFRI 2018-07055). USDA is an equal opportunity provider and employer.

I-XV Effect of prenatal stress on metabolism of heifers translocated to an unfamiliar environment.

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Objective: To evaluate the effects of translocation to an unfamiliar grazing environment in prenatally stressed (PNS) versus control (CON) yearling Brahman heifers. We have previously reported that these PNS heifers traveled farther each day and farther from water than CON. The PNS group selected a higher quality diet than CON but weight gain was not different between the two groups. **Methods:** Twelve half-sibling heifers (~12 months of age and 280±10 kg) born in spring 2019 at Overton, TX (1245 mm annual precipitation) were transported ~700 km southwest to Sonora, TX (610 mm annual precipitation) in April 2020. Six heifers were born to dams subjected to transportation stress during mid-gestation and six were born to non-stressed dams. Heifers grazed a series of 24-ha native range pastures (aboveground forage biomass; 1508±390 kg/ha). Serum samples, via coccygeal venipuncture, were obtained at 2-wk intervals from May through September. Differences between groups for metabolic parameters (albumin, blood urea nitrogen [BUN], glucose, cholesterol, beta hydroxybutyrate, and non-esterified fatty acids [NEFA]) were determined by a mixed model with treatment fixed and date repeated. Statistical significance was determined at $P < 0.05$. **Results**: Only BUN (mg/dL) differed ($P = 0.04$) between PNS (8.39±0.32) and CON (7.39±33). Albumin and glucose were numerically greater in PNS versus CON, while cholesterol and NEFA were numerically lower. **Conclusions**: Prenatal transportation stress enhanced adaptations to subsequent stressful situations in growing heifers via grazing behavior and diet selection. These adaptations resulted in greater circulating nitrogen concentration but did not result in greater weight gain. Further work with more animals and larger landscapes is required to determine how prenatal stress may fit grazing animals for future stress.

I-XVI Maternal Risk of Pre-eclampsia: Influence of Fetal rs1205 Genotype

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Objective: Pre-eclampsia (PE) is clearly an inflammatory state, but the question is whether inflammation is causal or simply a biomarker of some other primary factor. Placental mRNA expression of the C-reactive protein (*CRP*) gene is increased in women with PE, and infusion of CRP into pregnant mice reproduces some characteristics of PE. We have previously identified rs1205 and two other *CRP* gene variants, the maternal genotypes of which, increase the risk of PE. These findings were replicated in two non-American Indian populations. Considering potential pathophysiologic mechanisms, the rs1205 T allele is associated with reduced serum levels of CRP. Most analyses of genetic PE risk assume that maternal genotype confers risk, whereas the fetal genotype may be synergistic with the maternal genotype, or even determinative and the maternal genotype simply correlated with fetal genotype. **Method:** We enrolled only offspring of mothers known to be heterozygous for the rs1205 variant of *CRP* and experiencing either PE affected or normal pregnancies. Thus eliminating the maternal genetic influence of this variant. Offspring were then genotyped to determine if fetal rs1205 genotype was associated with PE. **Results:** Offspring of 24 of 31 normal pregnancies and 9 of 18 PE pregnancies exhibited the rs1205 T allele dominant genotype (Fisher's exact chi square p=0.048). Multivariate logistic regression analysis adjusted for maternal age, nulliparity and BMI gives an odds ratio of 0.275, p=0.072, 95% CI 0.067-1.123 for the fetal, T-dominant genotype. **Conclusion:** Among 49 women, heterozygous for the rs1205 allele, both chi-square and multivariate adjusted logistic analysis strongly suggest reduced risk of PE among pregnancies with fetal T allele dominant genotypes. This is consistent with previous findings of reduced risk associated with this genotype, and with a pathophysiologic model wherein less placental CRP expression reduces risk of PE. There have been 5 reported fetal variants associated with PE risk, but none previously related to *CRP*. (Supported by NIH P20GM103442)

II-I Preterm Cesarean versus Vaginal Birth Blunts Bile Acid- Fibroblast Growth Factor-19 Signaling in Neonatal Pigs

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Objectives: Birth by scheduled cesarean section has been shown to affect the development of the small intestine, brain, and microbiome. However, the impact of cesarean versus vaginal birth on the development of bile acid and fibroblast growth factor-19 (FGF19) signaling is unknown. In the fetus FGF19 is a potent growth factor, but postnatally, functions as a negative feedback mechanism for hepatic bile acid synthesis. The objective of this study was to determine the effect of birth modality (cesarean vs. vaginal) and gestational age (preterm vs. term) on plasma hormone levels, bile acid pool distribution, expression of genes in the bile acid-FXR-FGF19 pathway and plasma levels of FGF19 at birth and on day 3 of life in neonatal piglets. **Methods:** Four sows underwent a cesarean section on gestation day 105 (n=2) and 114 (n=2; term=115d), and two additional sows were allowed to farrow at term. Half of the piglets were euthanized at birth for tissue and blood collection, and the remaining pigs were nutritionally supported on total parenteral nutrition (TPN) then fed a bolus meal on day 3 of life, at which time tissue and blood were collected. Ex-vivo tissue explants were used to test tissue responsiveness to bile acids. **Results:** Piglets born vaginally had a markedly (30x) higher plasma FGF19 at birth than term pigs born via cesarean section, and 70x higher than preterm pigs (p<0.001). However, FGF19 gene expression in the distal ileum was similar in all groups (p >0.05). Ileal explants from cesarean and vaginally-derived pigs showed similar responsiveness to bile acid stimulation. Plasma FGF19 positively correlated with plasma cortisol (R=0.579; p <0.05). **Conclusions:** Exposure to maternal or endogenous glucorticoids in the perinatal period, which occurs during parturition, may have a profound effect on the development of the bile-acid-FGF19 pathway. Future work is focused on identifying the mechanism underpinning glucorticoid-FGF19 signaling in the perinatal period. (Support: USDA-ARS, NIH-NIDDK-RO1-DK094616-04A1)

II-II Antenatal Vitamin D Therapy Improves Pulmonary Endothelial Cell Growth and Response to Proangiogenic Stimuli in a Preeclampsia Model of Bronchopulmonary Dysplasia

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Objective: Preeclampsia (PE) is a major risk factor for preterm birth and the subsequent development of bronchopulmonary dysplasia (BPD), the chronic lung disease of prematurity. We have previously shown that antenatal (AN) exposure to soluble fms-like tyrosine kinase 1 (sFlt-1), an endogenous VEGF antagonist that is markedly increased in maternal blood and amniotic fluid in PE, causes abnormal lung structure and function in infant rats. We have also shown that AN vitamin D (VD; 1,25(OH)D) treatment improves infant lung structure and function after sFlt-1exposure in vivo. Since sFlt-1disrupts angiogenesis and VD has pro-angiogenic effects, we hypothesized that VD treatment improves lung structure through preserved pulmonary endothelial cell (PEC) growth after AN sFlt-1 exposure. To determine if VD treatment preserves rat PEC growth in vitro after AN sFlt-1 exposure. **Methods:** Fetal rats were exposed to saline (CTL), recombinant human sFlt-1 (sFlt-1), sFlt-1 + VD, or VD, via intra-amniotic (IA) injection at E20 and delivered at E22. At birth, PEC were isolated using CD-31 immunomagnetic cell separation. In vitro growth assays were conducted to assess baseline growth and response to VD or VEGF. **Results:** We found that AN exposure to sFlt-1 reduced PEC growth by 43% when compared to CTL PEC (p< .05). AN VD alone had no effect on PEC growth compared to CTL PEC, but when combined with sFlt-1exposure, VD prevented the suppression of PEC growth caused by sFlt-1alone (s-Flt-1 + VD v. s-Flt-1; p< 0.01) We next determined the effects of angiogenic stimuli on PEC growth. In CTL PEC, exogenous VEGF and 1,25(OH)D increased PEC growth by 44 % and 33%, respectively, compared to non-stimulated CTL PEC (p< 0.05). In sFlt-1exposed PEC, VEGF and 1,25(OH)D increased PEC growth by 70% and 68%, respectively, compared to non-stimulated sFlt-1 PEC (p< 0.01). In sFlt-1 + VD exposed PEC, VEGF and 1,25(OH)D increased PEC growth by68% and 55%, respectively, compared to non-stimulated sFlt-1 + VD (p< 0.05). In VD PEC, VEGF and1,25(OH)D increased PEC growth by 82% and 73% respectively compared to non-stimulated VD PEC (p<0.01). In CTL PEC, VEGF increased growth by 50% compared to sFlt-1 PEC treated with VEGF (p< 0.01). **Conclusions:** AN sFlt-1 exposure reduced PEC growth and blunted responsiveness to exogenous angiogenic stimuli invitro, and that AN VD treatment enhanced PEC growth and the response to angiogenic stimuli in this model. We speculate that VD treatment of sFlt-1 exposed pups preserves lung structure and function through enhanced pro-angiogenic signaling.

II-III Human Placental Lipid Metabolism in Maternal Obesity and across Gestation

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Introduction: Placental lipid metabolism alterations influence the delivery of lipids critical for fetal development and fetal lipid requirements may change across gestation. Maternal lipid metabolism is dysregulated in obesity. However, placental lipid metabolism in women with obesity and across gestation is poorly understood. We hypothesized that placental lipid content and metabolism increase across gestation and are elevated in obesity starting in first trimester. **Methods:** Placentas (4-40 weeks gestation) were collected from control (body mass index, BMI 18.5-24.9, n=37) and obese (BMI>30, n=19) pregnant women with informed consent. Tissue was homogenized and subjected to analysis of lipids (LC-MS/MS) and expression of lipid related enzymes (western blotting). Statistical analysis was performed using linear models and ANOVA with trimester and BMI as factors. **Results:** All 19 TAG and 9 of 35 identified PC species detected were higher in first trimester placenta ($P<0.05$). Four PC and 2 TAG species differed ($P<0.05$) often higher in obese mothers. Abundance of PC and TAG *de novo* synthesis enzymes GPAT3 and AGPAT2 as well as PC hydrolysis enzyme PLA2G4c were highest ($P<0.05$) in first trimester placenta. There were no differences in LPCAT4, which re-esterifies an acyl chain. Fatty acid binding protein 3 (FABP3) decreased whereas FABP5 increased across gestation and FABP5 was higher in obese mothers in second trimester ($P<0.05$). Abundance of mitochondrial transport proteins carnitine palmitoyltransferase (CPT)1a and CPT2 differed ($P<0.05$) by trimester and obesity, respectively. **Conclusion:** We corrected all placental lipids to protein content and hypothesized that would be increased across gestation and in obesity, rather placental lipid content was highest in first trimester with little impact of maternal BMI. The first trimester placenta is rapidly growing, which could explain elevated levels of PC, and has low oxygen tension, which has been shown to increase TAG abundance in other cell types. Fatty acid trafficking proteins were affected by both trimester and obesity, which may impact placental fatty acid transfer and beta-oxidation.

II-IV Maternofetal inflammation at mid-gestation impairs subsequent fetal growth, insulin secretion, and muscle-specific glucose metabolism

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Objectives: Maternofetal inflammation at 0.7 gestation causes intrauterine growth restriction (**IUGR**) in fetal sheep. However, inflammation during peak placental development has not been explored. Therefore, we determined the effects of maternofetal inflammation at 0.5 gestation on fetal glucose metabolism and insulin secretion near term. **Methods:** Pregnant ewes were injected every 3rd day from d50 to 65 of gestation (term=d150) with saline (controls; n=11) or lipopolysaccharide to induce maternofetal inflammation and IUGR (**MI-IUGR**; n=11). Fetuses were catheterized on d118. Hyperglycemic clamps and hyperinsulinemic-euglycemic clamps were performed on d123 and 124, respectively. Fetuses were necropsied at d125. **Results:** Basal plasma insulin did not differ between control and MI-IUGR fetuses, but glucose-stimulated insulin secretion was less ($P<0.05$) for MI-IUGR fetuses. Blood HCO_3, hemoglobin, Na^+, and K^+ were less ($P<0.05$) for MI-IUGR fetuses regardless of period, but blood glucose and lactate did not differ. Fetal hindlimb glucose uptake did not differ between groups at basal or hyperinsulinemia. Hindlimb glucose oxidation was less ($P<0.05$) for MI-IUGR fetuses, regardless of period. Plasma insulin and blood glucose did not differ between groups, but glucose-to-insulin ratios were greater ($P<0.05$) for MI-IUGR fetuses than controls under basal conditions. Blood O_2 was ~14% less ($P<0.05$) for MI-IUGR fetuses than controls, regardless of condition. At necropsy, MI-IUGR fetuses were 20% lighter ($P<0.05$) and their cannon bones were 6% shorter ($P<0.05$) than controls. MI-IUGR fetuses had smaller ($P<0.05$) hindlimbs and *semitendinosus*, *flexor digitorum superficialis*, *longissimus dorsi* muscles. Fetal heart, brain, liver, and kidney masses did not differ between groups. **Conclusions:** Maternofetal inflammation during peak placental development led to fetal hypoxemia but not hypoglycemia in later gestation. This coincided with poor β cell function, impaired hindlimb glucose oxidative capacity, and fetal growth restriction. These findings reflect metabolic phenotypes observed for other IUGR models and indicate some degree of placental insufficiency. (Supported by USDA-NIFA Foundational Grants 1018853, 1021843; NIGMS Grant 1P20GM104320; USDA-NIFA Hatch Multistate capacity funding 1011055, 1011126.)

II-V How does coronary flow in sheep change near birth?

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Objective: *Define perinatal changes in coronary perfusion of, and oxygen metabolism by the myocardium in normal development.* **Methods:** *Separate groups of late gestation fetal (N=7) and neonatal (N=6) lambs were instrumented with catheters (to measure systemic pressure and blood oxygen content, administer drugs), inflatable occluders (to transiently manipulate perfusion pressure), and a circumflex artery flow probe. Unanesthetized hemodynamics were recorded at 135d gestation (term 147d) or 5d postnatal. Pressure-flow studies were performed to determine coronary conductance and flow reserve with and without adenosine hyperemia. A subset (fetus N=4; neonate N=3) was anesthetized and left ventricular microvascular perfusion determined using myocardial contrast echocardiography. Separate fetuses (N=7) and lambs (N=4) were instrumented for simultaneous arterial and coronary sinus blood sampling to determine myocardial oxygen extraction (A-VO_2).* **Results:** *RPP (rate pressure product) was higher in neonates than fetuses (16,700±1,300 vs 7,900±400 mmHg min^{-1}, p<0.01), coronary flow was lower in neonates than fetuses (0.9±0.1 vs 1.7±0.3 mL $min^{-1}g^{-1}$, p<0.05), as was RPP- normalized oxygen delivery (6.5e-6±0.6e-6 vs 15.9e-6±1.7e-6 mL $mmHg^{-1}g^{-1}$, p<0.01). Coronary conductance was lower in neonates than fetuses at baseline (0.010±0.002 vs 0.027±0.004 mL $min^{-1}mmHg^{-1}g^{-1}$, p<0.01) and hyperemia (0.081±0.025 vs 0.176±0.023 mL $min^{-1}mmHg^{-1}g^{-1}$, p<0.05). Coronary reserve was similar between groups (5.0±0.9 vs 4.6±0.5 p>0.05). Microvascular perfusion was lower in neonates than fetuses (2.7±1.8 vs 9.6±1.6 mL $min^{-1}g^{-1}$, p<0.05). Coronary A-VO_2 was greater in neonates than fetuses (9.8±0.5 vs 3.8±0.4, p<0.0001), however when multiplied by flow, still indicated greater fetal than neonatal myocardial oxygen consumption.* **Conclusions:** *While coronary flow, microvascular perfusion, and oxygen delivery to, and consumption by, neonatal myocardium are lower than fetal myocardium, flow reserve is not different between ages. Reserve may be a set point around which other aspects of the coronary system develop. (Sponsored by NIH R01HL142483, R21HL152112).*

II-VI: Duration of Hypotension and Risk of Severe Intraventricular Hemorrhage in Periviable Infants

STUDY002601

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Objective: *Intraventricular hemorrhage (IVH) is a major neonatal complication of infants born before 26 weeks gestation. Factors that cause fluctuation in cerebral blood flow including hypotension, especially during the first week of life, are risks for IVH. Understanding the relationship between hypotension duration and risk of severe IVH could help guide our management of a hypotensive premature infant, especially when considering timing of intervention.* **Methods:** We performed a single-center retrospective cohort study. All liveborn infants with <26 weeks completed gestation between the years 2013 and 2020 were eligible for inclusion. Infants with multiple severe congenital anomalies, brain anomalies, severe congenital heart disease, death before head ultrasound, and outborn infants were excluded. Hourly mean arterial pressures (MAP) for the first 72 hours of life were extracted for each infant. Data for duration of hypotension was collected based on two commonly accepted definitions of hypotension: MAP below gestational age (MAP<GA) and MAP below 30 (MAP<30). The diagnosis and severity of IVH was assessed using head ultrasound at 7 days of life. Chi-squared test or Fisher's exact test was used to analyze categorical variables and independent sample T-test for continuous variables. We performed a multivariable logistic regression analysis to assess crude and adjusted associations between outcomes and predictive factors. **Results:** 198 infants met criteria for inclusion. Infants that were hypotensive for longer than 60 consecutive minutes had higher severity of IVH (p=0.008) when using a MAP<GA as the definition of hypotension. In our univariate analysis, mean birth weight, multiple gestation, and prolonged rupture of membranes were significantly associated with longer duration of hypotension (MAP<GA for longer than 60 minutes). There were no significant findings when using the MAP<30 definition. A multivariable logistic model revealed hypotension duration longer than 60 minutes to be independently predictive of IVH severity. **Conclusions:** Hypotension (MAP<GA) for longer than 60 consecutive minutes is associated with higher severity of IVH in periviable infants. *Travel Award: Sponsored by National Institutes of Health*

II-VII Investigating Transthyretin and Thyroid Hormones in CSH RNA Interference-Induced IUGR Pregnancies

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Introduction: *In vivo* lentiviral-mediated RNA interference of chorionic somatomammotropin (CSH) results in intrauterine growth restriction (IUGR) in sheep. Abnormal levels of thyroid hormones (TH; T_3 and T_4) have been reported in some animal models of IUGR pregnancies, with reductions in T_4 concentrations in both maternal and fetal circulation. Transthyretin (TTR) is a TH binding molecule produced by trophoblast cells that preferentially binds T_4 and may shuttle T_4 through the placenta. **Objective:** Assess TTR, T_3 and T_4 concentrations in both CSH RNAi IUGR and control pregnancies. We hypothesize that in this model of IUGR, a reduction of placental CSH affects day 135 TH levels in maternal and fetal circulation by impacting serum TTR levels. **Methods:** The trophectoderm of hatched blastocysts was infected with lentivirus expressing either a non-targeting sequence (NTS) shRNA or a CSH shRNA to generate a CSH RNAi model of IUGR. Uterine vein, uterine artery, umbilical vein, and umbilical artery blood was collected via catheterization, and maternal and fetal tissue was harvested near term (day 135) from CSH RNAi pregnancies (n=4) and NTS RNAi pregnancies (n=4). TTR protein abundance was determined through western blot analysis, and T_4 and T_3 levels were assessed using competitive ELISA assays. **Results:** TTR was reduced 61% (P=0.04) in the uterine artery and 64% (P=0.02) in the uterine vein, in CSH RNAi pregnancies. In the umbilical artery, TTR was reduced 51% (P=0.04), with no significant changes in umbilical vein concentrations. Umbilical artery T_4 concentrations were reduced 29% (P=0.02), whereas umbilical vein (16%; P=0.06), uterine artery (16%; P=0.10) and uterine vein (15%; P=0.10) T_4 concentrations tended to be reduced. There was no significant change in T_3 concentrations in CSH RNAi pregnancies. **Conclusion:** These results suggest that TTR protein abundance and T_4 abundance is reduced by CSH RNAi in maternal and fetal circulation. (Supported by NIH HD093701). *Travel Award: Sponsored by United States Department of Agriculture, National Institute of Food and Agriculture*

II-VIII Influence of maternal diabetes on the development of myocardial mitochondrial reticulum

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Objective: Maternal diabetes impairs mitochondrial dynamism and quality control, leading to poor energy efficiency and cardiac disease in offspring at birth and in adulthood. The objective of this study was to evaluate the effects of maternal diabetes on development of the myocardial mitochondrial reticulum over time. **Methods:** Left ventricle from control and diabetes-exposed newborn (NB), 3 week, and 4-month-old rats were processed for 3D serial block face-scanning electron microscopy (n=4/group at each timepoint). Stacks of approximately 500 images were obtained at 50nm increments. Each stack was aligned using Amira software, then analyzed and 3D-reconstructed with Reconstruct Software. Interfibrillar (IF) and Perinuclear (PN) mitochondria/standardized grid were quantified across 10 consecutive slices. Counts and whole mitochondria volume from 10 mitochondria/heart were compared using T-test at each timepoint. Local polynomial regression was used to examine differences over time/group with 95% CI and alpha of 0.05. **Results:** At birth, diabetes-exposed myocardium had 50% fewer PN and 20% fewer IF mitochondria ($p<0.0001$, $p=0.003$). In controls, PN count remained steady over time while IF count declined with expected fusion into a mature reticulum. In diabetes-exposed myocardium, PN and IF count increased so that by three weeks no difference remained, suggesting increased postnatal biogenesis. At 4 months, diabetes-exposed offspring had 35% more PN and 49% more IF mitochondria, but mitochondrial volume was significantly lower in diabetes-exposed myocardium at every developmental timepoint ($p=0.02$ for NB IF mitochondria and $p<0.0001$ for all others). **Conclusions:** Fetal exposure to maternal diabetes impairs myocardial mitochondrial reticulum development postnatally. Alongside previous confocal, mtDNA copy number, bioenergetics, and echocardiograph findings over time, we are confident that diabetes-mediated alterations in the mitochondrial reticulum explain developmentally programmed risk of adult cardiac disease in our model. (NIH/NIGMS-2P20GM103620-06) *Travel Award: Sponsored by National Institutes of Health*

II-IX Leptin Insensitivity and Impaired Lung Maturation during Maternal Overnutrition

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Objective: Maternal overnutrition has been linked to pregnancy-related complications, which extend into the neonate with higher incidences of respiratory distress syndrome and mortality. Maternal high-fat diet (HFD) rodent models suggest that impaired neonatal lung growth has long-term adverse health consequences. We hypothesize that pulmonary pathologies are linked through disruption in leptin signaling and altered metabolic pathways. The purpose of our study was to assess molecular markers of leptin insensitivity in newborn rat lungs birthed from HFD dams. **Methods:** Sprague-Dawley rats were placed on a control diet (CD; 18% calories as fat) or HFD (40% calories as fat) for 4 weeks before mating and continuing throughout pregnancy and parturition. Since dams on HFD had 2-fold greater postpartum circulation levels of leptin, SDS-PAGE/immunoblot was used for semi-quantitative analysis of pulmonary expression for leptin signaling proteins in P1 offspring from CD and HFD dams (n=8): leptin receptor (OBR-B), FOXO1 (p-ser249), STAT3, and PTP1B. **Results:** OBR-B expression increased 1.8-fold ($p<0.0001$) in maternal HFD offspring. Expression of terminal transcriptional factor of leptin signaling, STAT3, decreased 2.8-fold ($p=0.0087$). FOXO1, a negative regulator of STAT3 transactivation, increased 4.4-fold ($p<0.0088$) without any change in phosphorylation status (p-ser249 inhibits FOXO1-dependent STAT3 inhibition). There was no difference in the PTP1B levels between the two groups ($p=0.35$). **Conclusions:** Our data support the hypothesis that impaired leptin signaling could contribute to pulmonary pathologies in the offspring of mothers with overnutrition and obesity. Decreased STAT3 with increased FOXO1 expression suggests reduced expression of leptin-dependent target genes and likely compensatory upregulation of OBR-B. Ongoing studies assess expression of downstream leptin-dependent gene targets and metabolite profiles. This work is supported by The Children's Hospital Foundation Fellowship Research Award (awarded to ST Ahmed). *Travel Award: Sponsored by United State Department of Agriculture, National Institute of Food and Agriculture*

II-X Transcriptomic Analysis of Sheep Fetal Liver in Chorionic Somatomammotropin Deficient Pregnancies

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Objectives: *In vivo* chorionic somatomammotropin (CSH) RNA interference (RNAi) results in placental and fetal growth restriction. These fetuses are characterized by hypoglycemia, hypoinsulinemia and significant reductions in umbilical IGF1. We hypothesized that fetal livers from these growth-restricted CSH RNAi pregnancies would exhibit significant changes in the transcriptome. **Methods:** Hatched blastocysts at day 9 of gestational age (dGA) were collected and the trophectoderm was infected with a lentivirus expressing either a non-targeting sequence (NTS RNAi; n=4) or a CSH-specific shRNA (CSH RNAi; n=4) and were transferred into synchronized recipient ewes. Pregnancy was maintained to 135 dGA where the uteroplacental unit was excised and fetal liver tissue was harvested. **Results:** CSH RNAi fetal weights were significantly smaller (2.71 ± 0.37 vs 4.09 ± 0.14 kg: $P \leq 0.01$), as were the fetal liver weights (57.7 ± 11.6 vs 111.3 ± 7.3 g; $P \leq 0.01$). RNA-sequencing was performed on the Illumina NovaSEQ6000 platform and a total of 103 differentially expressed genes (DEGs) were identified via analysis using CLC Genomics Workbench. Functional analysis of DEGs were performed via DAVID. This revealed significant alterations in transcripts involved in metabolic pathways ($P \leq 0.01$), glycolysis/gluconeogenesis ($P \leq 0.01$), arginine and proline metabolism ($P \leq 0.05$), and positive regulation of fat cell differentiation ($P \leq 0.01$). **Conclusions:** Specific transcriptional changes include significant up-regulation of LDHA, G6PC1, and PCK1 (1.77-, 9.59- and 5.94-fold change, respectively), suggesting enhanced gluconeogenesis, in the face of fetal hypoglycemia in CSH RNAi pregnancies. ARG2 was also upregulated 5.96-fold, which could effectively reduce the arginine available for nitric oxide (NO) synthesis. Reductions in fetal hepatic NO could augment vasoconstriction and shunting of blood through the ductus venosus. These results support the hypothesis that CSH RNAi results in altered fetal liver transcription of metabolic pathways. By investigating transcriptional changes from CSH RNAi pregnancies we will better understand the pathways involved in the development of IUGR due to CSH deficiency. (Supported by NIH HD093701). *Travel Award: Sponsored by United States Department of Agriculture, National Institute of Food and Agriculture*

II-XI Maternal adiponectin supplementation prevents elevated muscle lipids that program insulin resistance in male offspring of obese dams.

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Objectives: Offspring born to obese mothers are at higher risk for developing insulin resistance, which can result in obesity and diabetes. Accumulation of diacylglycerols (DAGs) and ceramides (CER) in skeletal muscle is believed to be one common cause of insulin resistance. Obese mothers have lower levels of circulating adiponectin (ADN), which is associated with increased placental nutrient transport and fetal overgrowth. We have recently published that ADN supplementation in obese dams prevents insulin resistance and obesity in the offspring. We hypothesized that normalizing maternal ADN in obese pregnant mice prevents excess lipid accumulation within the skeletal muscle of 9-month-old offspring. **Methods:** Twelve-week-old C57/BL6J female mice were placed on either a control or obesogenic diet. Females were mated after obesogenic diet resulted in 25% increase in body weight. On embryonic day (E) 14.5, a mini osmotic pump was implanted subcutaneously. Control dams received infusion of phosphate-buffer saline (PBS, n=5), while obese dams received either PBS (n=5) or mouse recombinant full-length ADN (n=5) for 4 days. Dams delivered spontaneously and were maintained on their respective diets throughout lactation. Following weaning, offspring were maintained on standard chow. Skeletal muscle was obtained from 9-month-old offspring, homogenized and lipids were extracted. DAGs and CER were measured using liquid chromatography tandem mass spectrometry. **Results:** We found 1,2-di14:0DAGS and 1,2-di16:0DAGs were 53 and 80% higher, respectively, in male, but not female, offspring from obese mothers compared to offspring of obese+ADN mothers ($p<0.05$). Additionally, 16:0Cer was 72% higher in the male, but not female, offspring of obese mothers compared to the offspring of obese+ADN mothers ($p<0.05$). Normalization of maternal ADN levels in obese dams prevented the elevated muscle DAGs and CER in 9-month-old male offspring. **Conclusions:** These data suggest that low maternal ADN in obese dams is mechanistically linked to accumulation of lipids in skeletal muscle in male offspring, which could explain their insulin resistance. (Supported by R01HD065007). *Travel Award: Sponsored by University of Colorado*

II-XII Glucagon-like Protein-1 Receptor is Expressed in the Human Placenta and Activates ERK1/2 Signaling

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Objectives: Maternal obesity is associated with increased risk of fetal overgrowth. We previously found maternal plasma glucagon-like peptide-1 (GLP-1) is associated with fetal overgrowth in maternal obesity (Dumolt et al 2022. Reproductive Sciences Vol. 29, Supplement 1, 64A). The GLP-1 receptor (GLP-1R) is known to activate ERK1/2 signaling pathway and is thought to regulate cellular proliferation in non-placental tissues. However, the expression, localization, and function of GLP-1R in human placenta has not been previously described. We hypothesized GLP-1R is predominately expressed in the syncytiotrophoblast microvillous membrane (MVM) and activates the ERK1/2 signaling pathway. **Methods:** Placentas were collected from women with obesity (pre-pregnancy BMI > 30) delivering large for gestation age (LGA) infants (OB-LGA) or AGA infants (OB-AGA) at term. Placentas were homogenized and syncytiotrophoblast MVM and basal plasma membrane (BM) (n=17/group) were isolated. MVM and BM glucagon-like peptide-1 receptor (GLP-1R) and expression were measured by western blot and immunohistochemistry (IHC). Primary human cytotrophoblasts were isolated from term placental villous tissue (n=4). At 90 hours culture, cells were treated with the GLP-1 receptor agonist Exendin-4 and probed for pERK1/2 with immunoblot. Differences between OB-LGA and OB-AGA were determined by t-test. **Results**: Placentas from OB-LGA pregnancies weighed more ($p<0.05$) and positively correlated with birthweight (Pearson $r^2=0.59$, $p<0.05$). GLP-1R was identified in the MVM and BM by immunoblot and confirmed by IHC. GLP-1R expression was not different between groups ($p>0.05$), however, GLP-1R was predominately expressed on the maternal facing MVM ($p<0.05$). Placental GLP-1R activation with Exendin-4 increased pERK1/2 by 80% compared to controls ($p<0.05$). **Discussion:** We report for the first time that GLP-1R is present on the syncytiotrophoblast MVM and activates the ERK1/2 pathway which may contribute to the larger placenta observed in OB-LGA pregnancies. We speculate maternal GLP-1 may act as a novel regulator of placental function and fetal growth. *Travel Award: Sponsored by University of Colorado*

II-XIII Maternal Mastitis Infection During Pregnancy Impacts Hepatic Gene Expression in Bull Calves
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Objective: To determine if mastitis infection and/or high milk production during pregnancy can impact calf health, RNA-seq on offspring hepatic tissue was performed. **Methods:** Calves from dams that were high producers (HI; n = 4), high producers with mastitis (HIMAST; somatic cell count ≥ 200,000 cells/mL; n = 5) or moderate producers (MOD; n = 5) were slaughtered at approximately 11 weeks of age. Liver RNA was isolated and sequenced. Reads were aligned to the *Bos taurus* (BosTau9) reference annotation using HISAT2 and assembled using Stringtie. Differentially expressed genes (DEG) were identified using EdgeR ($q \leq 0.01$). Pathway analyses were performed using Panther version 17.0. **Results:** 421, 1,198, and 2,086 DEG were identified for MOD vs HI, MOD vs HIMAST, and HIMAST vs HI respectively. 40%, 65%, and 29% of DEG were upregulated while 60%, 35%, and 71% of DEG were downregulated in MOD vs HI, MOD vs HIMAST, HIMAST vs HI. For pathway analyses, 17 DEG were classified in the gonadotropin releasing hormone pathway and 13 DEG were involved in inflammation for HIMAST vs HI. Ten genes each were identified in the cholecystokinin receptor and inflammation pathways for MOD vs HIMAST. HIMAST calves exhibited a 15.06-fold reduction in *Talin (TLN)-1, variant X1* expression compared with HI ($q < 0.01$). Likewise, *TLN1, variant X1* expression was 15.16-fold greater in MOD vs HIMAST calves ($q < 0.01$). *Septin 7, variant X5* was reduced 15.31 and 14.66-fold in MOD compared with HIMAST and HI respectively ($q < 0.01$). Alternatively, Septin *7, variant X6* was 14.92-fold greater in MOD vs HIMAST calves ($q < 0.01$). C**onclusions:** We determined that maternal mastitis infection, as well as high maternal milk production during pregnancy, impacts the hepatic transcriptome of the male offspring. Proteomics analyses are being performed to determine how these changes in gene expression are reflected at the protein level. (Supported by USDA-AFRI-NIFA: 2018-06802 and USDA: RI0021-AH101)

II-XIV Racial Differences in the Metabolome and Inflammatory Status in Second Trimester Human Placenta
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Objectives: Fetal growth and the incidence of pregnancy complications have been reported to exhibit racial/ethnic differences. The placenta is metabolically active and supports the growth of the fetus, and placental insufficiency is implicated in the pathogenesis of preeclampsia and preterm birth. We hypothesized that the placenta may exhibit racial differences in the capacity of bioenergetics and metabolism during mid gestation, which may underlie the racial disparity in fetal growth and pregnancy complications. **Methods:** Focused on Black and White populations, which show the most differences in fetal growth and pregnancy complication rates, we performed metabolomics and Luminex assays in both male and female placentas (n=9 for males; n=10 for females) from second trimester pregnancies (18-22 weeks) to assess the differences of metabolomic signatures and cytokine/chemokine levels between Black and White patients. *t*-tests with $p<0.05$ were considered significantly different. **Results:** 866 metabolites were identified in the human placentas. Racial differences were profound in both genders. The levels of 317 and 332 metabolites were significantly different between Black and White patients in male and female placentas, respectively, and nearly all these metabolites were lower in Black compared to White placentas. Notable changes in metabolites that were significantly lower in Black vs. White placentas include metabolites in glycolytic and energy related pathways, fatty acid beta-oxidation, branched-chain amino acid metabolism, and oxidative stress. Furthermore, M-CSF and PDGF-AA levels were significantly lower in Black male vs. White male placentas. In female placentas, eotaxin, fractalkine, IFN-a2, IL-1a, IL-10, and MCP-1 levels were significantly different between Black and White patients. **Conclusions:** Our results demonstrate significant and biologically relevant racial differences in the placental metabolome and inflammatory status in Black and White populations. The observed differences that impact placental and fetal development may contribute to the racial disparity in fetal growth and pregnancy complications. (Supported by the March of Dimes).

II-XV IGF-1 infusion promotes linear growth without reducing insulin secretion in late gestation IUGR fetal sheep

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Objectives: Insulin and insulin-like growth factor-1 (IGF-1) are fetal growth hormones that have overlapping anabolic actions. Complications of pregnancy such as placental insufficiency can lead to intrauterine growth restriction (IUGR) with lower fetal insulin and IGF-1 concentrations and reduced glucose-stimulated insulin secretion (GSIS). We have demonstrated that a one-week infusion of the IGF-1 analogue, IGF-1 LR3, into normally grown fetal sheep increased body weight but lowered insulin concentrations and GSIS responsiveness. In this study, we test the hypothesis that a one-week IGF-1 infusion into IUGR fetuses known to have lower IGF-1 concentrations will improve fetal growth and potentiate GSIS. **Methods:** Pregnant sheep carrying twins were exposed to elevated ambient temperatures to produce placental insufficiency and IUGR (n=7). During late gestation, one fetus from each pregnancy was infused with IGF-1 LR3 (IGF-1) and the other fetus with vehicle (VEH) for one week. Plasma glucose, insulin, lactate, and arterial oxygen content were measured throughout infusion. On the final day of infusion (131-133 days gestation; term 147 days), GSIS was measured with a hyperglycemic clamp. **Results:** Fetal body weights tended to be heavier (IGF-1 2.27±0.41 kg vs VEH 1.99±0.36 kg; *P*=0.0856), and hindlimbs were 4% longer in IGF-1 (*P*=0.0322). Plasma glucose concentrations decreased over time in IGF-1 but not VEH (*P*=0.0238). Fetal insulin, lactate, and arterial oxygen concentrations were not different based on infusion. Fetal GSIS responses were similar between groups. **Conclusions:** A one-week infusion of IGF-1 LR3 increased linear fetal growth but did not potentiate GSIS. In IUGR fetuses, we speculate that exogenous IGF-1 can promote fetal growth without causing further disruption in β-cell function. This has important implications when considering pharmacological strategies to mitigate the adverse consequences of placental insufficiency on fetal growth and β-cell function (Supported by R01-DK088139 (PJR), T32-HD007186 (AW)).

II-XVI Fighting Maternal and Fetal Morbidity One Chemokine Axis at a Time

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Objectives: To further characterize the importance of the C-X-C motif chemokine receptor 4 (CXCR4) and its ligand CXCL12 on placentation and fetal growth through impacts on placental lactogen and members of the insulin-like growth factors (IGF) and their binding proteins (IGFBP1-3). **Methods:** Osmotic pumps were surgically implanted in sheep on day 12 of gestation to deliver either saline (control: n=6) or the CXCR4 inhibitor AMD3100 at a 1.5X dose, (n=8) or 3X dose (n=8) into the uterine over 14 days. At midgestation (d 90) and late gestation (d 135) placental and fetal liver tissues were harvested, and real time qPCR was performed to analyze gene expression. **Results:** Of the targets tested, mRNA expression was significantly decreased by AMD3100 treatment for both IGF-1 ($p = 0.05$) and IGF-2 ($p = 0.02$) primarily in maternal placenta tissues from d135. **Conclusion:** Our preliminary data shows an importance of the CXCL12- CXCR4 signaling on placentation and that impairment of this axis may alter IGFs in multiple tissue types later in gestation. Insights into this axis could lead to a greater understanding of placental development and its importance to the health of the mother and child. (Supported by NIH Grant 1SC1GM139712-01).

II-XVII PFOA Exposure Prior to Hepatocyte Differentiation Leads to DNA Methylation and Expression Changes Linked to Non-Alcoholic Fatty Liver Disease

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Objectives: Our objective was to characterize how perfluorooctanoic acid (PFOA) exposure during hepatocyte differentiation leads to the development of non-alcoholic fatty liver disease (NAFLD) through alterations in DNA methylation and transcription factor binding sites accessibility. PFOA is a persistent fluorinated compound with oil and water repelling properties found in cookware, food packaging and municipal water systems. **Methods:** HepaRG cells (human-derived hepatocyte progenitor cells) were treated with 0.5uM PFOA or vehicle for 48 hours followed by differentiation. RNASeq was performed and analyzed using DESeq2 ($q<0.05$). Genome-wide DNA methylation analysis via MethylSeq was completed to identify differentially methylated regions (DMRs), ($q<0.05$). Enrichment analysis of transcription factor binding motifs within DMRs (± 200 bp) was performed using HOMER**. Results:** PFOA treatment resulted in decreased expression of the transcription factors *EGR1*, *NR4A1*, *EGR2*, *KLF10*, and *FOSL1*, key genes linked to impaired hepatic insulin signaling, lipid metabolism, steatosis and fibrosis ($q<0.05$) in undifferentiated hepatocytes. Differentiated hepatocytes had decreased expression of *PGC1*α, *PPAR*γ, *FOXO1* and *PDK4*, genes linked to regulation of lipid metabolism and insulin signaling ($q<0.05$). MethylSeq identified 57 DMRs in undifferentiated hepatocytes ($q<0.05$) and 75 DMRs in differentiated hepatocytes ($q<0.05$). HOMER identified 29 known transcription factor binding motifs in undifferentiated hepatocytes ($p<0.05$) and 19 in differentiated hepatocytes ($p<0.05$), with significant changes in the EGR1 consensus sequence in both comparisons. **Conclusions:** We conclude that hepatocyte progenitor cells exposed to low dose PFOA results in changes in DNA methylation and expression of key metabolic genes linked to NAFLD, notably *EGR1*, a gene previously linked to NAFLD, suggesting PFOA exposure *in utero* has lasting effects. Funded by CHOP Pediatric Endocrinology T32 #5T32DK063688-17, NIEHS P30-ES013508, Pediatric Endocrine Society Research Fellowship Award.

TUESDAY, AUGUST 30, 2022

V-I Effects of poor maternal nutrition during gestation on colostrum and milk composition in F0 ewes

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Objectives: We previously reported that restricted- and over-feeding during gestation reduced offspring body weight (BW). To determine if lactation contributes to changes in offspring BW, we determined ewe colostrum and milk composition. We hypothesized that maternal restricted-nutrition would decrease and maternal over-nutrition would increase total solids, fat, and protein during early and transitional lactation, respectively. **Methods:** Forty-six multiparous Dorset ewes pregnant with twins were fed 100% (CON; n=13), 60% (RES; n=17) or 140% (OVER; n=16) of National Research Council requirements from d 30 ± 0.02 of gestation until parturition. Following parturition, animals were fed a similar lactation diet so that nutritional insult only occurred during gestation. Colostrum samples were collected within 24h of birth, and milk samples were collected at d3 and d21 postpartum. Colostrum and milk composition were evaluated using Brix Refractometry (total solids, g/dL) and spectrophotometry (crude fat, %; crude protein, %). **Results:** We did not detect an effect of diet on total solids, crude fat, and crude protein of colostrum nor milk ($P \geq 0.465$). A main effect of time was observed for all variables where colostrum had greater total solids, crude fat, and crude protein compared with milk at d3 and d21 ($P \leq 0.0001$). A treatment by time interaction was observed for crude fat where RES colostrum had less fat than CON colostrum ($P \leq 0.024$). **Conclusions:** In conclusion, reduced BW in OVER offspring are due to poor maternal diet during gestation and likely not a result of colostrum or milk composition. It is possible that early differences in RES offspring BW are due to decreased colostrum crude fat; however, the persistent reduced BW in RES and OVER offspring are likely due to diet during gestation. In addition, future studies are needed to determine if milk quantity is affected by maternal diet. *Travel Award: Sponsored by United State Department of Agriculture, National Institute of Food and Agriculture*

V-II Alterations of the Gastrointestinal Microbiome Associated with Western-Style Diet Feeding in a Primate Model of Testosterone Induced Polycystic Ovarian Syndrome May Modulate Reproductive Health

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Objectives: Polycystic ovarian syndrome (PCOS) is a prevalent endocrine disorder affecting the reproductive health of women driven by elevated testosterone (T; hyperandrogenemia) and an obesogenic diet. Given the endogenous microbiome may modulate fertility and pregnancy outcomes, we hypothesized these same microbiome communities may vary in association with different aspects of PCOS etiology. Thus, we leveraged a nonhuman primate (NHP) model to assess the individual effects of elevated T (PCOS levels), a high-fat, Western-style diet (WSD), and the combination of T+WSD on the microbiome community structure in these animals relative to controls (C). **Methods:** Rhesus macaque females (n=40) received subcutaneous implants of cholesterol (control; C) or T (serum T level ~1.4 ng/mL) and were fed either a low-fat control diet (CD; 14% fat) or a 36% fat WSD, resulting in four cohorts: 1) C+CD 2) T+CD 3) C+WSD and 4) T+WSD (n=10/group). Rectal and anal samples were collected at 1) baseline, 2) 18 months, and 3) at time of Cesarean delivery (~4 years). Microbial DNA was extracted from the samples (n=110), and rRNA V4 region amplicons of the bacteria-specific 16S rRNA gene were sequenced on the Ilumina platform. Customized bioinformatics pipelines were developed for longitudinal microbiome community and inferred functional analysis. **Results:** Alpha diversity was measured with Shannon index and statistical analysis was computed with pairwise Wilcox test, with $p<0.05$ considered significant. There were no statistically significant differences in alpha diversity between the control and treatment cohorts at baseline or at time of Cesarean delivery. However, there was a significant difference in alpha diversity between the C+CD and C+WSD cohorts ($p=0.001$) and the C+CD and T+WSD ($p=0.0001$) over time noted at 18 months. Permutational analysis of variance of beta diversity demonstrated a significant difference in the gut microbiomes across each of the four cohorts at 18 months ($p=0.001$) and at time of cesarean delivery ($p=0.001$). **Conclusions:** Treatment with chronic T, in both the absence and presence of WSD consumption, alters the community structure and function of the gut over time by reducing the alpha diversity of the microbiome. These findings suggest potential interactions between the microbiome, hyperandrogenism, and diet which may ultimately play a role in conception, fetal development, and pregnancy outcomes. [Supported by NIH/NICHD Women's Reproductive Health Research program K12 HD103087, NICHD P50 HD071836 (NCTRI), P51OD011092 (ONPRC)]. *Travel Award: Sponsored by United States Department of Agriculture, National Institute of Food and Agriculture*

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VIII-I Manipulating β2 adrenergic activity in IUGR-born lambs with daily clenbuterol injections improved glucose-stimulated insulin secretion and oxidative metabolism at 60 days of age.
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Objectives: Metabolic programming by intrauterine growth restriction (IUGR) includes reduced muscle β2 adrenoceptors, which persists after birth. We sought to determine whether increasing β2 adrenergic tone might improve metabolic outcomes in IUGR-born juvenile offspring. **Methods:** Pregnant ewes were housed under thermoneutral or hyperthermic (40°C) conditions from d35 to 95 of gestation to produce control and IUGR-born lambs. From birth to 60d of age, IUGR lambs received IM injections of saline (IUGR; n=10) or 0.8 µg/kg/d clenbuterol (IUGR+CLEN; n=10). Control lambs (n=11) were pair-fed and saline-injected. Lambs were catheterized on d55. Whole-body oximetry was performed on d30 and 57. Hyperglycemic and hyperinsulinemic-euglycemic clamps were performed on d58 and 59, respectively. Lambs were necropsied on d60. **Results:** Basal plasma insulin did not differ among groups. Glucose-stimulated insulin secretion was less ($P<0.05$) for IUGR lambs than controls and was intermediate ($P<0.05$) for IUGR+CLEN lambs. Basal and insulin-stimulated hindlimb glucose uptake did not differ among groups. Basal hindlimb glucose oxidation did not differ, and insulin-stimulated glucose oxidation was less ($P<0.05$) for IUGR but not IUGR+CLEN lambs compared to controls. Glucose-to-insulin ratios and high-density lipoproteins were greater ($P<0.05$) and blood urea nitrogen was less ($P<0.05$) for IUGR and IUGR+CLEN lambs than controls, regardless of period. Plasma triglycerides were not different for IUGR lambs but were greater ($P<0.05$) for IUGR+CLEN lambs than controls. Conversely, plasma non-esterified fatty acids were less ($P<0.05$) for IUGR but not IUGR+CLEN lambs compared to controls. Regardless of age, whole-body O_2 consumption was less ($P<0.05$) for IUGR and IUGR+CLEN lambs and CO_2 production was less ($P<0.05$) for IUGR but not IUGR+CLEN lambs than for controls. **Conclusions:** Deficits in metabolic substrate utilization and oxidative metabolism persisted in IUGR-born juvenile lambs but targeting underlying β2 adrenergic dysfunction effectively improved metabolic outcomes in these offspring. (Supported by USDA-NIFA Foundational Grants 1018853, 1021843; NIGMS Grant 1P20GM104320; USDA-NIFA Hatch Multistate 1011055, 1011126.) *Travel Award: Sponsored by United States Department of Agriculture, National Institute of Food and Agriculture*

VIII-II Maternal hyperglycemia increases uteroplacental oxygen utilization but fails to restore fetal glucose uptake in chorionic somatomammotropin RNAi pregnancies.
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Introduction: Chorionic somatomammotropin (CSH) RNA interference (RNAi) results in global impairment in nutrient uptake and transfer by the placenta. This includes substantial reductions in umbilical glucose uptake near-term (130 days of gestational age; dGA). Objective: To test for impaired maximal placental glucose transfer capacity in CSH RNAi pregnancies. **Methods:** Trophectoderm of sheep blastocysts (9 dGA) were infected with a lentivirus expressing either a non-targeting sequence (CON RNAi; n = 5) or CSH-specific shRNA (CSH RNAi; n = 7), prior to transfer into recipient sheep. At 126 dGA, pregnancies were fitted with vascular catheters. At 136 dGA, pregnancies underwent baseline steady-state metabolic studies with the ^3H_2O transplacental diffusion technique, followed by a 180-minute, maternal hyperglycemic clamp. **Results:** Fetal and placental weights were reduced ($P \leq 0.05$) in CSH RNAi animals. Basal uterine and umbilical glucose uptakes were suppressed ($P \leq 0.05$) along with umbilical insulin concentrations in CSH RNAi pregnancies. The hyperglycemic clamp normalized uterine glucose uptake. Despite similar uterine glucose uptakes, umbilical glucose and insulin concentrations in CSH RNAi fetuses tended ($P \leq 0.10$) to remain lower, as did uterine and umbilical blood flows ($P \leq 0.10$). While the slope of the relationship between umbilical glucose uptake and the maternal:fetal arterial glucose gradient was not statistically different ($P = 0.34$), the y-intercepts were lower in CSH RNAi ($P = 0.003$), indicating reduced maximal glucose transport capacity. This may be explained in part by elevated ($P \leq 0.05$) relative uteroplacental oxygen utilization, suggesting greater placental oxidation of substrates by the CSH RNAi placenta. **Conclusions:** Analyses suggest that perturbations in glucose transfer appear to be a combination of transfer mechanisms and reduced placental mass. Together, these data suggested that CSH likely plays a key role in modulating placental metabolism to ensure maximal placental glucose transfer. (Supported by NIH HD093701).
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VIII-III Single-cell transcriptomics identifies β-cell subpopulations in ovine FGR fetuses

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Objectives: Reductions in insulin secretion and β-cell mass were found in fetuses with placental insufficiency-induced fetal growth restriction (FGR). We have shown that the proportion of β-cells was smaller in FGR islets. Our objective was to sequence pancreatic islet cells and identify reductions in FGR β-cell sub-populations. **Methods:** FGR fetuses were generated by exposing pregnant ewes to environmental hyperthermia during mid-gestation. FGR fetuses were compared to control fetuses from thermoneutral ewes (n=3/group). Islets were isolated from fetuses near-term and disassociated into a single cell suspension. We used the 10X Genomics platform for single-cell RNA sequencing and analyzed the data with Seurat (P-adjusted value < 0.05). **Results:** FGR fetuses weighed less than controls (1.3±0.1 kg vs 3.3±0.3 kg, P<0.01). A total of 12,170 and 5,907 islet cells were sequenced from control and FGR fetuses, respectively. Fourteen cell-type classifications (clusters) were identified in a two-dimensional uMAP. Three clusters (0, 1, and 2) expressing insulin were identified as β-cell sub-populations. Because insulin expression was greater in cluster 2 (C2) compared to clusters 0 and 1, we grouped clusters 0 and 1 (C0-1) for further comparisons. The prevalence of GCK, MDH1/2, and VDAC1/2 was greater in C2 cells than in C0-1 cells. C2 β-cells also have greater expression of genes involved in carbon metabolism, oxidative phosphorylation, and endocytosis compared to C0-1 β-cells. This expression profile is reminiscent of signature genes in mature β-cells. Therefore, C2 β-cells exhibit a mature β-cell phenotype compare to C0-1 β-cells. C2 β-cells represent 19.4% of the total FGR islet cell population, whereas these cells make up only 7.2% of the control islet cells. In contrast, C0-1 β-cells represent 18% of the total FGR islet cells compared to 40% in controls. **Conclusions:** In conclusion, FGR islets are composed of a greater percentage of β-cells with a mature phenotype, but the percentage of immature cells was greater in control islets suggesting the immature pool of cells was inhibited in FGR islets resulting in the altered islet cell composition. *Travel Award: Sponsored by United State Department of Agriculture, National Institute of Food and Agriculture*

VIII-IV Increased Fetal Pyruvate Output and Placental Pyruvate Utilization during Intrauterine Growth Restriction

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Objectives: Glucose and lactate are major fetal nutrients. During hypoxia or intrauterine growth restriction (IUGR), fetal glucose concentrations are decreased and lactate concentrations are increased. However, the mechanisms regulating placental to fetal glucose and lactate flux remain incompletely understood. In hypoxic pregnancies, our prior data suggest an accelerated fetoplacental lactate-pyruvate shuttle whereby placental tissues preferentially use fetal pyruvate, over maternal glucose, to produce lactate for the fetus. We hypothesized that flux through this lactate-pyruvate shuttle is increased in IUGR. **Methods:** We exposed pregnant sheep to elevated temperatures to produce IUGR (n=10), compared to sheep at thermoneutrality (CON, n=6). Studies were performed at 0.9 gestational age to measure uteroplacental and umbilical net uptake rates of oxygen, glucose, lactate, and pyruvate in chronically-catheterized animals. Placental (cotyledon) tissue was collected at necropsy. **Results:** IUGR fetuses weighed 40% less and had decreased arterial oxygen and glucose and increased lactate and pyruvate concentrations (P<0.05). Uteroplacental rates of oxygen, glucose, lactate, and pyruvate uptake were similar between groups. In IUGR, fetal glucose uptake was decreased (P<0.05), and pyruvate output was increased (P<0.05). In IUGR placental tissue, pyruvate dehydrogenase (PDH) phosphorylation was decreased and PDH activity was increased, supporting increased pyruvate utilization. AMPK activation, mTOR signaling (S6K, S6, 4EBP1), and TBARS content, a marker of oxidative stress, were also increased. **Conclusions:** IUGR pregnancies had increased fetal to placental pyruvate flux and placental PDH activation, yet no increase in uteroplacental glucose uptake. This supports the preferential use of pyruvate as part of an accelerated lactate-pyruvate shuttle. However, we did not detect increased placental to fetal lactate flux. We speculate this is because IUGR fetuses have increased lactate production. Future studies tracing lactate flux are needed to test this. Mechanistically, AMPK activation and mTOR signaling may represent opposing signals in response to oxidative stress to increase placental pyruvate utilization during IUGR. *Travel Award: Sponsored by University of Colorado*