PROGRAM BOOKLET

8th PERINATAL BIOLOGY SYMPOSIUM

SNOWMASS, CO | AUGUST 24-27, 2019

Perinatal Exposures: Intersecting Mechanisms Leading to Developmental Outcomes

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ABOUT THE MEETING

The complex and diverse nature of perinatal events necessitates that perinatal research meetings themselves be interdisciplinary in nature, bringing together clinicians, as well as applied and basic scientists in various disciplines, from agricultural to biomedical and related fields.

The 2019 Aspen-Snowmass Perinatal Biology Symposium, which is the 8th in a series, has the overarching theme of the development of healthy offspring and whether there are common mechanisms that determine the long-term consequences of compromised development. This Symposium will bring together clinicians and scientists, established senior and junior investigators, from clinical medicine, basic research and applied livestock production, and from around the world to report and discuss their findings in an atmosphere conducive to frank yet amicable exchange. This will occur across all levels via plenary sessions, poster sessions, trainee workshops, and informal discussions, with time 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 2nd DJP Barker Memorial Lecture, 7 plenary sessions, as well as Trainee 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.

For the 3rd time, the venue for the meeting is the Viceroy Snowmass Hotel and Conference Center, in Snowmass Village, CO.

Snowmass Village, Aspen, and the surrounding area have a host of summertime activities (see: https://www.aspensnowmass.com/plan-your-stay/activities-and-lost-forest) including hiking, biking, kayaking and rafting, zip-lines, paint ball, sight-seeing via ski lift gondola, hot-air ballooning (https://www.gosnowmass.com/service-retail/hot-air-balloon-rides/), and the world-famous mountains called Maroon Bells (https://www.aspensnowmass.com/plan-your-stay/maroon-bells), as well as numerous outstanding dining and entertainment venues.

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

The Organizing Committee

ORGANIZING AND SCIENTIFIC COMMITTEES

ORGANIZING COMMITTEE

- **Larry Reynolds** – Co-Chair (larry.reynolds@ndsu.edu), Center for Nutrition and Pregnancy, and Animal Sciences Department, North Dakota State University, Fargo, ND
- **Stephanie Wesolowski** – Co-Chair (stephanie.wesolowski@ucdenver.edu), Department of Pediatrics, University of Colorado Anschutz Medical Campus, Denver
- **Sandra Davidge** (sdavidge@ualberta.ca), Women and Children's Health Research Institute, University of Alberta, Edmonton
- **Charles Ducsay** (cducsay@llu.edu), Lawrence D. Longo M.D. Center for Perinatal Biology, School of Medicine, Loma Linda University, Loma Linda, CA
- **Sonnet Jonker** (jonkers@ohsu.edu), Knight Cardiovascular Institute, Oregon Health and Science University, Portland, OR
- **Charles Wood** (woodc@ufl.edu), Department of Physiology and Functional Genomics, College of Medicine, University of Florida, Gainesville, FL

SCIENTIFIC COMMITTEE

- **Kirk Conrad**, Department of Physiology and Functional Genomics, College of Medicine, University of Florida
- **Mina Desai**, Department of Obstetrics & Gynecology, David Geffen School of Medicine, University of California, Los Angeles
- **Min Du**, Department of Animal Sciences, Washington State University
- **Kristen Govoni**, Department of Animal Science, University of Connecticut
- **Denise Hemmings**, Department of Obstetrics & Gynecology, Faculty of Medicine and Dentistry, University of Alberta
- **Caleb Lemley**, Department of Animal and Dairy Sciences, Mississippi State University
- **Ron Magness**, Department of Obstetrics & Gynecology, College of Medicine, University of South Florida
- **Janna Morrison**, School of Pharmacy and Medical Sciences, University of South Australia
- **William (Bill) Pearce**, Division of Physiology, School of Medicine, Loma Linda University
- **Becky Simmons**, Center for Research on Reproduction and Women's Health, Perelman School of Medicine, University of Pennsylvania

SPONSORS

The Aspen-Snowmass 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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Journal of Endocrinology

Journal of Molecular Endocrinology

The *Journal of Endocrinology* and the *Journal of Molecular Endocrinology* are proud to sponsor the upcoming 2019 Perinatal Biology Symposium. With impact factors of 4.381 and 3.744 respectively, these society owned journals aim to be the leading journals in basic endocrinology. Visit their websites for further information: https://joe.bioscientifica.com/ and https://jme.bioscientifica.com/

The *Journal of Endocrinology* is a leading global journal that publishes original research articles, reviews and science guidelines. Its focus is on endocrine physiology and metabolism, including hormone secretion; hormone action; biological effects. *Journal of Endocrinology* has an impact factor of 4.381 and is well established as a leading title in its field.

The *Journal of Molecular Endocrinology* is the leading society-owned basic molecular endocrinology journal that focuses on molecular and cellular mechanisms in endocrinology. The *Journal of Molecular Endocrinology* has an impact factor of 3.744, reaffirming the journal's standing as the leading basic journal dedicated to molecular endocrinology.

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SPEAKER BIOS

KJERSTI AAGAARD, an expert in maternal-fetal medicine, is theHenry and Emma Meyer Professor Chair in Obstetrics and Gynecology at Baylor College of Medicine and Texas Children's Hospital. She serves as Vice Chair of Research for Obstetrics and Gynecology and Professor in the Departments of Molecular and Human Genetics, Molecular and Cellular Biology, and Molecular Physiology and Biophysics. She is a co-director in the Baylor College of Medicine MSTP MD PhD program. Aagaard has worked globally for many years and has focused much of her global health efforts on understanding the causes and cures for the high rate of preterm birth in Malawi since 2011. Aagaard joined the faculty at Baylor College of Medicine and Texas Children's immediately after completing her fellowship in 2007. Her career as a physician-scientist has included active and supported efforts in research, clinical care, education, mentorship and public health advocacy. Her clinical interests include emerging infectious diseases, preterm birth, diabetes and hypertensive disorders, maternal smoking and environmental exposures, and the detection and diagnosis of congenital and genetic anomalies. Her translational research interests parallel her clinical interests, and focus on the role of the microbiome in pregnancy and early development, and the impact of key exposures in pregnancy (such as diabetes, maternal high fat diet, smoking, and environmental chemical exposures) on fetal development and later in life disease. She is dedicated to her role as a scientific mentor by engaging bright minds in often neglected arenas of scientific interest, engaging historically neglected minds in science and medicine, and retaining talent and earned knowledge in pregnancy and women's health research. Since receipt of her first post-student NIH award in 2005, Aagaard has been continuously funded by the NIH (NICHD, NIDDK, NIGMS and the Office of the Director). In addition, she has carried funding from the Burroughs Wellcome Fund Preterm Birth Initiative, March of Dimes Prematurity program, the Gates Foundation/USAID, and the Thrasher Foundation. Aagaard's research was previously was recognized with the NIH Directors New Innovator Award in 2007 and more recently as the recipient of the Michael E. Debakey Medal for Excellence in Research in 2015. In 2018 she was awarded the Nature prize for Outstanding Scientific Mentorship, and recently elected to the ASCI. You can find Aagaard caring for patients at Texas Children's Pavilion for Women and Ben Taub Hospital, leading her basic science and clinical research teams at Baylor College of Medicine and Texas Children's, teaching in the medical or graduate school, or volunteering in the community. You may also see her running the trails at Memorial with her husband, Dr. Jim Versalovic, and their two dogs (Sadie and Zoe), or spot Aagaard in the middle back of the pack at any one of several marathons around the globe.

MARISA BARTOLOMEI is the Perelman Professor of Cell & Developmental Biology and co-Director of the Epigenetics Program at the University of Pennsylvania Perelman School of Medicine. She received her BS from the University of Maryland and her PhD from the Johns Hopkins University School of Medicine. She trained as a postdoctoral fellow at Princeton University. In 1993, Bartolomei was appointed as an Assistant Professor at the University of Pennsylvania and was promoted to Associate Professor with tenure in 1999 and Professor in 2006. In 2006, Bartolomei received the Society for Women's Health Research Medtronics Prize for Contributions to Women's Health. In 2011, Bartolomei received the Jane Glick Graduate School Teaching Award for the University of Pennsylvania School of Medicine and a MERIT award. She was elected as a Fellow of the American Association for the Advancement of Science in 2014 and is recipient of the 2017 Genetics Society Medal from the UK Genetics Society. Her laboratory investigates genomic imprinting mechanisms.

SEBASTIEN BOURET received a PhD in neuroscience from the University of Lille (France) in 2001. He subsequently joined the laboratory of Dr. Richard Simerly in the Department of Neuroscience at the Oregon Health and Science University where he did his postdoctoral work. In 2005, Bouret was appointed Faculty in the Developmental Neuroscience Program of The Saban Research Institute at the University of Southern California in Los Angeles. He is currently a tenured Associate Professor of Pediatrics at the Keck School of Medicine of the University of Southern California. Bouret has a broad background in the field of metabolic programming and the neurobiology of obesity (key papers: Bouret et al., Science, 2004; Coupe et al., Cell Metabolism, 2012; Steculorum et al., JCI, 2015; van der Klaauw et al., Cell, 2019). He has published more than 80 articles, reviews, and book chapters in the field of developmental programming. Bouret's research has directly led to several breakthroughs in the understanding of the complex hormonal signals and neurodevelopmental substrates responsible for appetite regulation (key review: Bouret et al, Physiol Reviews, 2015). Most notably, he discovered that metabolic hormones (such as leptin and ghrelin) play a crucial role in hypothalamic development and lifelong metabolic regulation. In addition, Bouret has served on numerous journal editorial boards (including Endocrinology, Molecular Metabolism, JCI Insight), organizing committees and grant review panels (he is currently a member of the Neuroendocrinology, Neuroimmunology, Rhythms and Sleep study section of the NIH) and has been invited to lecture internationally.

STEPHANE BOURQUE is an Assistant Professor in the Departments of Anesthesiology & Pain Medicine, Pharmacology and Pediatrics at the University of Alberta. He currently holds a Tier 2 Canada Research Chair in Developmental and Integrative Cardiovascular Pharmacology. He received his PhD from Queen's University in 2009, and then pursued a postdoctoral fellowship at the University of Alberta before joining its faculty in 2014. His research program encompasses two broad areas of cardiovascular pharmacology. The first focuses on understanding how iron deficiency in pregnancy affects growth and development of the fetus, and in turn predisposes the offspring to cardiovascular disease in later life. Iron deficiency Is the most common nutritional deficiency worldwide, and pregnant women are among the most susceptible. Diagnosis and treatment for iron deficiency in pregnancy is deceptively complex, which underscores the high prevalence despite widespread supplementation and food-fortification efforts. The goal of his work is to develop tools to diagnose iron deficiency and anemia earlier in pregnancy, and novel therapeutics to improve outcomes in these complicated pregnancies. The second focuses on understanding the mechanisms underlying the development of vasoplegia and cardiovascular collapse in the progression from sepsis to septic shock. More recently, his team has also begun studying the implications of neonatal sepsis and recovery on subsequent cardiovascular development and function in adulthood. His research program is currently funded by the Canadian Institutes of Health Research, the Women and Children's Health Research Institute at the University of Alberta, the Canadian Foundation for Innovation, and the Royal Alexandra Hospital Foundation.

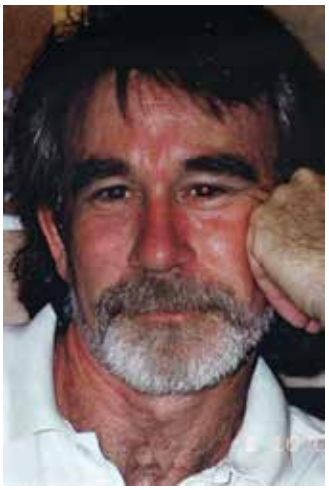
KRISTEN BOYLE

is a leading expert in the regulation of human stem cell metabolism and phenotyping in the context of obesity and diabetes. She earned her Bachelor of Science with Honors from the University of Massachusetts and her PhD in Bioenergetics from East Carolina University, where her work focused on the skeletal muscle metabolic response to high fat feeding in humans and in primary human cells. During her Postdoctoral fellowship she researched gestational diabetes and muscle metabolism with Dr. Jed Friedman at the University of Colorado School of Medicine. Boyle's early independent career was supported by a Building Interdisciplinary Research Careers in Women's Health (BIRCWH) Scholarship from The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) and by The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). During this time, she began using primary infant mesenchymal stem cells, derived from umbilical cord tissue, to investigate stem cell phenotype and epigenetic signatures as a model for developmental programming in humans. She discovered that cells from infants born to mothers with obesity have epigenetic and metabolic perturbations associated with greater neonatal adiposity, which may elucidate why these children are at increased risk for developing obesity and diabetes later in life. Boyle is currently an Associate Professor in the Department of Pediatrics, Section of Nutrition at the University of Colorado Anschutz Medical Campus. Her current research program is supported by the American Diabetes Association and the NIDDK to investigate mesenchymal stem cell metabolism as a predictor of child metabolic health outcomes, and to determine epigenetic mechanisms for altered metabolism in cells from infants born to mothers with obesity.

SEBASTIAN CANOVAS

is a DVM (2002), and has a Master's degree in Biology and Technology of Reproduction (2005), and a PhD in Biomedical Experimental Sciences (2007). He has more than 15 years of research experience in different laboratories (Univ. of Murcia in Spain, Michigan State University, and Laboratory of Cell Reprogramming-LARCEL, Seville, Spain). He has participated as researcher and Principal Investigator in several competitive national and international grants and research contracts with companies around fertilization and cellular reprogramming. Canovas has received international awards from Bedford Research Foundation (MA, USA) to support his research and a scholarship from Burroughs Wellcome Fund to participate in the prestigious Advanced Summer Course "Frontiers in Reproduction" at the Marine Biological Laboratory (Woods Hole, MA, USA) during the 2012 summer. Canovas has participated as Co-Chair in the International Congress of Animal Reproduction-ICAR 2016 and he is Co-Chair of the Local Organization Committee for the 35th Scientific meeting of the AETE (September 2019). He has more than 50 peer-review publications (34 JCR publications) and 7 book chapters, including papers in PNAS, eLife, Bioessays and Mol Hum Rep. The results have been presented in numerous international conferences. He participates as reviewer of grants/projects for several national and international institutions, and scientific journals. The international dimension of his career is further reflected by his participation in several international programs and networks, including as Project Manager of the European Program-REPBIOTECH-ITN-EJD (H2020-Marie Curie). He combines his expertise in Physiology of Reproduction and Epigenetics, and his research is focused in the epigenetic impact of Assisted Reproductive Technologies in large animal models, such as pig and cow, and in human. Currently, he is Associate Professor of Physiology (tenure track) in the University of Murcia and Academic Coordinator in the Master of Biology and Technology of Reproduction in Mammals program.

JOEL CATON attended New Mexico State University for his BS, University of Missouri for his MS, and New Mexico State University for his PhD. After a postdoctoral fellowship at the University of Missouri, he accepted a research and teaching position at North Dakota State University where he has continued to work in nutrition, metabolism, digestive physiology, and developmental outcomes. He is Professor of Animal Nutrition, and holds the Engberg Endowed Professorship. His collaborative research program in maternal nutrition and developmental programming has been active for over 25 years. Caton teaches both undergraduate and graduate students and has advised or co-advised 45 graduate student degree programs thus far in his career. He has published extensively in scientific journals and conference proceedings, and has given numerous invited presentations at national and international venues. Caton recently served on the NRC committee to update the Nutrient Requirements of Beef Cattle, 8th Revised Edition, as the Associate Editor-in-Chief for the Journal of Animal Science, and on the American Society of Animal Science Board of Directors. He currently serves on the National Animal Nutrition Program (NRSP-9) coordinating committee. Caton has received numerous awards from North Dakota State University and the American Society of Animal Science for his research accomplishments



ALAN CONLEY is Professor, and former Chair, in the Department of Population Health and Reproduction at the University of California, Davis, School of Veterinary Medicine. He also is Director of the Clinical Endocrinology Laboratory, School of Veterinary Medicine, and among his many honors he holds the John P. Hughes Endowed Chair in Equine Reproduction, is a Fellow of the Royal College of Veterinary Surgeons (UK) and was elected an honorary Diplomate of the American College of Theriogenology. He received his BVSc from Melbourne University. During his years as a veterinary practitioner, dairy and mixed animal, in Australia (3 years) and Scotland (2 years), he became interested in steroids as universal regulators of the estrous cycle and pregnancy, but also realized how little was known about their metabolism in different species, which became the focus of his work. After a clinical residency in Theriogenology at Iowa State University, he completed his MS and PhD there with Dr. Steven Ford, focusing on placental synthesis and uterine metabolism of sex steroids. Subsequently, he held postdoctoral positions funded by both NIH (Cecil H. and Ida Green Center for Reproductive Biology Sciences, University of Texas Southwestern Medical Center, Dallas TX) and USDA (US Meat Animal Research Center, Clay Center NE), where he was involved in numerous projects evaluating the role of steroid metabolism in establishment and maintenance of pregnancy as well as sexual differentiation. After a brief stint as Assistant Professor of Animal Sciences at North Dakota State University in Fargo, he migrated westward to his current department, where he has established himself as one of the premiere investigators of steroid metabolism and its role in reproductive function including initiation of parturition.

JUSTIN DEAN is an Associate Professor in the Department of Physiology, the University of Auckland. Dean received his PhD in Physiology in 2006 from the University of Auckland, New Zealand. His PhD studies examined neuroprotective strategies for treatment of newborn hypoxic-ischemic brain injury. Dean completed a research fellowship in the laboratory of Dr. Carina Mallard/Dr. Henrik Hagberg in Sweden, examining the effects of early life infection on development of the white matter structures of the brain. He also completed a research fellowship in the laboratory of Dr. Stephen Back in the USA, where he defined roles for the extracellular matrix in controlling oligodendrocyte maturation, and for impaired neuronal maturation in controlling cortical maldevelopment, in preterm ischemic brain injury. Using in vitro systems and small and large animal models, the current research interests of Dean's lab include: the mechanisms by which infection and hypoxia-ischemia regulate oligodendrocyte and neuronal survival and maturation; the role of the extracellular matrix in neuronal development and signaling; and drug treatment strategies to promote normal brain development following infection and hypoxia-ischemia. The long-term objectives of the studies in Dean's lab are to develop imaging techniques to identify subtle changes in brain development, to develop interventions that promote normal brain development, in infants born prematurely. Dean has published over 50 research articles, and his research has been supported by grants from the Health Research Council of NZ, the Marsden Fund, Auckland Medical Research Foundation, Neurological Foundation of NZ, and Cure Kids NZ.

MINA DESAI received her Bachelor of Science and Master's degrees from Maharaja Sayaijirao University in Baroda, India and her doctorate in Clinical Biochemistry was awarded by the University of Cambridge, United Kingdom. She began her professional career at the University of Cambridge, first as a training Fellow for the International Atomic Energy Agency and, later, as a Research Associate in the Department of Clinical Biochemistry. In the year 2000, she joined the Department of Obstetrics and Gynecology at Harbor-UCLA, as a faculty member at the David Geffen Medical Center and in 2006 was appointed the Director of Perinatal Research at LA BioMed. She is a recipient of a numerous awards including from the International Atomic Energy Agency, the Cambridge Commonwealth Scholarship, University of Cambridge Overseas Research Students Award, Perinatal Research Society Award and the Richard E. Weitzman Memorial Award. In 2010, she was enlisted as an Associate Editor for the Cambridge University Press Journal of Developmental Origins of Health and Disease. She was also an appointed member of NIH/NIDDK IPOD study section. Together with her colleague Dr. Michael Ross, she performed critical research to understand the mechanisms by which infants exposed in utero and/or nursing periods to perturbed maternal environment, develop obesity and metabolic syndrome. Altered maternal environment includes under- and over-nutrition as well as exposure to environmental chemical endocrine disruptors (e.g., bispheol A) during pregnancy and/or lactation. Remarkably, these divergent maternal exposures result in similar offspring outcomes, that is, hyperphagia, increased adiposity and fatty liver. Desai's mechanistic approach encompasses a spectrum of molecular and cellular studies that involve stem cells, epigenetics, gene expression and cellular signaling paradigms. Her research is funded by the National Institute of Health, American Heart Association, American Diabetes Association and March of Dimes. She is also devoted to mentoring undergraduate and post-graduate students, including medical fellows in biomedical research.

MIN DU earned his BS from Zhejiang University in 1990 and MS from China Agricultural University (CAU) in 1993. Then, Min worked in the same institution as an instructor for 5 years while pursuing a ScD degree in Biochemistry and Molecular Biology. He earned his PhD in Animal Science at Iowa State University (ISU) in 2001 with distinction. During his PhD study, he received both the Research Excellence Award from the ISU Graduate College and the David R. Griffith Research Excellence Award from Nutritional Sciences Council at ISU. Under the support of a prestigious NSERC postdoc fellowship from the Canadian Government, he obtained postdoctoral training in Cell Biology and Signaling in the Department of Biochemistry at University of Alberta, Canada. He was hired as an Assistant Professor in Muscle Biology and Animal Physiology at the University of Wyoming (UW) in 2003 and was later promoted to Associate Professor. In 2011, he moved to Washington State University as a Professor and Endowed (Funded) Chair. His current research focuses on the impacts of maternal physiological factors on the development of fetal skeletal muscle and adipose tissue, and the long-term effects on offspring health. The total funding, to date, is more than $24 million. He has published 238 peer-reviewed publications (Google Scholar H-index 54). He has trained more than 40 graduate students, postdocs and visiting scientists. He has served as the Associate Editor for the Journal of Animal Science and as reviewers for a large number of scientific journals and grant funding agencies. Currently, he is a standing member for the NIH Diabetes, Endocrinology and Metabolic Diseases Study Section. He was the recipient of the Young Scientist Award from the Western Section of the American Association for Animal Science (ASAS); the Early Career Achievement Award from ASAS; Research Award from the Center for Cardiovascular Research and Alternative Medicine at UW; the UW College of Agriculture Outstanding Advisor Award; Excellent Service Award from the Physiological Genomics Group of the American Society of Physiology; the Animal Growth and Development Award, and Physiology and Endocrinology Award from ASAS; and the Faculty Excellence in Research Award from WSU. Min is also highly active internationally. He is a Fulbright Specialist of the US Department of State and visited China, Indonesia and Brazil to help animal science research and production. He serves as Adjunct Professor at several universities and research institutes in China.

NEIL EVANS graduated with a BSc (Hons) in Genetics from The University of Nottingham, UK, and a PhD focused on ovine reproductive endocrinology from the University of Edinburgh, UK. Following a postdoc at the University of Michigan, Ann Arbor, MI, USA, Neil returned to the UK, and worked at the BBSRC Babraham Institute, Cambridge, UK before taking at post at the University of Glasgow. His research interests encompass the neuroendocrine regulation of the reproductive and stress axes with a focus on programming by events that occur either prenatally or during the peripubertal period. This work encompasses the effects of endogenous hormones and medical manipulation of the reproductive axis and the effects of exposure to endocrine disrupting chemicals, in particular the effects of real-life mixed chemical exposure. While most of Neil's work has used ovine models, some of the work has used avian and companion animal models and studies of wild avian and mammalian species.

ANTONIO FRIAS is a Professor in the Division of Reproductive and Developmental Sciences at the Oregon National Primate Research Center (ONPRC) and a Professor and Maternal Fetal Medicine (MFM) subspecialist in the Department of Obstetrics & Gynecology at Oregon Health and Science University (OHSU). He completed medical school at the Mayo Clinic, both residency training in Obstetrics & Gynecology and fellowship training in MFM at the University of Utah. With his collaborators at OHSU, his laboratory is a leader in advanced imaging to assess placental function in vivo. He is a principal investigator and co-investigator on multiple grants from the NICHD Human Placenta Project (HPP). He serves on the HPP Technology Development Committee, is a reviewer for NIH study section, and is a member of the NICHD Strategic Planning Working Group. In addition to receiving multiple teaching awards, Frias is also the recipient of the OHSU Faculty Mentorship Award and serves as a research mentor for young faculty investigators through the NIH Reproductive Scientist Development Program (RSDP) and the Women's Reproductive Health Research (WRHR) Career Development Program. He has previously served as the Director of the MFM Fellowship Program at OHSU and now serves on the leadership group and advisory council for the OHSU WRHR and BIRCWH programs.

HELEN JONES is currently an Associate Professor in the Department of Surgery at the University of Cincinnati and serves as Head of Research for the Center for Fetal and Placental Research at Cincinnati Children's Hospital Medical Center. She received her Biochemistry degree from the University of St. Andrews and her Ph.D. in Biomedical Sciences (Physiology) from the University of Aberdeen. While training in Aberdeen with Drs. Ken Page, Harry McArdle, and Cheryl Ashworth, Jones discovered her passion for placental biology. She has expertise in many aspects of the maternal-fetal interface but maintains significant interest in placental physiology in the context of normal and abnormal pregnancies such as intra-uterine growth restriction (IUGR), preterm birth, gestational diabetes and Placenta Accreta Spectrum as well as in Congenital Heart Defects. She currently holds an NICHD R01 to develop targeted, placental-specific in utero therapeutics and through the use of both animal models and isolated human placental tissue identifies potential pathways that can be targeted for treatment. Other current projects include the characterization of a novel murine model of placental accreta spectrum and the role of the placenta in the development or exacerbation of congenital heart defects. Jones maintains multiple collaborations within Cincinnati Children's with members of the Center for Prevention of Preterm Birth, the Center for Inflammation and Tolerance and the Heart Institute.

SEAN LIMESAND

is a Professor of Endocrinology in the School of Animal and Comparative Biomedical Sciences at the University of Arizona. His research is dedicated to placental function and fetal development, specifically investigating early life risk factors for metabolic diseases, such as intrauterine growth restriction. His research program uses a pertinent ovine model that allows for a truly integrative approach at the whole animal, isolated organ, cell, and molecular level to determine developmental responses in pancreatic β-cells that disrupt insulin secretion and permanently affect the life course of the fetus. Limesand continues to expand his research to incorporate critical aspects involved in insulin action in skeletal muscle to identify mechanisms influencing growth and metabolism. His investigations are ongoing with funding from the National Institute for Health. He has also received support from the Bill and Melinda Gates Foundation and other private foundations.

CARRIE E. MCCURDY,

Ph.D., is an Associa Professor at the University of Oregon in the Department of Human Physiology. Her research is focused on identifying key signaling pathways that regulate cellular metabolism and insulin sensitivity in response to acute nutrient challenges (over- or under-feeding), obesity or hormonal stress (hyperandrogenemia) and more so how disruption of these pathways leads to metabolic diseases like type 2 diabetes. Her current projects center on identifying the cellular signals for adipocyte-immune cell crosstalk in response to short-term over-feeding and points of dysregulation in these signals with obesity resulting in unresolved inflammation and insulin resistance. Over the last decade, McCurdy has also been a part of team science effort to investigate the impact of maternal obesity or a western-style diet during pregnancy on metabolic and behavioral programming in offspring using a non-human primate model. She leads the research group studying changes in cellular networks that regulate metabolism, mitochondrial dynamics and insulin sensitivity in offspring skeletal muscle. McCurdy received her Bachelor of Science degree in Biochemistry at the University of Notre Dame in South Bend, Indiana and her Doctor of Philosophy in Nutritional Science at the University of Wisconsin-Madison. Her postdoctoral training at the University of Colorado Anschutz Medical Campus in the Department of Pediatrics, Neonatology launched her interest in maternal-fetal physiology. Her work is funded through grants from the National Institutes of Health.

MELLISSA MANN received her doctorate in Dr. Susannah Varmuza's laboratory at The University of Toronto. She then trained with Dr. Marisa Bartolomei at The University of Pennsylvania. In 2005, Mann joined the Departments of Obstetrics & Gynecology, and Biochemistry at The University of Western Ontario, and the Children's Health Research Institute in 2005. In 2011, she was appointed to Associate Professor. In 2015, she joined the University of Pittsburgh and the Magee Women's Research Institute. Mann's laboratory studies the molecular mechanisms that regulate genomic imprinting. Research in her lab focuses on the effects of assisted reproductive technologies on genomic imprinting during gametogenesis and early embryo development, as well as imprinted domain regulation and the role of long noncoding RNAs in stem cells and early embryos.

STEPHEN MATTHEWS is Professor of Physiology, Obstetrics and Gynaecology and Medicine at the University of Toronto and Director of Research at the Alliance for Human Development, Lunenfeld-Tanenbaum Research Institute, Sinai Health System. Matthews received his PhD from the University of Cambridge, UK. He was appointed to the University of Toronto in 1996 and served as Chair of Physiology (2007-2014). Matthews' research is focused towards understanding how the fetal environment affects developmental trajectories leading to modified neurologic and endocrine function. He has established that these effects can extend across multiple generations and are linked to altered susceptibility to chronic disease. His research team is determining the mechanisms by which such 'programming' can occur. In parallel, his group is investigating transport mechanisms in the placenta and developing brain, with a focus on strategies to protect the fetus. He is also deeply committed to translating fundamental research. He was founding co-director of the MAVAN program, which followed neurocognitive development in children following adverse early experience. He is currently co-leading large pregnancy intervention studies (Healthy Life Trajectories Initiative; HeLTI) in India and Africa focused towards improving maternal, infant and child health. His research has been funded by CIHR, NSERC and the Gates Foundation, and he has published over 200 research papers. He has served as a member and chair of CIHR Peer Review Panels and on the Editorial Boards of several Journals. He is on Council for the Society for Reproductive Investigation and for the International Society of Developmental Origins of Health and Disease (DOHaD); in 2015, he co-founded DOHaD Canada. Matthews has also worked closely with the leadership of UNICEF in the translation of science to policy.

TERRY MORGAN

is a Professor of Pathology, Obstetrics & Gynecology, and Biomedical Engineering at Oregon Health & Science University in Portland, OR. He has been a NIH-funded investigator since 2012 and has authored dozens of papers, a number of book chapters, and two books about pathology, including serving as an editor of Pathology of the Placenta: A Practical Guide published in 2019. He is also part of the multi-disciplinary OHSU uteroplacental imaging group that has recently made significant contributions to our understanding of the relationship between uteroplacental pathology and blood flow in animal models and humans. His transgenic mouse model has provided insights into how maternal genotype and fetal sex affect uterine spiral artery growth and uteroplacental blood flow, affecting fetal kidney development and fetal programming of adult onset hypertension in males.

PETER NATHANIELSZ

obtained his scientific training and Bachelor's and Medical degree and PhD as well as an ScD from University of Cambridge in England. For six years, he was a Fellow of St. Catharine's College, Cambridge. After a period on the faculty at University of Cambridge, he assumed the position as Director of the Laboratory of Fetal Physiology at the University of California, Los Angeles; He then joined the Faculty at the College of Veterinary Medicine, Cornell University, as the Director of the Laboratory for Pregnancy and Newborn Research. He moved to New York University School of Medicine where he was Director of the Center for Women's Health Research from 2002–2004. In 2004, the whole of the Center for Women's Health Research relocated to the University of Texas Health Science Center at San Antonio and formed the Center for Pregnancy and Newborn Research (CPNR). In 2015, he accepted the Distinguished Professor Chair in Life Course Health at University of Wyoming. The whole group working on development moved to the Southwest National Primate Research Center where he is an Adjunct Scientist and they formed the Texas Pregnancy and Life Course Health Center. Peter Nathanielsz' laboratory focuses on a comparative approach to developmental programming in rodents, sheep and nonhuman primates. They have now taken up the story of how developmental programming and aging interact to influence life course health. Peter Nathanielsz' book Life in the womb: the origin of health and disease, published in 1999, was the first book for the general reader on developmental programming. The NIH has continuously funded Peter Nathanielsz' group since 1976. Their Program Project Grant is in year 26 and together they were awarded an NIA U19 in September 2018. Among the awards he has received are: James Law Professor of Reproduction Physiology, Cornell University, Ithaca, NY; Honorary Member, Society of Perinatal Obstetricians (now the Society for Maternal-Fetal Medicine); Fulbright Distinguished Scholar Award; and Honorary Fellow of the Royal College of Obstetrics and Gynaecology (FRCOG). He is a member of the Mexican Academy of Medicine.

DANIEL NETTLE is Professor of Behavioural Science at Newcastle University. He originally trained in biological anthropology, and much of his work has been based on longitudinal cohort studies from the UK and other human populations. However, more recently, in collaboration with Melissa Bateson, he has developed the European starling as a system for understanding the impact of early-life conditions on later behavioural phenotypes and aging biomarkers. The starling has some surprising commonalities to humans—biparental care and long life, for example—and the cross-fertilization of knowledge from humans and birds was the theme of his major European Union funded project 'COMSTAR: Understanding developmental plasticity in humans and starlings'. Nettle is interested not just in the empirics of how early life affects adult outcomes, including aging, reproduction, decision-making and obesity, but also in improving our theories about why it should do so, which involves setting development in its evolutionary and ecological context, and constructing formal and computational models. In recent years, Nettle and Bateson have developed a line of research modeling telomere dynamics, as an example of an ageing biomarker. Nettle is also a science writer and recently published 'Hanging On To The Edges: Essays on Science, Society and the Academic Life' (2018).

VASANTHA PADMANABHAN, MS, PhD, is Professor of Pediatrics, Obstetrics, and Gynecology, Molecular and Integrative Physiology, and Environmental Health Sciences, and Director of Pediatric Endocrine Research at the University of Michigan. She received her PhD from the Indian Institute of Science, India; completed her postdoctoral fellowship at Michigan State University. Padmanabhan's research is translational and mainly centers on understanding the fetal origin of pubertal and adult reproductive and metabolic disorders. Specifically, her laboratory focuses on the impact of maternal exposure to native steroids (testosterone, estradiol) and environmental pollutants such as bisphenol-A in altering developmental trajectory of fetus and programming adult reproductive and metabolic diseases. Utilizing integrative approaches ranging from cell and molecular biology as well as in vitro systems to whole animal physiology her research emphasis is to understand the mechanisms by which native and environmental steroids program reproductive neuroendocrine and ovarian defects and insulin resistance as well as adipose defects such as that seen in hyperandrogenic disorders like Poly Cystic Ovarian Syndrome (PCOS) and identify prevention and treatment strategies. As PI of a Program project (P01-HD44232: Prenatal programming of reproductive health and disease), she was instrumental in developing the sheep model of PCOS phenotype and testing intervention strategies. She is also PI of a P30 Children's center (NIH/NIEHS P01ES022844 Life course Exposures & Diet: Epigenetics, Maturation & Metabolic Syndrome) that addresses the impact of developmental exposure to endocrine disrupting toxicants on metabolic function. She has served as a member of the expert panel for the 2010 Joint Food and Agriculture Organization/World Health Organization Expert Meeting to review toxicological and health aspects of bisphenol A and as standing member of the REN and ICER Study Sections. She is a member of the editorial board of Endocrinology, DOHAD journal, Reproduction and Environmental Health Perspectives.

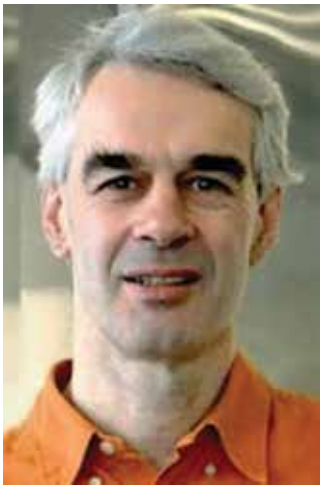
SARA PINNEY is currently an Assistant Professor of Pediatrics at the Perelman School of Medicine at the University of Pennsylvania (Penn) and an attending physician in the Division of Endocrinology and Diabetes at the Children's Hospital of Philadelphia (CHOP). Pinney received her medical degree from the University of Cincinnati College of Medicine and completed her pediatric residency at Children's Memorial Hospital in Chicago. Following residency training she joined the fellowship program in Pediatric Endocrinology at CHOP. Afterwards she completed a post-doctoral fellowship in the laboratory of Dr. Rebecca Simmons, Professor of Pediatrics at Penn and also completed the Master of Science in Translational Research degree program at Penn. She opened her own lab at CHOP in 2011. The principal focus of the research program in the Pinney Lab is to determine the molecular mechanisms that link an adverse intrauterine milieu to the development of diabetes and obesity later in life. The lab is currently investigating how intrauterine growth restriction, gestational diabetes, and in utero exposure to environmental toxicants including bisphenol A (BPA), bisphenol S (BPS) and perfluorooctanoic acid (PFOA) contribute to the development of diabetes and obesity in the offspring. The research team uses human samples, animal models, and cell culture systems to study molecular mechanisms, including epigenetic modifications responsible for fetal programming of adult metabolic disease. Specifically, the lab has been investigating the molecular mechanisms that are responsible for the development of diabetes, non-alcoholic fatty liver disease and obesity in offspring after exposure to an altered intra-uterine environment.

SARAH REED is an Associate Professor in the Department of Animal Science at the University of Connecticut. Reed earned her MS in Animal Science and her PhD in Animal Molecular and Cellular Biology at the University of Florida. She then spent two years in the Department of Physical Therapy at the University of Florida as a post-doctoral researcher. Reed's current research interests focus on the role of maternal diet during gestation on offspring muscle development and post-natal growth. Most recently, her lab has focused on how maternal diet during gestation alters metabolism, oxidative stress, and satellite cell function in offspring skeletal muscle. She teaches and advises extensively in the UConn Animal Science program, teaching Horse Breeding Farm Management, Advanced Broodmare and Foal Management, Comparative Exercise Physiology, Scientific Writing in Comparative Exercise Physiology, and advising approximately 50 equine and pre-vet undergraduate students.

TIM REGNAULT

received his undergraduate degree in Rural Science (Hons) from the University of New England in Armidale, Australia. Following graduation, he undertook positions as a District agronomist and then a District livestock officer at Goodwindi and Hay, Australia respectively. He completed his PhD studies through a CSIRO/ University of Western Sydney scholarship at CSIRO Prospect, studying the role of litter size and pregnancy nutrition upon placental lactogen. He then moved to Denver, CO, in 1996 to undertake postdoctoral training, and subsequent faculty positions, under the mentorship of Drs. Anthony, Battaglia, Meschia and Wilkening. During his time in Denver, his investigations focused on areas such as placental angiogenesis, fetal hypertension, placental and fetal oxygenation and placental nutrient transport, in the IUGR sheep model. In 2005 he moved London, Ontario in Canada, to join the Perinatal Research group there led by Drs. Richardson, Gagnon and Han. While continuing aspects of sheep work with a focus on cardiovascular perturbations in IUGR, he commenced abnormal pregnancy (IUGR/LBW, deficient nutrient supply and excess energy supply) and postnatal dietary interactive outcome studies using guinea pig, rat and rabbit, cell culture systems and imaging techniques (CT/PET/MRI, hyperpolarized MRI). The laboratories current focuses are upon detecting early abnormal placental failure in vivo and in vitro and on understanding the in-utero origins and postnatal dietary interactions resulting in the development of pre-clinical markers such as insulin resistance (in multiple tissues) and non-alcoholic fatty liver disease (NAFLD) and other early markers of later life metabolic disease.

MICHAEL E. SYMONDS



has an international reputation for research in nutrition during pregnancy and brown adipose tissue development and its role in later obesity. He is Professor of Developmental Physiology. His research has been supported by a substantial number of funding bodies to the sum of ~£60M including the United Kingdom's Medical Research Council, BBSRC, National Institute for Health Research (NIHR), Royal Society, Wellcome Trust, British Heart Foundation, Diabetes UK and Nutricia Research Foundation as well as the European Union. He obtained his BSc in Agricultural Science from the University of Nottingham (1983); his PhD on Nutrition, Pregnancy and Size at Birth from the University of Reading (1987); undertook post-doctoral positions at the Universities of Oxford, Nottingham and Reading and a Wellcome Trust Lectureship (1993) before moving to Child Health in Nottingham (1997). He was made a full Professor in 2004. To date he has published >200 peer-reviewed manuscripts, >80 review articles, 15 book Chapters, 2 books and given >100 invited lectures at international meetings. He has successfully supervised >35 PhD students.

PROGRAM

2019 Aspen-Snowmass Perinatal Biology Symposium
"Perinatal Exposures: Intersecting Mechanisms leading to Developmental Outcomes"

https://www.asas.org/meetings/perinatal-home/perinatal-2019

SATURDAY AUGUST 24, 2019

4:00 – 7:45 pm	Registration
5:00 – 6:30 pm	**Opening Reception** *Sponsored by Mead Johnson Nutrition*
6:30 – 6:45 pm	**Welcome and Opening Remarks** Larry Reynolds PhD; Organizing Committee Co-Chair, and Stephanie Wesolowski, PhD; Organizing Committee Co-Chair

Session 1 / Evening Session – Keynote Address: Aspen-Snowmass Perinatal Biology Symposium
Sponsored by Mead Johnson Nutrition
Chair: Stephanie Wesolowski, Department of Pediatrics, University of Colorado Anschutz Medical Campus

6:45 – 7:45 pm	Daniel Nettle, Center for Behaviour and Evolution, Newcastle University **The long reach of early life: Developmental experience and the organization of the adult phenotype**
7:45 pm	Networking (on your own)

SUNDAY, AUGUST 25, 2019

7:00 – 8:00 am	**Trainee workshop 1 – Collaborating in Perinatal Biology** - with Continental Breakfast *Sponsored by Abbott Nutrition*

Session 2 – Early events that program embryonic, fetal and postnatal development
Sponsored by Agriculture and Food Research Institute, USDA
Co-Chairs: Min Du, Washington State University, and Rebecca Simmons, University of Pennsylvania

8:15 – 8:45 am	Joel Caton, Animal Sciences Department, North Dakota State University **Maternal nutrition and early programming events**
8:45 – 9:15 am	Marisa Bartolomei, Epigenetics Institute, Department of Cell and Developmental Biology, Perelman School of Medicine, University of Pennsylvania **Epigenetic reprogramming in the germline and early development**
9:15 – 9:45 am	Mellissa Mann, Magee Womens Research Institute, University of Pittsburgh **Assisted reproductive technologies (ART) and genomic imprinting**
9:45 – 10:15 am	Early Career Speaker: Sebastian Canovas, Physiology Department, University of Murcia **Role of reproductive tract secretions in embryonic development and early programming**
10:15 – 10:45 am	Networking and refreshment break

Session 3 – Cellular pathways I: Programming of perinatal growth and development
Sponsored by Mead Johnson Nutrition
Co-Chairs: Joel Caton, North Dakota State University, and Sara Pinney, University of Pennsylvania

10:45 – 11:15 am	Mina Desai, David Geffen School of Medicine, UC-Los Angeles **Cellular pathways of adipogenesis**
11:15 – 11:45 am	Min Du, Animal Sciences Department, Washington State University **Cellular pathways of myogenesis**
11:45 am – 12:15 pm	Michael Symonds, School of Medicine, University of Nottingham **Programming of adipose development**

12:15 –12:45 pm — Kjersti Aagaard, Maternal-Fetal Medicine, Baylor College of Medicine
Microbiome and perinatal outcomes

12:45 – 6:45 pm — Networking/Organized (and Unorganized) Activities

Session 4 / Evening Session – Maternal nutrition/body composition and programming
Sponsored by Agriculture and Food Research Institute, USDA
Co-Chairs: Janna Morrison, University South Australia, and Sebastien Bouret, University Southern California

6:45 – 7:15 pm — Tim Regnault, Western University, London, Ontario
Maternal diet/body composition in programming of fetal and placental development

7:15 – 7:45 pm — Sarah Reed, Department of Animal Science, University of Connecticut
Maternal nutrition and fetal programming: Developmental changes in the muscle

7:45 – 8:15 pm — Kristen Boyle, Department of Pediatrics, University of Colorado Anschutz Medical Campus
Umbilical stem cells – programmed risk?

8:15 – 9:30 pm — Poster Session 1

MONDAY AUGUST 26, 2019

7:00 – 8:00 am — **Trainee workshop 2 – Grant Writing in Perinatal Biology** - with Continental Breakfast
Sponsored by Mead Johnson Nutrition

Session 5 – Programming of insulin sensitivity and insulin action
Sponsored by NIDDK
Co-Chairs: Antonio Frias, Oregon Health and Science University, and Ronald Magness, University of South Florida

8:15 – 8:45 am — Carrie McCurdy, College of Arts and Sciences, University of Oregon
Impact of maternal diet and obesity on insulin signaling and metabolism in offspring skeletal muscle

8:45 – 9:15 am — Sean Limesand, College of Agriculture and Life Sciences University of Arizona
Development of glucose intolerance through tissue-specific programming

9:15 – 9:45 am — Vasantha Padmanabhan, Department of Pediatrics, University of Michigan
Developmental programming of insulin resistance: Is androgen the culprit?

9:45 – 10:15 am — Early Career Speaker: Sara Pinney, School of Medicine, University of Pennsylvani
From sweet to seq: Mechanisms by which gestational diabetes programs fetal development

10:15 – 10:45 am — Networking and refreshment break

Session 6 – Cellular Pathways II: Development of brain and feeding circuits
Sponsored by Abbott Nutrition
Co-Chairs: Kristen Govoni, University of Connecticut, and Stephane Bourque, University of Alberta

10:45 – 11:15 am — Justin Dean, Department of Physiology, and Centre for Brain Research, in the Faculty of Medical and Health Sciences, the University of Auckland
Cell death versus impaired cell maturation in preterm brain injury

11:15 – 11:45 am — Sebastien Bouret, Keck School of Medicine, University of Southern California
Hormonal and molecular signals that direct development of brain feeding circuits

Trainee oral presentations

11:45 am – 12:00 pm — Eli J. Louwagie, University of South Dakota-Sanford School of Medicine, Vermillion
Prenatal exposure to diabetes but not high-fat diet increases mitochondria-mediated cell death in adult rat cardiomyocytes

12:00 – 12:15 am — Laura B. James-Allan, Department of Ob-Gyn, University of Colorado
Exosomes isolated from women with gestational diabetes cause insulin resistance and fail to stimulate islet insulin secretion in non-pregnant mice

12:15 – 6:00 pm — Networking/Organized (and Unorganized) Activities

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

Session 7 / Evening Session – DJP Barker Memorial Lecture
Sponsored by NICHD
Chair: Larry Reynolds, North Dakota State University

7:30 – 8:30 pm	Peter Nathanielsz, University of Wyoming, and Southwest National Primate Research Center, San Antonio **Developmental programming and aging**
8:30 – 9:45 pm	Poster Session 2

TUESDAY, AUGUST 27, 2019

7:00 – 8:00 am	**Trainee Workshop 3 – Obtaining a faculty appointment in the field of perinatal biology** - with Continental Breakfast *Sponsored by Agriculture and Food Research Institute, USDA*

Session 8 – Stress and the micronutrient deficiency
Sponsored by NIDDK
Co-Chairs – William Pearce, Loma Linda University and Kristen Boyle, University of Colorado

8:00 – 8:30 am	Steve Matthews, Physiology, University of Toronto **Stress hormones and developmental programming**
8:30 – 9:00 am	Neil Evans, Institute of Biodiversity, Animal Health & Comparative Medicine, University of Glasgow **Developmental programming by exposure to real-life mixtures of environmental chemicals: Lessons from large animal models**
9:00 – 9:30 am	Early Career Speaker: Stephane Bourque, Faculty of Medicine and Dentistry, University of Alberta **Early mechanisms of cardiovascular programming by iron deficiency**

Trainee oral presentations

9:30 – 9:45 am	Caitlin Cadaret, University of Nebraska, Lincoln **Intermittent materno-fetal O2 supplementation during late gestation rescues placental insufficiency-induced intrauterine growth restriction, skeletal muscle growth capacity, and glucose metabolism**
9:45 – 10:00 am	Anna Mikolajczak, Libin Cardiovascular Institute of Alberta, and Alberta Children's Hospital Research Institute, University of Calgary **Premature adipose tissue development and heightened adipogenic potential in offspring born to metabolically compromised pregnancy**
10:00 – 10:30 am	Networking and refreshment break

Session 9 – Placental function and programming
Sponsored by NICHD
Co-Chairs: Mina Desai, University California-Los Angeles, and Sebastian Canovas, University of Murcia

10:30 – 10:45 am	Alan Conley, School of Veterinary Medicine, UC-Davis **Steroids and the preparation for parturition: Comparative models**
10:45 – 11:15 am	Helen Jones, Cincinnati Children's Hospital Medical Center **Placenta and heart: concurrent maldevelopment in congenital heart defects.**
11:15 – 11:45 am	Terry Morgan, School of Medicine, Oregon Health and Science University **Maternal vascular remodeling and developmental programming of cardiovascular disease**
11:45 – 12:15 am	Antonio Frias, School of Medicine, Oregon Health and Sciences University **Imaging methods to detect abnormal uteroplacental development**
12:15 – 12:45 pm	**Conference Closure – final comments and election of next Organizing Committee**

ABSTRACTS

SUNDAY, AUGUST 25, 2019

I-I Immunoblot analysis of biceps from fetuses born of hypercortisolemic ewes in late gestation

B. Alava, S. Joseph, M. Keller-Wood, *Department of Pharmacodynamics, University of Florida College of Pharmacy, Gainesville, FL*

Introduction: There is an increased incidence of perinatal mortality at term in an ovine experimental model of maternal stress induced by infusion of cortisol. Chronic stress is known to decrease or damage mitochondria; mitochondrial DNA expression was decreased in the cardiac septum of the fetuses in this model. Transcriptomic analysis of the biceps suggested changes in pathways related to mitochondrial metabolism and content. It is therefore hypothesized that maternal hypercortisolemia alters expression of mitochondrial proteins in fetal skeletal tissue as well. **Methods:** Cortisol (1mg/kg/day) was continuously infused into pregnant ewes starting at 115 d of gestation, and animals were sacrificed at labor. Proteins were extracted from the fetal bicep tissues of control (n = 7) and CORT (n = 6) fetuses by sonication in the presence of protease and phosphatase inhibitors. Western Blot analysis was used to determine whether maternal hypercortisolemia changed citrate synthase, COX4, Cytochrome-c, PDHE1 S293 alpha total and phosphorylated protein density. The intensity of signals generated were normalized to total protein and compared by t-test. **Results:** Although mRNA for citrate synthase was reduced in biceps, the protein expression tended to be greater in the biceps of CORT fetuses. ($P < 0.06$, CORT: 5689 ±655 vs control: 4102±426). There were no changes in expression of the other proteins in CORT vs control fetal biceps. **Conclusions:** Overall there is no significant impact of maternal hypercortisolemia on expression of mitochondrial proteins in biceps muscle of fetuses of hypercortisolemic ewes. (Supported by NIH Grant R01 HD087306)

I-II Caloric restriction during gestation affects offspring ovarian reserve in mice

C. Bespalhok Jacometo[1], B. Machado Zanini[2], K.R. Silva Andrade[2], D. Neske Garcia[2], L.A. Cruz[2], R. Gianela Mondadori[2], A. Schneider[2], [1]*Facultad de Ciencias Agropecuarias, Universidad de La Salle, Bogotá DC, Colombia,* [2]*Universidade Federal de Pelotas, Pelotas, RS, Brazil*

Objective: To evaluate the effect of maternal caloric restriction during gestation on mice offspring ovarian follicular reserve. **Methods:** 14 female and 7 male mice of the C57BL/6 lineage were maintained with standard diet and water *ad libitum* under controlled light and temperature conditions. Mice were mated and 10 d after confirmation of copulation, females were divided into control (CT) group (n = 7) and caloric restriction (CR) group (n = 7), which received a diet consisting of 50% of what was consumed by the CT group in the previous day, during 6 d. After delivering and weaning females were separated according to maternal group, received *ad libitum* diet, weighed every 14 d, and submitted to euthanasia at 3 months of age, when the ovaries were collected. For histological evaluation the ovarian samples were submitted to serial cut in a microtome, stained with hematoxylin-eosin and follicles were classified as primordial, transition, primary, secondary and tertiary. Ovarian *Amh*, *Akt1*, *Foxo3a* and *Pten* mRNA expression was evaluated by real time PCR. Statistical analyzes were carried out using a t test, at 5% significance level. **Results:** Weight gain was increased in females from CR group after weaning (average weight: CT=16.2±0.4g vs CR=18.0±0.5g; P <0.007). Primordial (CT=2740±231 vs CR=1064±128) and transition (CT=2914±210 vs CR=1042±131) follicles numbers was decreased in mice from CR compared to CT group (P<0.05 for both comparisons). The mRNA expression of *Amh* (CT=1.0±0.14 vs CR=1.58±0.29), *Akt1* (CT=1.0±0.19 vs CR=0.79±0.11), *Foxo3a* (CT=1.0±0.14 vs CR=0.79±0.11) and *Pten* (CT=1.0±0.18 vs CR=0.96±0.16) was not affected by CR ($P > 0.05$ for all comparisons). **Conclusions:** Maternal CR during gestation increased body weight gain and reduced the ovarian reserve in the offspring; however, no effect was detected in the expression of genes related to primordial follicle activation, indicating a temporal-specific effect on fetal follicle formation. (Supported collectively by CAPES, CNPq and FAPERGS awards).

I-III Western diet consumption alters lipid profiles in dam circulation and placenta

K.L. Bidne[1], A.L. Rister[2], A.R. McCain[1], E.D. Dodds[2], J.R. Wood[1], [1]*Department of Animal Science, University of Nebraska – Lincoln, Lincoln, Nebraska, USA,* [2]*Department of Chemistry, University of Nebraska – Lincoln, Lincoln, Nebraska, USA*

Objective: Identify changes in lipid profiles in the circulation of diet-induced obese dams which are transmitted to the mid-gestation mouse placenta. **Methods:** Female C57BL/6J mice (5 weeks of age) were placed on either a control diet (normal diet, ND, n = 7) or a high-fat, high-sucrose diet (western diet, WD, n = 5). After eight weeks, mice were mated with ND C57BL/6J males. Observation of a copulatory plug was considered embryonic day 0.5 (e0.5). Dams were euthanized at e12.5, with weights, blood, tissues, and fetal/placenta pairs collected. Serum lipids were extracted and analyzed via liquid chromatography-mass spectrometry. Mass spectrometry imaging was performed to identify and localize lipids in the placenta. **Results:** Dams on WD were heavier than their ND counterparts (28.53 ± 0.78g, 24.44 ± 0.66g, respectively, mean ± SEM), $P < 0.01$. Relative quantitation of serum lipids revealed increases in circulating 16:1, 18:1, 20:0, 20:2, and 20:3 fatty acids in WD dams, $P < 0.05$. Female fetuses from ND dams weighed less than the male fetuses (89.3 ± 2.4mg, 96.5 ± 2.6mg, respectively), $P < 0.05$. However, there was no weight difference between female and male fetuses from WD dams (94.7 ± 2.9mg, 97.5 ± 3.1mg, respectively), $P > 0.05$. In ND dams, female placental weights were also reduced compared to males (84.0 ± 2.4mg, 91.1 ± 2.8mg, respectively), $P < 0.05$. Similarly, female placentas from WD dams tended to be smaller than their male counterparts (80.3 ± 2.9mg, 86.7 ± 3.2mg, respectively), $P < 0.1$. Interestingly, preliminary studies showed differences in specific lipid species and their distribution in placentas from ND and WD dams. **Conclusions:** Fetuses from ND, but not WD, dams had sex-dependent weight differences, suggesting that maternal obesity altered mid-gestation fetal growth. Furthermore, placental lipid species mirrored those in the maternal circulation indicating that these lipids may impact early fetal growth. (Funding from University of Nebraska Foundation).

I-IV Histone lysine demethylase function in placental trophoblast cells

G.J. Bouma[1], A. Ali[1], E.S. McWhorter[1], R.C. West[1,2], Q.A. Winger[1], [1]*Animal Reproduction & Biotechnology Laboratory, Department of Biomedical Sciences, Colorado State University, Fort Collins, CO,* [2]*Current Address: Colorado Center for Reproductive Medicine, Lone Tree, CO*

Objectives: To elucidate the function of histone lysine demethylase (KDM) 1A in trophoblast cells and placental development, we determined its ability to modulate androgen receptor (AR) and estrogen receptor (ESR1) levels *in vitro*, and inhibit its function in the trophectoderm *in vivo*. **Methods:** Coimmunoprecipitation experiments were performed to determine KDM1A binding to AR and ESR1 in ACH-3P trophoblast cells. Furthermore, CRISPR-Cas9 gene targeting constructs were designed to mutate and knockout KDM1A. The effect of KDM1A knockout on AR, ESR1 and vascular endothelial growth factor (VEGFA) was assessed in ACH-3P cells. Finally, trophectoderm-specific KDM1A knockout was conducted in sheep blastocysts, and the subsequent effects on embryo elongation was determined *in vivo*. **Results:** KDM1A localizes to trophoblast cells in sheep and human placentae, and is present throughout pregnancy. Similar to cancer cells, KDM1A binds to AR and ESR1 in ACH-3P cells, and abolishment of KDM1A leads to significant ($P < 0.05$) decreased levels of *AR* and *ESR1*. Furthermore, angiogenic factor *VEGFA* was significantly ($P < 0.05$) decreased in KDM1A knockout ACH-3P cells. Finally, preliminary *in vivo* experiments reveal that KDM1A knockout starting in day 9 blastocysts results in significant ($P < 0.05$) decreased levels of *AR* and impaired elongation at day 16 of gestation. **Conclusions:** KDM1A binds AR and ESR1 in trophoblast cells, and possibly regulates VEGFA expression. Importantly, KDM1A gene targeting *in vivo* leads to impaired elongation during early pregnancy. These data suggest an important function for KDM1A in sex steroid receptor signaling and early placental development. [Supported by Colorado State University CVMBS College Research Council, NIH Institutional National Research Service Award Training Grant (T32 NRSA) "Biomedical Research Training for Veterinarians," and USDA AFRI 2019-67015-29000].

I-V Disruption of IGF-1 pathways in placental villous tissue in idiopathic spontaneous preterm birth.

H. Brockway, L. Muglia, H. Jones, *Cincinnati Children's Hospital Medical Center*

Objectives: Preterm birth is global public health concern. Although multiple risk factors have been identified, the underlying molecular mechanisms of truly idiopathic spontaneous preterm birth (isPTB) remain unclear. Recent pathological studies of isPTB suggest placental hypermaturity has a role in adverse pregnancy outcomes. We sought to identify transcriptomic signatures of placental hypermaturity associated with isPTB. **Methods:** We conducted transcriptomic analyses in precisely phenotyped cohorts of PTB due to either intra-amniotic infection (IAI) or isPTB, and healthy term placentas. We utilized IAI samples from the same gestational age range as the isPTB samples to be able to assess differences in gene expression due to isPTB pathology versus those due to gestational age. Validation of expression was determined by immunohistochemistry on villous samples. **Results:** Transcriptomic analyses revealed candidate genes for both isPTB (n = 170) and IAI (n = 170) pathologies. Pathway analyses of the isPTB candidates revealed gene enrichment for IGF signaling regulation, with the upregulation of *IGFBP1*, *IGFBP2*, and *IGFBP6*. Specific roles for these genes in the regulation of IGF signaling in villous tissue has not yet been clearly defined. Additionally, 68 isPTB candidate genes' expression patterns demonstrate a hypermaturity signature. Of those 68, three genes downstream of the IGF signaling pathway were significantly upregulated: ceruloplasmin (*CP*), tenascin-C (*TNC*) and complement 3 (*C3)* by a minimum of a 2-fold upregulation with FDR<0.05.

Conclusions: Distinct placental transcriptomic signatures between isPTB and IAI births imply different mechanisms underlying their respective placental pathophysiology and pregnancy outcomes. The isPTB transcriptional signature supports a placental hypermaturity hypothesis indicating a disconnect between the fetal and placental development during gestation. Increased maternal C3 serum levels have been previously closely associated with sPTB. The increase of *C3* transcription via the IGF signaling pathway in our isPTB samples suggests a placental role for increasing C3 serum levels, likely indicating a premature activation of the complement system and thus, inflammatory pathways associated with birth. (Supported by NIH R01HD091527, Gates Foundation OPP1113966, and March of Dimes Ohio Prematurity Center)

I-VI Intermittent maternofetal O_2 supplementation during late gestation rescues placental insufficiency-induced intrauterine growth restriction, skeletal muscle growth capacity, and glucose metabolism

C. Cadaret, R. Posont, R. Swanson, J. Beard, T. Barnes, K. Beede, D. Yates, *University of Nebraska-Lincoln, Lincoln, NE, USA*

Objectives: Placental insufficiency (PI) results in fetal nutrient deprivation and is the most common cause of intrauterine growth restriction (IUGR) in humans. Fetal hypoxemia drives *in utero* adaptations, leading to low birthweight and a predisposition to metabolic syndrome in adulthood. However, the underlying mechanisms are not well understood. Our objective was to determine whether intermittent maternal O_2 supplementation during late gestation improves fetal hypoxemia and in turn IUGR, postnatal growth, and metabolic pathologies. Methods: Pregnant ewes were heat stressed (40°C, 35% RH) from the 40th to 95th day of gestation (dGA) to induce PI (IUGR, n = 6; thermoneutral controls, n = 12). A 2nd group of IUGR ewes received 100% O_2 supplementation (10L/min, intra-tracheal) for 8 hours/day from dGA130 to parturition (IUGR+O_2, n = 9). Lambs were weaned at birth, hand-reared, and fitted with femoral arterial and venous catheters and a blood flow probe at 25 d of age. Glucose-stimulated insulin secretion (GSIS) and hindlimb-specific hyperinsulinemic-euglycemic clamp (HEC) studies were performed at 28 and 29 d of age, respectively. At 30 d of age, lambs were euthanized and an *ex vivo* HEC study was performed on primary skeletal muscle. Birthweight, day-30 bodyweight (BW), and brain weight/BW were less ($P < 0.05$) in IUGR lambs but did not differ between IUGR+O_2 lambs and controls. GSIS tended to be lower ($P < 0.10$) in IUGR lambs but was similar between IUGR+O_2 lambs and controls. Insulin-stimulated glucose oxidation rates in hindlimb tissues of live lambs and in primary skeletal muscle at necropsy were decreased ($P < 0.05$) in IUGR compared to controls and IUGR+O_2 lambs. Conversely, *in vivo* hindlimb and *ex vivo* skeletal muscle glucose uptake rates did not differ among groups.

Conclusions: These data show that fetal hypoxemia was implicit in IUGR growth and metabolic deficiencies and that intermittently improving fetal O_2 during late gestation via maternal O_2 supplementation improved muscle-centric metabolic pathologies. (Supported by NIH/NIGMS Grant 1P20GM104320, J. Zempleni, Director).

I-VII Intrauterine growth restricted ovine fetal skeletal muscle has reduced cell cycle activity corresponding with lower rates of myogenesis

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Objectives: We reported that the rates of myoblast proliferation, differentiation, and fusion to form myonuclei were reduced in intrauterine growth restricted (IUGR) fetal muscle compared with controls. Furthermore, total myofiber number was lower and individual fiber size was smaller in IUGR. We hypothesized that reduced rates of myogenesis in the IUGR fetal hindlimb were associated with slower cell cycle progression and not an increase in cellular apoptosis. **Methods:** Biceps femoris was harvested from IUGR (n = 13) and control (n = 8) fetal sheep (134-day gestation; term = 147 d). Genes that regulate cell cycle, apoptosis, and muscle maturation were measured using real-time qPCR, and normalized to the average of housekeeping genes: *ACTIN*, *S15*, *RPL37A*. Protein levels of caspase3 and p130 were measured by western blot. Student's T-test or Mann-Whitney test were used, and $P < 0.05$ was designated as significant. **Results:** Gene expression of cyclins (*CCNA2, CCNB1, CCNB2, CCNE2*) and cyclin dependent protein kinases (*CDK1*, *CDK2*, *CDK6*) were 30-60% lower ($P < 0.05$), and inhibitors of the cell cycle were 2-fold higher (*CDKN1A*/p21; $P < 0.05$) in IUGR. Both gene and protein expression of RBL2/p130, a G0 phase marker, were similar in both groups. Gene expression of apoptosis markers were either similar (*BCL2, BAX, APAF1, CASP9*), or 30-40% lower (*BAD*, *CASP3*, *CASP8*; $P < 0.05$) in IUGR. Protein expression of caspase3 was similar in both groups. The muscle regulatory factors and myogenesis inhibitor myostatin were 30% lower (*MYOD*, *MYF6*, *MYOG*, *MSTN*, $P < 0.05$) in IUGR. **Conclusions:** In IUGR fetal muscle, gene and protein expression patterns indicate slower myoblast progression through cell cycle versus increased rates of apoptosis, cell senescence in G0, or increased myostatin expression. Lower anabolic hormone concentrations in the IUGR fetal circulation could be responsible for slower rates of myogenesis. Correction of slower rates of myogenesis during gestation has the potential to increase myofiber number and size, thus improving the trajectory of muscle mass growth into adulthood. (Supported by NIH-R01-HD079404.)

I-VIII Hyperglucagonemia results in lower fetal weight, α-cell mass, and insulin concentrations in late gestation fetal sheep

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Objective: Glucagon potentiates postnatal glucose-stimulated insulin secretion (GSIS), but whether this also occurs in the fetus is unknown. Therefore, we investigated the effects of chronic fetal hyperglucagonemia on *in vivo* fetal insulin secretion in late gestation sheep. **Methods:** Late gestation fetal sheep received a direct intravenous infusion of glucagon (5 or 50 ng/kg/min; GCG-5 or GCG-50) or vehicle control for 8-10 d. Fetal GSIS was measured in response to acute (3 hour; control n = 7-10, GCG-5 n = 9-11) and chronic (8-10 d; control n = 4-7, GCG-5 n = 5-7) hyperglucagonemia. After 8-10 d of infusion, we measured fetal and organ weights, in addition to pancreatic vascularity, β-cell mass, and α-cell mass utilizing immunofluorescent staining (control n = 7-10, GCG-5 n = 7, GCG-50 n = 5). **Results:** There were no differences in GSIS following acute or chronic hyperglucagonemia (GCG-5). There was a 3-fold decrease in basal plasma insulin concentrations in the GCG-5 fetuses by study end (GCG-5 baseline 0.29±0.04ng/mL, GCG-5 final 0.10±0.02ng/mL, $P < 0.001$). Pancreatic weight was lower in hyperglucagonemic fetuses in a dose-dependent manner (control 3.62±0.19g; GCG-5 2.94±0.25g; GCG-50 2.57±0.18g; $P = 0.01$), as was α-cell mass (control 71.7±8.6mg; GCG-5 49.5±3.8mg; GCG-50 36.9±12.8mg; $P = 0.03$). There also was a dose-dependent trend toward lower fetal weight (control 3354±151g; GCG-5 2971±109g; GCG-50 2830±218g; $P = 0.07$) and β-cell mass (control 93.3±11.9mg; GCG-5 83.8±15.0mg; GCG-50 52.1±12.2mg; $P = 0.16$). The lower fetal weight achieves statistical significance with all hyperglucagonemic fetuses combined (GCG 2913±107 g, $P = 0.02$). **Conclusions:** These findings show that fetal hyperglucagonemia does not stimulate *in vivo* insulin secretion or potentiate GSIS under either acute or chronic conditions in the late gestations fetal sheep, but rather results in lower plasma insulin concentrations over time. This study adds important information regarding fetal endocrine pancreatic function by illustrating that the developing β-cell response to glucagon is a postnatal event, while strongly implicating an inhibitory role for glucagon in the regulation of fetal and pancreatic growth. (Supported by NIH Grant R01 DK088139.)

I-IX Effects of TGFβ-induced transgelin expression on endothelial progenitor cells exposed to gestational diabetes

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Objectives: To investigate whether the TGFβ pathway contributes to transgelin overexpression and impaired vasculogenic function in fetal endothelial colony forming cells (ECFCs) exposed to gestational diabetes mellitus (GDM). **Methods:** GDM-exposed ECFCs were treated for 48-72 hours with a TGFβ pathway inhibitor (ALK5 inhibitor SB431542 at 5μM) or vehicle control. Treated ECFCs were then evaluated for nuclear pSmad3 and transgelin expression via western blotting, transwell migration using a serum gradient, and network formation using a matrigel assay. **Results:** To confirm that SB431542 inhibited the TGFβ pathway, nuclear localization of pSmad3 was evaluated. Nuclear pSmad3, which is elevated in GDM-exposed ECFCs, was reduced following SB431542 treatment. In addition, transgelin expression decreased approximately 30% after a 48-hour treatment with SB431542 (n=7, p=0.03). To assess whether inhibition of the TGFβ pathway enhanced GDM-exposed ECFC function, transwell migration and matrigel assays were conducted. ECFC migration was increased in SB431542 treated ECFCs compared with vehicle controls (n = 10, $P = 0.008$). Importantly, SB431542 treatment also enhanced network formation compared with vehicle controls, including increased network numbers, as well as thicker nodes and branches, suggesting increased network stability. Network formation from these inhibitor-treated GDM-exposed ECFCs was similar to untreated, uncomplicated controls. **Conclusion:** The TGFβ pathway has a significant role in mediating aberrant transgelin expression and subsequent ECFC vasculogenic function. (Supported by: U54 DK106846 and Riley Children's Foundation)

I-X Wharton's jelly and cord blood-derived 3D organized culture to measure biological development

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Our objective was to create a human-based model used to determine whether perinatal exposures affect biological development through programmed cell susceptibility or cell-signaling from an adverse developmental microenvironment (DME). To do this, we created *Invitro*WOMB which uses human umbilical cord-derived mesenchymal stem cells (hu-MSC) on a proprietary 3D cord blood scaffold to study precision-based cellular proliferation and differentiation. **Methods:** Hu-MSCs were isolated by overnight digestion. After expansion, purity was confirmed using flow cytometry. Cells were seeded to 3D ECM made from cord plasma, crosslinking, and stability solutions by a patent-pending method. Cell viability, proliferation, and differentiation were evaluated and compared to standard 2D culture. The developmental niche was evaluated with and without cells using an antibody array to quantify TNFa, IL6, IL10, IFG1, FGF9, HGF and VEGF. Oxygen was measured using PreSens optical sensors. Rigidity was measured using atomic force microscopy (AFM). **Results:** Flow cytometry confirmed hu-MSC purity with ≥95% expressing MSC markers and <2% expressing hematopoietic, endothelial, or fibroblast markers. Doubling time was 39.7h. In our 3D matrix, hu-MSC remained multipotent and could be differentiated into adipocytes and osteocytes 50% faster than in traditional culture (7d vs. 14d). *Invitro*WOMB accelerated cardiogenic differentiation and yielded more mature cardiomyocytes. Confocal z-stack imaging demonstrated 7 layers of morphologically aligned cells for better cell-cell and cell-ECM interactions. Cell-seeded *Invitro*WOMB had lower and depth-dependent partial pressure of oxygen that more closely mimics *in utero* conditions. AFM demonstrated that stiffness can be manipulated to test biomechanical forces on development. *Invitro*WOMB had personalized hormone, growth factor, and pro-inflammatory cytokine profiles at baseline and during differentiation. Current studies take a cross-over approach to determine whether differences in cell fate are due to inherent cell susceptibility and/or perturbations in cell-signaling from an adverse DME. **Conclusion:** *Invitro*WOMB is a novel, human-based model for studying the effects of normal and adverse exposures on biological development. We expect it will be a useful tool for Developmental Biology, Reproductive Toxicology, and DOHaD.

I-XI IUGR causes pancreatic inflammation in the neonatal rat

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Objectives: The intrauterine milieu influences fetal development and perturbations can have lifelong effects on the offspring. Intrauterine growth restriction (IUGR) is a common complication of pregnancy and increases the risk of type 2 diabetes (T2D) in the offspring. Using a rat model of IUGR, bilateral uterine artery ligation at embryologic d18 (e18), we identified immune pathways that are causal to beta cell failure and the eventual development of diabetes. Previously we have shown that Th2 cytokines are transiently elevated at day 19 in islet lysates of IUGR fetuses. Neonatal administration of interleukin 4 (IL4) neutralizing antibody to IUGR pups on d1-6 reduced cytokine expression at postnatal day 14 (PD14) and ameliorated the IUGR phenotype in adult IUGR rats. The aim of this study was to identify which immune cell populations are responsible for the IUGR phenotype in the pancreas during the fetal and neonatal periods following IUGR surgery. **Methods**: Immune cell populations were enumerated by flow cytometry, RNAseq and immunohistochemistry at e19, PD1, PD7 and PD14. **Results**: At PD7, but not earlier, the number of immune cells increases in the islets and exocrine portion of the pancreas in male IUGR pups. Specifically, T cells and a subset of macrophages ($HIS48^{HI}$) increase in both the islets and exocrine pancreas. By PD14, immune cell numbers return to control levels, however, RNAseq and immunohistochemistry demonstrate a persistent change in immune cell activation. Administration of IL4 neutralizing antibody on d1-6 of life, prevents the increase in T cells and reduces the magnitude of the increase in $HIS48^{HI}$ macrophages in PD7 islets. Interestingly, IL4 neutralizing antibody does not prevent changes in the immune cell populations in IUGR exocrine pancreas, demonstrating that immune cells in the *islet* are responsible for the IUGR ß-cell phenotype. **Conclusions**: These results suggest that activated T cells and $HIS48^{HI}$ macrophages are causal to T2D in IUGR rats. [Supported by R01DK55704 (RAS) and T32ES09851 (TG)]

I-XII *In utero* exposure to maternal western style diet alters offspring skeletal muscle transcriptome

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Objectives: Skeletal muscle insulin resistance is a primary defect in the development of type 2 diabetes. Studies have shown that fetal exposure to a maternal diet high in fat predisposes offspring to a greater risk of obesity and insulin resistance. The objective of our study is to understand how *in utero* exposure to maternal Western Style Diet (WSD) transcriptionally programs offspring skeletal muscle for altered function. **Methods and Results**: We employed a previously established non-human primate model of WSD-induced maternal obesity to investigate the effect of maternal diet on offspring skeletal muscle. Adult females were fed a control (CON) diet or WSD for 2-7 years prior to and during pregnancy. Offspring either remained on the maternal diet, or their diet was switched post-weaning (PW), creating four treatment groups based on maternal and PW diet exposure. RNAseq was performed on RNA isolated from gastrocnemius muscle of offspring at 3 years of age. Principal component analysis of the RNAseq data showed clustering based on sex and maternal diet, and not based on PW diet, indicating that maternal diet strongly influences offspring skeletal muscle at the transcriptional level. To understand how transcriptional changes may influence skeletal muscle function, we performed differential gene expression analysis. More than 1,100 genes were differentially expressed based on maternal diet, while only 32 genes were differentially expressed based on PW diet. Pathway analysis using KEGG, and Gene Ontology (GO) databases indicate that transcriptionally, maternal WSD causes downregulation of the insulin signaling pathway, oxidative phosphorylation, Wnt signaling, ubiquitin mediated proteolysis, and chemokine signaling. A variety of RNA processing pathways were upregulated by maternal WSD exposure, including biosynthesis, processing, and transport pathways. **Conclusions**: Our data indicates that exposure to maternal WSD *in utero* alters offspring skeletal muscle function at the transcriptional level, dysregulating environmental signaling pathways, developmental pathways, and cellular quality control. Interestingly, altered RNA processing may be an important factor contributing to changes in the transcriptome. (R24 DK090964)

I-XIII Greater pyruvate dehydrogenase phosphorylation and sustained concentrations of tricarboxylic acid intermediates in hypoxemic fetal livers

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Introduction: Fetuses exposed to sustained hypoxemia maintain normal oxygen consumption rates; however, the mechanisms supporting this are not completely understood. Our objective was to determine the contribution of the fetal liver to whole body metabolism during hypoxemia by measuring pyruvate dehydrogenase (PDH) complex regulation and tricarboxylic acid (TCA) cycle metabolites. **Methods:** Surgeries were performed on late gestation pregnant ewes to place indwelling catheters in the maternal and fetal vasculature and maternal trachea. Hypoxemia was induced for 9 d by tracheal nitrogen insufflation to reduce maternal and subsequently fetal arterial pO_2 (HOX; n = 11; fetal pO_2 = 14.6±0.5 mmHg) compared with fetuses from ewes receiving compressed air (CON; n = 7; fetal pO_2 = 18.33±1.0 mmHg). At 133±1 d gestation, fetal liver biopsies were collected for qPCR, western blotting, ^{1}H NMR metabolomics, and citrate synthase activity. Data were analyzed by student's t-test, presented as mean ± SE, and significance accepted at $P \leq 0.05$. **Results:** The ratio of phosphorylated (S293) to total PDH protein was 40% greater in livers from HOX fetuses compared to CON ($P < 0.05$). Gene expression for PDH kinase isoforms *PDK1, PDK2* and *PDK4* were not different between groups. Both mRNA and protein expression of lactate dehydrogenase (*LDHA* gene; LDH-A protein) were 2-fold greater in HOX compared with CON ($P < 0.05$). Liver concentrations of pyruvate precursors, alanine and lactate, were not different between groups. Liver concentrations of TCA intermediates: citrate and succinate, and amino acids: glutamine, glutamate, and alanine were similar between groups. Hepatic citrate synthase activity was similar between CON and HOX (24.9±4.3 vs 24.8±3.8 nmol/min/mg protein). **Conclusion:** Greater PDH phosphorylation indicates reduced pyruvate oxidation in HOX fetal livers, yet mitochondrial content is maintained based on citrate synthase activity. We speculate that the TCA cycle is sustained with amino acids as an oxidative fuel source in HOX livers. This demonstrates metabolic flexibility in the fetal liver during hypoxemia. [Support: NIH R01-DK-108910 (SRW); F32-DK-120070 (AKJ).]

I-XIV Developmental changes in mitochondria respiratory function between fetuses in labor and 2-day old lambs.

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The fetus undergoes rapid changes in its transition to a newborn in terms of breathing and circulation. The present study was done to test the hypothesis that the mitochondrial respiration of the cardiac intraventricular septum and diaphragm of newborn lambs differs from the fetus. **Methods:** Cardiac interventricular septum (IVS) and diaphragm (DIA) were collected from fetuses of ewes in labor and from 2-day old lambs. Mitochondrial respiration was assessed by high-resolution respirometry from mechanically separated fibers of IVS and DIA at 39 ^{0}C. The protocol assessed leak respiration (L) in the presence of substrates, addition of ADP (PCI), followed by succinate (PCI+II). Integrity of the outer membrane was assessed by addition of cytochrome c. Titration of the uncoupler, FCCP, induced maximal uncoupled respiration (ECI+II) and subsequent measurement of ECII by addition of rotenone to block complex I. Maximal Complex IV activity (ECIV) was determined by addition of the substrate TMPD in the presence of the antioxidant ascorbate. Oxygen flux (pmol O_2/s/mg wet weight was analyzed. Statistical analysis was performed by Student t-test ($P < 0.05$). **Results:** We found that leak flux (p= 0.04, 10.8±3.1 vs 3.6±1.0), and PCI ($P = 0.05$, 51.3± 6.1 vs 34.1 ± 5.3), was significantly increased in the DIA of lambs compared to the fetuses. Though the other states were increased in the lamb, they were not statistically significant. In the IVS, leak flux showed a tendency to significantly increase ($P = 0.06$, 6.2±1.3 vs 11.5 ±2.1). There were no significant changes in other states in the IVS. **Conclusion:** Despite the increase in activity of the diaphragm at birth, mitochondrial respiratory capacity appears to be similar to postnatal capacity in both cardiac muscle and diaphragm by the time of labor. However, the increase in leak may reflect an increase in basal activity in the tissues postnatally. This indicates that in normal fetuses, mitochondria are mature by the time of birth. (Funding source: NIH R01 HD087306)

I-XV Insulin effect during *in vitro* oocyte maturation on insulin and IGF-receptor gene expression in bovine blastocysts

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Objectives: Metabolic imbalance and hyperinsulinemia are influencing reproductive health. Metabolic and reproductive disorders are strongly related, while the molecular mechanisms behind are only partly explained. Insulin and insulin-like growth factors (IGF) are expressed during early development (Schultz *et al.* 1992, Wang *et al.* 2009) with anti-apoptotic effects and functions in glucose-, lipid- and protein metabolism and regulation of the cell cycle. In this study, insulin was added during *in vitro* oocyte maturation, and changes in gene expression of bovine day 8 blastocysts (BC8) were investigated by transcriptome analysis. **Methods:** Abattoir-derived oocytes (n = 882) were divided into 3 groups and *in vitro* matured for 22 h by adding insulin (INS10=10µg/ml; INS0.1=0.1 µg/ml and INS0=control). After routine *in vitro* production, BC8 (n = 120) were pooled in groups of 10 and total RNA was extracted by parallel gDNA-and total RNA-extraction (AllPrepDNA/RNA micro kit, Qiagen®) for analyses of the transcriptome. Amplified aRNA was hybridized on the Agilent-manufactured EmbryoGENE-slides in a 2-color-dye-swap design. An empirical Bayes moderated t-test was applied to search for the differentially expressed transcripts (DET) between control and insulin-treated groups, using the 'limma' package in R (www.r-project.org). DET were defined as having a 1.5 fold-change difference between treatment and control with $P < 0.05$. **Results:** BC8 rates were significantly lower in INS10 and INS0.1 versus control ($p<0.05$). While changes in gene expression of IGF1, IGF2 and the insulin receptor did not reach significance, IGF2-receptor was overexpressed in both insulin groups (INS10: 1.628 and INS0.1: 1.545). IGFBP7-levels were only increased in INS0.1 (1.557). **Conclusions:** Overexpression of IGF2R and IGFB7 as consequence to hyperinsulinaemic stimuli during oocyte maturation might further impact the developmental potential of the blastocysts, having impact on the regulation of insulin signaling. Hyperinsulinemia influences important cellular functions in growth and energy metabolism. (Funded by FORMAS).

I-XVI Prenatal exposure to diabetes but not high-fat diet increases mitochondria-mediated cell death in adult rat cardiomyocytes

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Objective: To determine the role of mitochondrial-mediated cell death in developmentally programmed heart disease, we used reproducible, real-time, live-cell imaging studies to objectively measure cardiomyocyte responses to metabolic stress. **Methods:** Newborn rats prenatally exposed to streptozocin-induced diabetes, maternal high-fat diet, or combination were cross-fostered to healthy dams and aged in controlled environments. At 12-13 months, adult rat cardiomyocytes (ARCM) were isolated and live-cell video-imaging performed before and after FCCP-induced mitochondrial uncoupling. Videos were analyzed for rates of mitochondrial membrane potential (MMP) loss, mitolysosome formation, and time to cell death. Groups were compared by two-way ANOVA for diet, diabetes, and interaction effects and unpaired T-test for sex-specific differences. **Results:** Diabetes-exposed but not diet-exposed ARCM had significantly faster MMP loss ($P < 0.0001$) and a shorter time to cell death as quantified by volume loss ($P = 0.004$) or pyknosis ($P = 0.013$). Sex-specific differences were evident. Normal and diabetes-exposed female ARCM had a higher number of baseline mitolysosomes than males, suggesting better physiologic mitochondrial homeostasis through culling and turnover. In diabetes-exposed offspring, males had a faster MMP loss ($P < 0.0001$) and shorter time from MMP to cell death ($P < 0.0001$) than females which was not explained by rates of mitophagy. Diet-exposed female but not male ARCM had fewer baseline mitolysosomes (physiologic turnover) and higher rates of mitophagy after FCCP compared to same sex controls. **Conclusions:** Prenatal exposure to maternal diabetes increased the risk of mitochondrial-mediated cell death in adult male cardiomyocytes. Higher rates of physiologic mitophagy may play a cardioprotective role in females. Findings highlight sex-specific differences and the role of mitochondria in developmentally programmed heart disease, specifically the risk of damage from myocardial infarction. (Supported by NIH-NICHD K08HD078504 and NIH-GMS P20GM103620).

I-XVII Perinatal iron deficiency combined with a high salt diet causes sex-dependent oxidative stress and mitochondrial dysfunction in adult rat kidneys

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Objectives: Iron deficiency (ID) is the most common nutritional deficiency worldwide. Perinatal ID is associated with increased reactive oxygen species (ROS) generation and mitochondrial dysfunction in the fetal kidney, though it is unclear whether these persist into adulthood. We aimed to elucidate the effects of perinatal ID on the kidney of adult offspring and hypothesized that perinatal ID causes sex-dependent oxidative stress and mitochondrial dysfunction in which will be exacerbated by high-salt intake. **Methods:** Dams were fed either a control or iron-restricted diet prior to and throughout gestation. After birth, dams were fed an iron-replete diet. On postnatal day (PD) 138 offspring randomly received either a high-salt (HS) or normal-salt (NS) diet for 6 weeks. Tissues were collected on PD 180. Cytosolic and mitochondrial superoxide were assessed in cryosectioned kidneys with dihydrotheium and MitoSox-Red dyes, respectively, and quantified with fluorescence microscopy. Mitochondrial respiration was measured using an Oroboros -O2k Oxygraph. **Results:** ID resulted in 34% and 52% decreases in maternal and offspring hemoglobin levels compared to controls at birth. In 6-month old male offspring, cytosolic superoxide was increased by HS in the cortex ($P = 0.04$), and by ID in both the medulla and cortex ($P < 0.001$). Mitochondrial superoxide production was increased in the medulla of males subjected to HS ($P = 0.04$), but not in females. Mitochondrial respiration was increased in the medulla of male offspring subjected to HS ($P < 0.05$), albeit ID males exhibited reduced complex II respiration ($P < 0.05$). Within the cortex, an interaction between HS and ID was observed whereby complex IV respiration was reduced by HS only in ID offspring ($P = 0.01$). Females exhibited no alterations in mitochondrial function. **Conclusion:** These results suggest perinatal ID causes long-term sex-dependent patterns of oxidative stress and mitochondrial dysfunction, with males more susceptible than females.
(Funding: Canadian Institutes of Health Research, and University of Alberta Women and Children's Health Research Institute.)

I-XVIII Premature adipose tissue development and heightened adipogenic potential in offspring born to metabolically compromised pregnancy

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Objectives: Determine the effect of maternal metabolic dysfunction on developmental adipogenesis and later-life adipogenic potential. **Methods:** Two mouse models were used. First, females heterozygous for leptin receptor deficiency ($Lepr^{db}$/+) have higher adiposity, hypertriglyceridemia and hyperinsulinemia during pregnancy. Our lab revealed this model to program early-onset cardiovascular risk factors in the offspring. To isolate effects of intrauterine hyperinsulinemia, we used females heterozygous for prolactin receptor deletion ($Prlr^{+/-}$), which develop gestational hyperglycaemia due to impaired pregnancy-induced β-cell adaptations. Wild type (Wt) females served as control; neonates were cross-fostered onto CD1 dams and only Wt offspring studied. Adipocyte maturation was assessed in neonatal inguinal subcutaneous adipose tissue (iSAT), by measuring cell size distribution, expression levels of adipogenic markers and circulating levels of adipokines. At 7 wks of age, Wt offspring were randomized to control or high fat/sugar (HF/HS) diet. In adulthood, preadipocytes isolated from the stromal vascular fraction of iSAT were induced to differentiate and Oil Red-O staining used to measure lipid accumulation. **Results:** Both $Lepr^{db}$/+ and $Prlr^{+/-}$ pregnancies resulted in accelerated iSAT maturation. In iSAT from Wt neonates born to $Prlr^{+/-}$ vs. Wt dams, newly formed adipocytes (< 30μm) were less abundant ($P < 0.0001$), while mature adipocytes (> 70 μm) more abundant ($P < 0.05$). Protein expression of insulin-mediated adipogenic mediators in iSAT (SREBP1 & SCD1) and plasma leptin levels [males: 2-fold ($P < 0.0001$); females: 1.7-fold ($P < 0.01$)] were higher in Wt neonates from $Prlr^{+/-}$ dams. In isolated preadipocytes, optical density of extracted Oil Red-O was higher at D4 ($P < 0.05$) and D7 ($P < 0.05$) in Wt offspring from $Lepr^{db}$/+ vs. Wt dams after HF/HS feeding. **Conclusions:** Heightened adipogenic potential is programmed in offspring born to pregnancies complicated by maternal metabolic disease and our data suggest *in utero* hyperinsulinemia to be the primary stimulus. (Supported by LCIA, CIHR, Heart and Stroke Foundation and NIH).

I-XIX Postnatal catch-up growth in protein-restricted IUGR offspring leads to elevated hepatic p66Shc: Mechanism of mitochondrial dysfunction?

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Introduction: Epidemiological studies suggest an inverse relationship between birth weight and long-term metabolic disease. Postnatal catch-up growth exacerbates this relationship; however, the underlying molecular mechanisms remain elusive. Given that mitochondrial dysfunction occurs with metabolic pathologies, we investigated the role of mitochondrial stress marker p66Shc in livers of low birth weight offspring exposed to maternal protein restriction (MPR). **Objectives:** To determine if MPR offspring exhibit hepatic mitochondrial dysfunction following postnatal catch-up growth. We hypothesized that adult MPR offspring with catch-up growth exhibit elevated p66Shc and oxidative stress. Since hepatic endoplasmic reticulum (ER) stress is also present in these offspring by adulthood, we further predicted that ER stress promotes increased expression of p66Shc. **Methods:** Pregnant Wistar rats were fed a control (20%) protein diet or a low protein (LP, 8%) diet. Control offspring were fed a control diet, while MPR offspring were maintained on a LP diet (LP1) or switched to a control diet post-weaning (LP2) or at birth (LP3). To investigate the relationship between ER stress and p66Shc, HepG2 cells were treated with tunicamycin, an inducer of ER stress. Transcript and protein abundances were assessed via qRT-PCR and western immunoblotting, respectively. **Results:** Protein levels of p66Shc and its isomerase Pin1 were increased in LP2 offspring at four months ($P < 0.05$), along with increased oxidative stress markers 4-hydroxynonenal ($P < 0.01$), superoxide dismutase (SOD)-1 ($P < 0.05$) and SOD2 ($P < 0.01$). LP2 offspring further displayed aberrant markers of aerobic metabolism, including increased phosphorylated pyruvate dehydrogenase ($P < 0.05$), decreased citrate synthase ($P < 0.001$) and decreased succinate dehydrogenase ($P < 0.0001$). *In vitro* protein levels of p66Shc were increased following tunicamycin treatment ($P < 0.05$). **Conclusion:** Our results suggest that MPR followed by catch-up growth is detrimental to hepatic mitochondrial function, and this may be mediated by ER stress. Overall, our data indicates that timing of nutritional restoration for IUGR offspring could influence long-term hepatic metabolism via modulation of mitochondrial function.

I-XX *In utero* exposure to bisphenol A is associated with sex specific changes in the methylome and transcriptome in human fetal stem cells

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Introduction: Prenatal exposure to bisphenol A (BPA) has been linked to obesity and diabetes in adults but the molecular mechanisms driving these phenomena are not known. Studies in mice found that gestational BPA exposure alters DNA methylation and gene expression of key metabolic tissues. **Objective:** To profile changes in genome-wide DNA methylation and expression in second trimester human amniocytes, a fetal stem cell, exposed to *BPA in utero*. **Methods:** A nested case control study design was performed in 16 pairs of amniocytes discordant for *in utero* BPA exposure and matched for offspring sex, maternal race/ethnicity, maternal age, gestational age at amniocentesis and gestational age at birth. Genome wide DNA methylation analysis was performed with enhanced reduced representation bisulfite sequencing (ERRBS) and gene expression was assayed via RNA-Sequencing (RNA-Seq). Sequencing data analysis was performed to determine differentially methylation regions and significant changes in gene expression. **Results:** RNA-Seq identified 101 genes with altered expression in male amniocytes ($q<0.05$) with enrichment in biological pathways including hepatic fibrosis, axonal guidance, collagen signaling and adipogenesis. Sex-specific analysis of ERRBS data identified 508 and 498 single CpGs with an absolute change in methylation >15% ($q<0.05$) in male and female analysis, respectively. In addition, we identified 36 differentially methylated regions (DMR) in male BPA exposed amniocytes and 14 in female amniocytes ($q<0.05$). **Conclusion:** In a unique repository of human amniocytes exposed to BPA *in utero*, we identified novel sex-specific changes in gene expression and DNA methylation using genome-wide assays.

I-XXI Placental proteins: A new approach to prematurity

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Objectives: Extreme prematurity (23 to <28 weeks) continues to be a leading cause of infant morbidity and mortality and increases the risk of significant long-term sequelae such as cerebral palsy, respiratory and neurodevelopmental disease. Emerging evidence from animal experiments indicates that factors secreted by the placenta are critical for normal fetal organ development. One fundamental difference between fetal and postnatal life is the instantaneous discontinuation of the umbilical circulation, depriving the premature infant of placental factors potentially critical for fetal organ development. We recently reported that 341 proteins are secreted by the term human placenta into the fetal circulation. Using bioinformatic approaches, we found that these proteins were involved in neurogenesis (18%), angiogenesis (11%), inflammatory processes (19%), embryogenesis (6%), and lung development (1%) implicating a role in fetal organ development and maturation. However, it is currently unknown if these proteins are expressed earlier in gestation. To determine if genes for these proteins are highly expressed in the placenta during late second trimester. **Methods**: Placenta villous tissue was collected after informed consent from preterm (range 26.1-32.6 weeks; n = 9) and term healthy pregnancies (range 39.0-39.1 weeks; n = 4), homogenized on ice and stored at -80˚C. We selected 7 candidate proteins with the highest umbilical venous-artery concentration differences at term with predicted roles in development. Placental mRNA was extracted, and qPCR was used to determine placental gene expression. **Results**: We found that mRNA expression for properdin, a known factor in the coagulation cascade, had a 3.1 fold increase in very premature when compared to full term placentas ($P < 0.05$) and genes encoding endoglin, neuropilin-1, platelet derived growth factor α and β, and semaphorin-6A and 6B were expressed at similar levels in preterm and term placentas. **Conclusions**: These data suggest that the late second trimester human placenta expresses genes encoding proteins predicted to be involved in neurogenesis, angiogenesis, and lung development. Further research is needed to understand the role of these proteins in the development of fetal organs.

I-XXII Maternal obesity linked to hypertrophy in adipogenic differentiating infant MSCs: The Healthy Start ECHO Cohort

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Objectives: Maternal obesity increases the risk of neonatal adiposity and future risk of obesity. Previously, we reported greater adipogenesis in mesenchymal stem cells (MSCs) cultured from umbilical cords of human infants of mothers with obesity (Ob-MSCs) compared to those of normal weight mothers (NW-MSCs), which positively correlated with neonatal adiposity. However, it is unclear if greater adipogenesis is due to increased adipocyte number (hyperplasia) or size (hypertrophy), the latter of which is linked to proinflammatory markers and insulin resistance in adults with obesity. **Methods:** To test the hypothesis that Ob-MSCs are larger and store more lipid than NW-MSCs, we compared 20 NW-MSCs with 17 Ob-MSCs (without gestational diabetes) after inducing adipogenesis for 14 d in 3-dimensional hydrogels. The hydrogels allowed better quantification of adipocyte hypertrophy than traditional cell culture. We stained hydrogels for BODIPY (neutral lipids), Wheat Germ Agglutinin (cell membrane), and DAPI (nucleus), and imaged them with confocal microscopy. We used Fiji to quantify fluorescence intensity, double-measuring 200 image Z-stacks (step size 1 μm) of > 100 cells/subject (avg repeatability > 0.88). **Results:** We used T-tests to determine differences between groups. The Ob group had a higher pre-pregnancy BMI (NW = 21.7±0.1; Ob = 33.8±0.8 kg/m^2; $p < 0.0001$), and higher fasting maternal insulin (NW = 7.3±0.4; Ob = 13.1±2.1 μU/mL; $p = 0.01$) at mid-gestation (15-23 wks), but no difference in glucose levels. Infants were born ≥ 37 wks and had similar gestational age and rates of cesarean delivery. Ob-MSCs stored 157% more lipid ($P = 0.0007$) and were 138% larger ($P = 0.0005$) than NW-MSCs, indicating hypertrophy. **Conclusions:** Adipocyte hypertrophy in infant MSCs may explain, in part, how infants of obese mothers have a heightened risk for obesity and insulin resistance later in life. (NIH DK117168, UG3OD023248).

I-XXIII Potentiation of adipogenesis by bisphenol A and its common substitute, bisphenol S

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Objective: Bisphenol A (BPA) is a commonly used plasticizer detected in the urine of 93 percent of US adults and associated with metabolic and cardiovascular diseases. Amid growing consumer concern, manufacturers turned to Bisphenol S (BPS); however, its safety was not determined before introduction to market. Thus, exposure to BPS is on the rise, including from products labeled "BPA-free". Since bisphenols cross the placenta, they are likely to impact fetal development. Our aim is to determine the impact of BPA or BPS exposure on developmental adipogenesis, a key developmental even that starts *in utero*. **Methods:** The stromal vascular fraction (SVF) was isolated from inguinal subcutaneous adipose tissue of juvenile male C56BL/6 mice. SVF-mesenchymal stem cells were cultured with preadipocyte growth medium and treated with vehicle or variable doses of BPA or BPS [2.5nM (levels in drinking water); 250nM (permissible limit) and 25μM]. At 48-hours post-confluency (contact inhibition), cells were treated with differentiation medium. At day 4 and 7 of differentiation, Oil Red-O staining was used to measure lipid droplet formation and mRNA expression of adipogenic genes was determined. **Results:** At day 4 and day 7 of differentiation, lipid droplet formation as determined by the optical density of Oil Red-O, was increased in both BPA and BPS-treated cells ($P < 0.001$). The pro-adipogenic response of BPA was dose-dependent, while that of BPS was biphasic with the greatest response at the lowest dose. The expression levels of adipogenic mediators (PPAR-γ and SREBP-1) were also higher in differentiated cells exposed to BPA or BPS ($P < 0.05$). At 48-hours of contact inhibition (pre-differentiation), the expression of ZFP-423 (early adipogenic marker) was increased following BPA or BPA exposure ($P < 0.05$). **Conclusion:** Adipogenic potential is enhanced in preadipocytes exposed to BPS or BPA at doses lower than the permissible limit. Studies are underway to determine the effect of maternal BPS exposure on developmental adipogenesis and explore DNA methylation as a potential mediator. (Supported by Heart and Stroke and CIHR grant).

I-XXIV A Dreadful childhood: The long shadow of American slavery

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This project analyzes birth and death lists from plantation records, heights recorded on shipping manifests required by the coastwise trade, and taxable wealth records for the state of Georgia in 1900 and 1910. Young slaves endured extreme childhood deprivation, characterized by profoundly seasonal neonatal mortality rates, infant mortality rates of 35 per cent, and very short stature (at the first percentile of modern height standards). These conditions had significant negative implications for cognitive development. Attenuated breastfeeding and a low protein diet stunted growth among children and a low-energy diets created lethargic children, which reduced the need for expensive adult supervision. Catch-up growth and declining mortality rates followed after age 10 when children entered the workforce and received adult rations that included meat protein. Thus young slaves caught-up physically to the heights of well-nourished free workers such as Union Army recruits, but were unable to do so cognitively. On approximately one-half of southern plantations, meals were prepared in central kitchens, in which case it was easy to enforced dietary segregation; the children were simply fed separately. If food was distributed to the parents for preparation, it was destined to feed the slaves who worked in the fields, whose typical ration was ½ pound of pork per day. If the parents gave some meat to their young children, the workers in the family would have lacked the protein required for a full day's work and would have been punished. Therefore, parents could not protect their young children from hunger. There was a structural break in nutrition associated with emancipation and hence in the cognitive abilities of southern blacks arranged by birth cohort. Black children born after emancipation were better able than their older siblings to compete in a market economy. This is revealed by the amount of taxable wealth owned by blacks linked from the census manuscripts of population in 1900 and 1910 to tax rolls; controlling for age and other socioeconomic conditions, the post-Civil War cohort owned approximately 3 times as much wealth as those born prior to emancipation. Soon Jim Crow laws and lynching emerged as methods of social control.

I-XXV Performance of growing beef cattle produced under divergent perinatal rangeland resource environments

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Objective: To examine the effect of perinatal environment - as dictated by precipitation - on indicators of growth and performance in rangeland cattle. **Methods:** Performance records of *Bos taurus* calves born January-April of 2000-2016 to dams maintained as a single herd on the University of Arizona's V Bar V Experiment Station (31,000 ha; 36.4N, 111.7 W) were sorted by standardized precipitation index (SPI) during 3-month pre-natal (Aug-Oct) and post-natal (Mar-May) periods. Records from animals identified as having experienced either "dry" (SPI < -0.1, n = 5 periods; n = 1,269 animals) or "wet" (SPI > 0.5, n = 4 periods; n = 992 animals) pre- and post-natal environments were included in a mixed model analysis. Perinatal environment was considered fixed and year of birth random. Weaned steers were fed and harvested at commercial facilities. Performance measures included adjusted birth (n = 984) and weaning (n = 960) weight (kg), as well as carcass weight (kg), fat thickness (cm) and ribeye area (cm^2); carcass measurements n = 171. Weaned heifers were developed on pasture. Performance measures included adjusted birth (n = 1,262), weaning (n = 1,220) and yearling (n = 798) weight (kg), as well as pelvic height (cm), pelvic width (cm) and pelvic area (cm^2); pelvic measurements n = 918. **Results:** "Dry" steers were lighter ($P < 0.01$) at birth (35.84 ± 0.50 vs 37.90 ± 0.56,) and harvest (355.69 ± 3.51 vs 379.75 ± 3.07), and produced smaller ($P < 0.01$) ribeye's (87.03 ± 1.02 vs 91.71 ± 0.89), than their "wet" counterparts, respectively. "Dry" heifers were lighter ($P < 0.01$) at birth (32.66 ±0.34 vs 34.44 ± 0.39) but had greater ($P < 0.05$) pelvic height (14.08 ± 0.58 vs 12.26 ± 0.65) than their "wet" counterparts. respectively. **Conclusions:** Perinatal environment affected subsequent indicators of growth and performance in rangeland beef cattle.

I-XXVI Effect of high altitude on human placental amino acid transport

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Introduction: Non-native women who are pregnant at high altitude give birth to smaller babies than at sea level. Placental amino acid transport capacity is positively associated with fetal growth and placental mechanistic target of rapamycin signaling, which activates placental amino acid transport, is suppressed at high altitude. Severe environmental hypoxia reduces System A (SysA)-mediated amino acid transport in human trophoblast and the mouse placenta. We hypothesized that microvillous membrane (MVM) SysA and System L (SysL) amino acid transporter activity is lower in placentas of women living at high altitude, compared to low altitude controls. **Methods:** Placentas were collected, at term, from healthy pregnant women residing at high altitude (HA, >2500m, Summit County, CO, n = 14), low altitude (LA, 1600m, Denver, CO, n = 14) or sea level (SL, 200m, San Antonio, TX, n = 14), following planned Caesarean-section without labor. Villous tissue was dissected, homogenized and the MVM isolated by differential centrifugation and Mg^{2+}-precipitation. SysA and SysL activity in MVM were determined by Na^+-dependent ^{14}C-methylaminoisobutyric acid uptake and BCH-inhibitable ^{3}H-leucine uptake, respectively. Intergroup differences and linear interdependence of variables were assessed by one-way ANOVA and Pearson correlation. **Results:** Birth weight, but not placenta weight, was 13-15% lower in HA pregnancies (2.88±0.10kg) compared to either LA (3.30±0.07kg, $P < 0.01$) or SL neonates (3.39±0.29kg, $P < 0.01$). Both birth weight (R=-0.53) and placenta weight (R=-0.34) inversely correlated with maternal altitude of residence ($P < 0.05$). However, MVM Sys A and Sys L activity was similar in HA, LA and SL groups and did not correlate with altitude of residence. The effect of altitude was similar when data were stratified by infant sex. **Discussion:** Low birth weights in the neonates of women residing at high altitude are not a consequence of reduced placental amino acid transport capacity. These observations are in general agreement with studies of IUGR babies at low altitude, in which MVM SysA activity is down-regulated only in IUGR babies with significant compromise.

I-XXVII Maternal allergic asthma during pregnancy alters fetal lung and immune development in sheep

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Objectives: Asthma is prevalent in pregnancy and increases the risk of respiratory disease in offspring. We aimed to elucidate the prenatal mechanisms by which maternal asthma increases this risk using a sheep model. **Methods:** Singleton-bearing ewes were either sensitized before pregnancy to house dust mite via three intradermal injections (allergic, n = 7) or remained non-allergic (control, n = 5). Ewes received airway challenges with house dust mite (allergic group, every four weeks) or saline (controls, fortnightly) throughout gestation. At 140±1 d gestational age (term, ~147 d), lung tissues were collected for histology (fetal lung structure) and immune tissues for flow cytometry (immune phenotype). **Results:** The number of type II alveolar epithelial (surfactant protein C-immunostained) cells was lower in fetuses from allergic ewes compared to controls ($P < 0.001$). Lung tissue-to-airspace ratio (an estimate of airspace) and leukocyte and macrophage densities did not differ. The proportion of thymic lymphocytes positive for $CD44^+$ (receptor involved in allergic inflammation) was higher in fetuses from allergic ewes compared to controls ($P < 0.05$). **Conclusions:** Type II alveolar epithelial cells promote lung expansion after birth, thus lower numbers may contribute to increased risk of neonatal respiratory distress in infants of asthmatic mothers. Therefore, interventions to promote lung maturation could improve neonatal outcomes. If the elevated lymphocyte expression of CD44 persists postnatally, this could be a mechanism by which maternal asthma confers greater susceptibility to allergic diseases in offspring. (Supported by the Jack Brockhoff Foundation and the Victorian Government).

II-I Development of the human fetal ad≥renal medulla and the influence of maternal smoking

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Objective: to determine the impact of exposure to maternal smoking on the development of the human fetal adrenal medulla. Cigarettes contain many potential endocrine disruptors (EDs). Fetal exposure via maternal smoking can disrupt normal fetal programming and has been linked with an altered postnatal stress response in the offspring, possibly due to altered catecholamine release by the adrenal medulla. Some programming effects of maternal smoking may be due to altered fetal adrenal medulla development or function. **Methods:** We have examined development of prechromoblast cells (which form catecholamine-secreting chromaffin cells) in the adrenal medulla from 109 human fetuses exposed, or not, to maternal smoking. Adrenals from elective terminations (11-21 weeks of gestation; REC 04/S0802/21) were grouped by sex, gestational age and maternal smoking. Medulla development was examined by immunohistochemistry. mRNA and protein were quantified by RT-qPCR and Western Blot. **Results:** Transcripts and proteins involved in catecholamine biosynthesis (tyrosine hydroxylase (TH), Phenylethanolamine N-methyltransferase (PNMT), dopamine beta-hydroxylase (DBH) and DOPA decarboxylase (DDC)) were highly expressed in the developing medulla. Relative levels of DBH and DDC transcript decreased between 12 and 19 weeks of gestation ($P = 0.033$ & $P = 0.028$). Protein levels of PNMT (n = 60) and TH (n = 38) also decreased ($P < 0.001$ & $P = 0.002$). Maternal smoking was not associated with any changes in these enzymes at transcript or protein level. Immunostaining for TH and PNMT showed that prechromoblast cells are divided into two subpopulations of cells either positive for TH (producing norepinephrine) or PNMT (converting norepinephrine to epinephrine). **Conclusions:** Developing adrenal medullary cells actively express enzymes required for second trimester catecholamine synthesis, localized into two distinct subpopulations. Expression of key enzymes in this pathway is not affected by maternal smoking. Maternal smoking may not affect medullary development or the effects may occur later in gestation. (Supported by Medical Research Council)

II-II Novel variants of the *CRP* gene in an American Indian pre-eclampsia cohort

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Objectives: While the etiology of pre-eclampsia (PE), is unknown, multiple lines of evidence implicate immunologic factors as important contributors. C-reactive protein (CRP) is a prominent component of the innate immune system. We previously reported inherited genetic variants that increase PE risk. We sought to discover novel genetic variants among these American Indian cases. **Methods:** Cases (n = 95) exhibiting well defined PE were randomly selected. A total of 177,525 base pairs were sequenced from ~168 Kb 5' to 7 Kb distal to the CPR gene, using the Illumina MySeq platform. Reads were aligned to hg19 and processed using GATK best practices, and the resulting variants were annotated using SnpEff in GEMINI. Quality control filters in vctf tools excluded variants with a call rate < 95%, those with Hardy-Weinberg equilibrium $P < 0.01$, and genotypes with quality<15. Mean sequencing depth was 158x coverage (range 45-268). **Results:** There were a total of 1,809 variants (including 93 deletions and 23 insertions) following quality control and 1,254 (69%) have not been reported in dbSNP. Among apparently novel variants there were 510 singletons, 548 occurring in 3 or more individuals, and one found in 40 instances. One individual was homozygous for a novel SNP. There are 8 novel coding variants, of which 3 predict truncated or non-functional protein and 5 indicate amino acid substitutions. **Conclusion:** Although ascertained from a cohort of only 95 pre-eclampsia cases, there appears to be considerable, hitherto unrecognized genetic variation remaining to be discovered, validated and evaluated for functional effects among this population.
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II-III Role of maternal preconception nutrition and BMI on infant DNA methylation of human metastable epialleles: Findings from the women first study

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Objectives: To test if timing of a maternal lipid-based nutrient supplement (LNS) and pre-pregnancy BMI (ppBMI) leads to differential DNA methylation (DNAme) of humans metastable epialleles (MEs) in Guatemalan infants at birth. MEs are systemically methylated regions and reported to be altered by maternal nutritional status at conception. This study is part of the Women First RCT that tested whether preconception LNS improved birth length. The study groups were: 1) women consumed LNS ≥ 3mos prior to conception (n = 45); 2) women consumed the same LNS commencing at 12wks gestation (n = 45); or 3) no LNS (n = 44) across ppBMI (20.1–38.4 kg/m^2). **Methods:** DNAme libraries were constructed from amnion tissue collected at birth using RocheNimbleGen CpGiant and sequenced via NovaSeq. A linear model to test for the interaction between maternal LNS and ppBMI on infant DNAme within 275 previously identified MEs was used for subjects that passed quality control (131/142), significance level adjusting for the 275 regions was $P \leq 0.000182$. **Results:** We identified 5 MEs with significant interactions, demonstrating differential ME DNAme due to intervention arm was dependent on ppBMI. We also identified 3 CpGs associated with ppBMI regardless of LNS and 1 CpG associated with

LNS regardless of ppBMI suggesting independent effects of maternal LNS and ppBMI on ME DNAme. **Conclusions:** Our findings indicate that timing of maternal LNS and ppBMI contribute to DNAme of MEs in infants at birth, suggesting epigenetic influences due to *in utero* exposures. (Supported by Bill & Melinda Gates Foundation OPPI055867, NIH/ODS U10 HD076474, K01DK109077, NIH/NCATS Colorado CTSA UL1TR002535).

II-IV Impact of ergot alkaloid consumption on fetoplacental growth and development across late gestation in sheep

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Objective: To evaluate the impact that ergot alkaloid consumption has on fetoplacental growth and development at multiple stages during late gestation. **Methods:** Suffolk ewes (n = 18; 87 ± 7.8 kg) bred to a Texel ram and estimated to be carrying twins were assigned to endophyte-infected tall fescue seed (E+; 4.14µg ergovaline + ergovalinine/g seed) or a control diet (CON; 0µg ergovaline + ergovalinine). Ewes were individually fed CON or E+ seed from d 86 to d 133 of gestation. Ewes were harvested at d 85 (pretreatment; n = 3), d 110 (n = 4/treatment) or d 133 (n = 4/treatment). The full uterus was tied off at the cervix, excised, and weighed. Fetuses, placentomes, and membranes were removed from the intact uterus and weighed. Fluid volume was calculated by difference. Placentomes were separated into cotyledon and caruncle and weighed individually. Data were analyzed with treatment as fixed effect and means adjusted for lamb number. Orthogonal contrasts were used to compare means at specific time points (d 110 vs pretreatment, d 133 vs 110, E+ vs. CON at d 110, E+ vs. CON at d133). **Results:** Full uterus, membrane, uterine fluid, and empty uterine weights were increased ($P < 0.05$) at d 110 compared to d 85. Full uterus, membrane, and empty uterine weights were increased ($P < 0.05$) at d 133 compared to d 110. Fetal weights increased ($P < 0.05$) by 301% between d 85 and d 110 and by 105% between d 110 and d 133. Cotyledon weights were decreased ($P < 0.05$) at d 110 compared to d 85 with no difference between d 133 and d 110. Cotyledon weights were decreased ($P < 0.05$) in CON compared to E+ at d 133. **Conclusion:** Fetal growth increases rapidly during late gestation while cotyledon weights decline. Additionally, E+ treatment appears to alter growth of the cotyledon at d 133. Further analysis is necessary to evaluate the impact on placental development at the cellular level.

II-V Developmentally regulated innate immune NFκB signaling mediates IL-1α expression in the neonatal lung

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Objective: The objective of our study was to determine whether systemic inflammatory stress induces IL-1α expression in the neonatal lung, and if so, whether this expression is mediated by innate immune NFκB signaling. **Methods:** Fetal (e15, e19), neonatal (P0) and adult wild type (WT) and IκBβ overexpressing (AKBI) mice were exposed to endotoxemia. IL-1α mRNA and protein expression, cytosolic degradation of NFκB inhibitory proteins, and nuclear translocation of NFκB subunits were assessed. The role of NFκB in regulating IL-1α expression was evaluated using genetic and pharmacologic approaches to inhibit NFκB activity isolated macrophages (RAW 264.7 and BMDM). **Results:** We found that endotoxemia induced IL-1α expression during the saccular stage of neonatal lung development and was not present in the other neonatal organs or the adult lung. This IL-1α expression was dependent upon sustained pulmonary NFκB activation, which was specific to the neonatal lung. Using *in vivo* and *in vitro* approaches, we found that pharmacologic and genetic inhibition of NFκB signaling attenuated IL-1α expression.
Conclusions: These findings demonstrate that innate immune regulation of IL-1α expression is developmentally regulated and occurs via an NFκB dependent mechanism. Importantly, the specific role of developmentally regulated pulmonary IL-1α expression remains unknown. Future studies must determine the effect of attenuating innate immune IL-1α expression in the developing lung before adopting broad IL-1 receptor antagonism as an approach to prevent neonatal lung injury.

II-VI Impact of lipid-based nutrient supplementation on placental mTOR signaling and IGF-1 gene methylation and fetal growth

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Objective: The Women First (WF) Preconception Trial Study has demonstrated that intrauterine linear fetal growth was improved with maternal lipid-based nutrient supplementation (LNS) prior to conception in low-resource countries. Fetal growth is regulated by Insulin-like growth factor 1 (IGF-1) and dependent on nutrient availability and placental transfer capacity, which is regulated by the nutrient sensing mechanistic target of rapamycin (mTOR) pathway. We investigated the effect of LNS on placental mTOR signaling and *IGF-1* gene methylation and its correlation to fetal growth. **Methods:** Placental samples were obtained from Guatemala and Pakistan WF sites (n: 12 LNS, 12 Control per site). We determined the expression and phosphorylation of downstream mTOR targets (4E-BP1(T37/46)/4E-BP1 and rpS6(S235/236)/rpS6), AMPKα(T172)/ AMPKα and IGF-1R by western blot and DNA methylation of the *IGF-1* gene promoter by bisulfite pyrosequencing. **Results:** Maternal pre-pregnancy BMI differed between participants in Guatemala (26.5±1.3) and Pakistan (19.8±0.7). Placentas of LNS Pakistani women had increased ratios of 4E-BP1(T37/46)/4E-BP1 and rpS6(T37/46)/rpS6 and decreased expression of AMPKα(T172)/AMPKα. *IGF-1* DNA methylation was not different between LNS and control groups and was not correlated with birth weight or length. In placentas from Guatemala, we found no differences in the phosphorylation of mTOR targets between LNS and control. Birth weight and length were negatively correlated with *IGF-1* promoter methylation and positively with IGF-1R expression. **Conclusion:** Based on our preliminary data, we speculate that in Pakistani women, with poor maternal nutritional status, LNS resulted in an activation of the placental mTOR pathway to promote nutrient transfer to the fetus. In contrast, in Guatemalan mothers who were not nutritionally deprived, the IGF-1 signaling pathway plays a greater role in determining fetal growth.

II-VII Maternal high fat diet attenuates fetal brown adipose tissue development via suppression of monoallelic DIO3os expression

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Objectives: Maternal high fat diet and obesity (MO) predisposes obesity and metabolic dysfunction in offspring. We previously identified that MO impairs offspring brown adipose tissue (BAT) function that decreases energy expenditure, but underlying mechanisms remain elusive. Because intracellular thyroid hormone signaling regulates brown adipogenesis, we hypothesized that attenuation of thyroid hormone signaling mediates the negative effects of MO on fetal BAT development. **Methods**: To test, female C57BL/6J mice were fed a control diet (10% energy from fat) or an obesogenic diet (45% energy from fat) for 10 weeks, mated and maintained on their respective diet during pregnancy and lactation. After weaning, offspring were challenged by high fat diet (60% HFD) for 12 weeks. **Results**: MO not only decreased BAT mass and thermogenic function (UCP-1, PGC-1a), but also profoundly decreased the density of brown adipogenic progenitors (Lin-/PDGFRa+/EBF2+) in fetal BAT, which impaired BAT plasticity in adaption to cold exposure. The surface temperature of offspring mice was substantially reduced due to MO. When challenged with 60% HFD, MO offspring at 4 months old had higher weight gain and glucose intolerance, showing susceptibility to obesity and metabolic diseases. In fetal BAT, MO decreased the concentration of T3 but did not affect the concentrations of T3 and T4 in fetal circulation. Consistently, MO elevated the expression of Dio3, which encodes D3, an enzyme inactivating T3 due to inner ring deiodination. The promoter of a corresponding antisense LncRNA, Dio3os, was hypermethylated and suppressed in fetal BAT due to MO. Furthermore, we ablated Dio3os transcription in brown adipogenic progenitors *in vitro*, which increased Dio3 expression, reduced T3 concentration and brown adipogenesis. **Conclusions**: In summary, we discovered that MO increased DNA methylation in the promoter of Dio3os, which attenuated intracellular thyroid hormone signaling and fetal BAT development, a novel mechanism explaining susceptibility of MO offspring to metabolic dysfunction in later life.

II-VIII Effects of glucose level and one-carbon metabolite supplementation on NIH/3T3 cell growth and mitochondrial respiration

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Objectives: The objective of this study was to determine if supplementation of one-carbon metabolites (OCM: methionine, folate, choline, and vitamin B_{12}) to mouse embryonic fibroblasts (NIH/3T3) in divergent glucose media would affect cell growth and mitochondrial respiration. **Methods:** Cells were cultured in DMEM medium containing 1 g/L (Low) or 4.5 g/L (High) of glucose with no added OCM (CON), or 2.5, 5, or 10 times folate, choline, and B_{12} (2.5X, 5X, or 10X, respectively) in the CON media. Methionine was limited to 2X CON. Cells were passaged three times in their respective treatment medium before being plated for proliferation assay or analysis by Seahorse XFe24. Cells were plated at 0 h; incubated for either 1, 12, 24, 36, 48, or 72 h; fixed in NBF; stained with anti-Ki67 for cell proliferation index; and counterstained with DAPI for total cell counts. Growth rate was determined as the slope after natural log transformation of cell number. Mitochondrial respiration parameters were measured as O_2 consumption (pmol/min) scaled to 10,000 cells. Only significant comparisons are reported. **Results:** Total growth rate (1 to 72 hr) was greater ($P < 0.01$) in Low 5X compared with High 2.5X and 10X cells with Low 10X being less than all other treatments. O_2-Linked ATP synthesis was greater ($P < 0.01$) in Low 5X cells compared with High CON, 5X, and 10X, with High 10X being less than all other treatments. Non-mitochondrial respiration increased linearly with increasing OCM supplementation in Low glucose and decreased linearly with increasing OCM in High glucose cells. **Conclusions:** These data suggest that increasing OCM supplementation decreases proliferation and cellular respiration in High glucose media; however, in the case of energy restriction (Low glucose), OCM appear to increase cell proliferation through mitochondrial and non-mitochondrial respiration pathways. USDA is an equal opportunity provider and employer. (Supported by USDA-NIFA-AFRI: 2017-07016).

II-IX Maternal low protein diet during gestation programs adult offspring glucose intolerance regardless of the postnatal plane of nutrition in female mice

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Objective: Our objective was to determine if the contributions of a poor nutritional environment during gestation and/or neonatal life to adult onset diabetes is exacerbated when there is a mismatch in the offspring's plane of nutrition in the transition between developmental stages. **Methods:** Mice were exposed to one of two nutritional planes during gestation (G) by being born to FVB dams fed a control (CON; 20% protein, 7.5% fat) or a low protein diet (LP; 8% protein, 7.5% fat) and cross-fostered at birth to one of three nutritional planes: dam fed CON and either 7 pups (CON) or 4 pups/dam (over-nourished, OV); dam fed LP with 8 pups/dam for a total of 6 groups: CON-CON, CON-LP, CON-OV, GLP-CON, GLP-LP, GLP-OV. Female offspring were weaned to the CON diet. At 1 and 2 years of age body composition was measured by quantitative magnetic resonance and i.p. glucose and insulin tolerance tests (ipITT) were performed. **Results:** At 1 yr: GLP offspring were leaner than CON ($P = 0.01$), and all pups suckled by LP dams were leaner than postnatal CON or OV pups. GLP-CON and GLP-LP offspring were glucose intolerant ($P < 0.05$) compared to all other groups, but GLP-LP had improved ($P < 0.05$) insulin tolerance compared to CON-OV and CON-CON; no other differences in ipITT were observed. At 2yrs: only postnatal nutrition affected adiposity, LP offspring remaining leaner than all other groups ($P < 0.05$). All GLP offspring were glucose intolerant ($P < 0.001$) regardless of postnatal nutrition. Adiposity independently contributed to glucose intolerance ($P < 0.001$). CON-CON females were the most insulin sensitive, while CON-OV were the least ($P < 0.05$). GLP effects on insulin sensitivity were minimal. **Conclusions:** A maternal LP diet during gestation programmed glucose intolerance in the offspring at both one and two years of age, regardless of the degree of mismatch between pre- and postnatal planes of nutrition. (Funded by USDA/ARS 3092-51000-056-01S).

II-X Neonatal growth and BIA-estimated body composition in lambs are diminished in two models of IUGR

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Objectives and Methods: Stress during critical windows of development reduce postnatal muscle mass, alter body composition, and impair growth. Lean-to-fat proportions are indicative of metabolic health and wellbeing, and bioelectrical impedance analysis (BIA) is an objective tool for assessing body composition in adults. Our objective was to determine growth and BIA-estimated body composition at 3 and 25 d of age in intrauterine growth-restricted (IUGR) lambs produced by two different models of *in utero* stress: maternal hyperthermia-induced placental insufficiency (PI-IUGR) or bacterial endotoxin-induced maternal inflammation (MI-IUGR). A 2nd group of PI-IUGR ewes were supplemented with 100% O_2 (10L/min, endotracheal) for the last 3wk of gestation (PI-IUGR+O_2). **Results**: Bodyweight (BW) at birth and at 3, 25, and 30 d of age was less ($P < 0.05$) in PI-IUGR and MI-IUGR lambs but not PI-IUGR+O_2 lambs compared to controls. PI-IUGR lambs did not exhibit catch up growth, as body length, abdominal girth, and head circumference were less ($P < 0.05$) than controls at birth and remained so at 30 d. At 3 d of age, BIA did not detect differences among groups for fat-free mass (FFM) or carcass components, and estimates were inconsistent and unrealistic. At 25 d of age, however, BIA-estimated FFM/BW, moisture content, and fat content was reduced ($P < 0.05$) and protein content tended to be reduced ($P < 0.10$) in PI-IUGR and MI-IUGR lambs compared to PI-IUGR+O_2 and controls, which would be consistent with reduced soft tissue growth. **Conclusions**: From these findings, we conclude that PI-IUGR and MI-IUGR diminishes lean tissue growth in neonatal lambs and that BIA reasonably estimates stress-induced changes in body composition, except in very young animals. [Supported by NIH/NIGMS Grant 1P20GM104320, J. Zempleni, Director, and by NE AES Hatch Multistate Research capacity funding (Accession Numbers 1011055, 1009410) through USDA NIFA)]

II-XI Effects of oral citrulline:malate administration to ewes fed ergot alkaloids during late gestation on neonatal serum amino acids and growth

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Objectives: The objective of this study was to evaluate oral citrulline:malate administration to ewes fed ergot alkaloids during late gestation on lamb serum amino acid levels and growth. **Methods**: Suffolk ewes (n = 10; 87kg) estimated to be carrying twins at d85 of gestation were randomly assigned to citrulline:malate 2:1 (81mg/kg citrulline in 35ml water, CT) or control treatment (35ml water). All ewes were fed endophyte-infected tall fescue seed (4.14µg ergovaline+ ergovalinine/g) in a total mixed ration from d86-parturition. Maternal doppler ultrasounds were conducted on d76±4 (pretreatment) and d112±4 of gestation (treatment). Maternal serum prolactin concentrations were determined by RIA. Blood was collected from lambs within 12h of birth and serum amino acid content was analyzed by LC-MS/MS. The first-born male lamb was harvested within 12h of birth and all muscle from the right side was collected for proximate analysis. **Results**: Doppler ultrasounds and prolactin concentrations were not altered ($P > 0.05$) by CT treatment. Doppler ultrasounds showed vasoconstriction ($P < 0.10$) from pretreatment to post-treatment and prolactin concentrations increased ($P < 0.05$) during gestation. Lamb birth and carcass weight did not differ ($P > 0.05$). Concentrations of glutamine, ornithine, isoleucine, and leucine were lower ($P < 0.05$) in lambs from CT ewes. Ewes on CT treatment produced lambs with smaller ($P < 0.05$) thymus weight, total fat weight, and crude fat percentage. Rumen weight, large intestine weight, and crude protein percentage were larger ($P < 0.10$) for lambs from CT ewes. Brown fat and kidney fat weights were smaller ($P < 0.10$) for neonates from CT ewes. As percentages of empty body weight, CT ewes produced lambs that had larger ($P < 0.05$) rumen and large intestine weights, and smaller ($P < 0.05$) kidney fat and total fat weights. Liver, quadriceps femoris, and semimembranosus and adductor percentages were larger ($P < 0.10$) for lambs from CT ewes. **Conclusions**: Oral administration of citrulline:malate to ewes fed ergot alkaloids alters fetal growth warranting more research into dose levels and administration.

II-XII Exosomes isolated from women with gestational diabetes cause insulin resistance and fail to stimulate islet insulin secretion in non-pregnant mice

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Introduction: The mechanisms underpinning the adaptation of maternal glucose metabolism in normal pregnancy and the failure of these changes to occur normally in gestational diabetes (GDM) remain poorly understood. Exosomes isolated from women with GDM carry a specific miRNA signature that is predicted to regulate glucose metabolism. We hypothesized that exosomes isolated from healthy pregnant women promote pancreatic beta cell insulin secretion and insulin resistance and that exosomes from women with GDM fail to stimulate insulin secretion and exacerbate insulin resistance. **Methods:** Blood was collected from non-pregnant, healthy and GDM pregnant women at 24-28 weeks gestation. Exosomes were isolated and infused into non-pregnant mice via a jugular vein catheter and mini-osmotic pump. Following 4 d of infusion, animals were fasted, and a glucose tolerance test performed. Pancreatic islet cells were isolated and glucose-stimulated insulin secretion (GSIS) determined. Muscle was incubated with insulin and the insulin signaling pathway determined. **Results:** The area under the blood glucose curve was increased ($P < 0.01$) in mice infused with exosomes from GDM women compared to exosomes from non-pregnant women. Fasting insulin was elevated in mice infused with exosomes from normal pregnancy compared to non-pregnant women ($P < 0.01$) and GDM pregnancies ($P < 0.05$). Islet GSIS was increased in mice infused with healthy pregnancy exosomes compared to non-pregnant ($P < 0.0001$); islet GSIS from mice infused with GDM exosomes did not differ from islets of mice infused with exosomes from non-pregnant women. Muscle insulin responsiveness was attenuated by exosomes from normal pregnant women, GDM exosomes inhibited basal and insulin-stimulated muscle IRS-1 and Akt phosphorylation. **Conclusion:** Exosomes from normal pregnant women elicited changes in glucose metabolism in non-pregnant mice characteristic of normal pregnancy. Exosomes from GDM women failed to stimulate islet insulin secretion and lead to pronounced insulin resistance. Therefore, exosomes may play a novel role mediating the maternal metabolic adaptation in normal and GDM pregnancies.

II-XIII GRB2-associated binding protein 3 limits trophoblast invasion into the decidua

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Abstract not available

II-XIV Effects of maternal ergot alkaloid exposure on male offspring carcass composition and yield

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Objectives: The objective of this study was to assess how maternal exposure to ergot alkaloids during two stages of gestation alters male lamb growth postnatally. **Methods**: Ewes (n = 51; BW 83 kg) were confirmed pregnant and randomly assigned to dietary treatment; endophyte-free tall fescue seed (E-; 0μg ergovaline+ergovalinine/g) or endophyte-infected tall fescue seed (E+: 4.14μg ergovaline+ergovalinine/g) fed during two stages of gestation (d35-85 and d86-parturition). This created four dietary treatment groups: E-/E-, E-/E+, E+/E-. E+/E+. At parturition ewes were removed from treatment and lambs were weaned at d75. Birth and weaning weights were lower ($P < 0.05$) for lambs born to ewes fed E+ fescue during late gestation. Post-weaning wether lambs (n = 44) were individually fed a high energy diet and finished to 59kg or d185 post-weaning. At harvest, hot carcass weight was obtained and carcasses were scanned using a dual-energy x-ray absorptiometry scanner (DXA) to measure carcass fat and lean percentage. After 24h of chilling, carcasses were scanned again with the DXA and carcass data collected. Individual muscles from the left side were excised and weighed. Total lean and fat were removed from the right side for proximate composition. **Results**: Percent lean or fat and carcass quality traits did not differ ($P > 0.05$) by maternal treatment. Longissimus muscle weight and as a percent of EBW were greater ($P < 0.10$) for wethers from E+/E- ewes compared to E-/E- and E-/E+. Wethers from E+/E+ ewes did not differ from any group. The cold carcass DXA scans showed a linear relationship to the carcass fat mass as estimated by DXA (r^2=0.75). **Conclusions**: In this study, male lambs born to ewes fed E+ fescue were smaller at birth and weaning but were able to compensate when fed a high energy diet postweaning to slaughter.

II-XV Chronic maternal hypercortisolemia during late gestation alters neonatal arterial blood pressure

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Objectives: In previous studies we found that chronic maternal hypercortisolemia in late gestation increases the incidence of perinatal mortality. Fetal blood pressure and heart rate were lower in late stages of labor and delivery. We hypothesized that arterial blood pressure and heart rate might also be adversely impacted in the neonates of ewes treated with cortisol during late gestation. **Methods**: Ewes were infused with cortisol [CORT; 1mg/kg/day; gestational age (GA) day 115 to delivery, n = 7]; control ewes were not treated with cortisol (Control; n=6). A telemetry transmitter was implanted on GA day 125± 3 for measurement of fetal aortic pressure during labor and delivery and in the early neonatal period. Aortic pressures as systolic (SP), diastolic (DP), and mean arterial (MAP) and heart rate (HR) from 5h prior to birth to 42h after birth were calculated as hourly means and analyzed by two-way ANOVA for repeated measures across time. P values <0.05 were considered significant. **Results**: We found that there was no significant overall difference in SP, DP, MAP or HR over the entire 47h analyzed. However, the pattern of blood pressure differed in the immediate peripartum period; SP, DP and MAP were significantly different for the 8 hours surrounding birth ($P < 0.001$; group x time effect). MAP was higher in the CORT lambs in the hour prior to birth (CORT: 63.8±2.1; Control: 52.2±2.3 mmHg) and MAP was lower in the CORT lambs in 1-2 hours after birth (CORT: 57.0±2.3, Control: 66.3±2.5 mmHg). Although there was no significant overall difference in HR between CORT and Control lambs, the lower HR of CORT lamb in the hour prior to birth (CORT: 137±10, Control: 148±11 bpm) showed a similar trend as in our previous study. **Conclusions**: We conclude that chronic maternal hypercortisolemia during late gestation alters the transition in arterial pressure from *in utero* to *ex utero* life. (This study was funded by National Institutes of Health Grant HD-087306 to MKW)

II-XVI Norepinephrine spares adipose tissue in ovine fetuses complicated with placental insufficiency

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Objectives: Placental insufficiency (PI) causes hypoxemia and hypoglycema leading to intrauterine growth restriction (IUGR), which elevates norepinephrine (NE) concentrations. IUGR disrupts fetal metabolism including adipose and increases the risk of developing metabolic diseases. Persistent NE causes adrenergic receptor β_2 desensitization in adipose that impairs lipid mobilization postnatally. This may direct IUGR offspring to obesity. Our objective was to identify the molecular effects of chronic hypoxemia and elevated NE concentrations on perirenal adipose from near-term PI-IUGR fetal sheep. **Methods**: PI-IUGR was induced by maternal hyperthermia. At 65% gestation, fetuses were randomly assigned to a sham (SH) or bilateral adrenal demedullation (AD) surgical procedure. Perirenal adipose was collected from control (CON) and IUGR fetuses at 90% gestation. Physiological assessments were used to confirm AD. RNAseq (n=4/group) was performed on adipose mRNA to determine differentially expressed (DE) genes among CON-SH, IUGR-SH, CON-AD and IUGR-AD groups. DE genes were modeled to functional pathways. Gene expression was confirmed with qPCR in an expanded cohort (n = 7/group) and analyzed by ANOVA and post hoc LSD test. **Results**: IUGR-AD had lower plasma NE concentrations than IUGR-SH fetuses despite being hypoxemic and hypoglycemic (612±100 vs 3,478±674 pg/mL). IUGR-AD fetuses weighed more than IUGR-SH (2.3±0.6 vs 1.3±0.2kg, P<0.05). Perirenal adipose weight relative to total body weight was greater in IUGR-SH fetuses compared to IUGR-AD and CON fetuses. RNAseq identified 592 DE genes in IUGR-SH compared to CON-SH, 297 DE genes in IUGR-SH compared to IUGR-AD, and 223 DE genes in CON-AD compared to IUGR-AD. Metabolism and PPAR signaling were enriched pathways in DE genes across comparisons. DE genes within enriched pathways were measured with qPCR, and the majority of genes were increased in IUGR-SH compared to CON-SH. The expression of three metabolic regulators with a known role in adipose tissue, ADIRF, PDK4, and GLUT1, were decreased in IUGR-AD compared to IUGR-SH, indicating NE-dependent IUGR response. **Conclusions**: Upregulation of PPAR and ADIRF may promote adipogenesis. (RO1 DK084842)

II-XVII Perinatal nutrient availability and neonatal vigor are affected by parity in cattle

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Objectives: We have previously demonstrated that decreased placental and fetal growth in first parity dams are accompanied by altered neonatal energy metabolism of calves exposed to cold stress. Our current objective was to determine effects of parity on perinatal nutrient availability for calves in thermoneutral conditions. **Methods:** Fall-calving primiparous (n = 13) and multiparous (parity 3 or 4; n = 11) beef females were managed to meet or exceed nutrient requirements for the last third of pregnancy. Females were monitored intensively at calving to collect calf vigor measures and expelled placentas. Calf jugular blood was obtained at 0 (pre-colostrum), 6, 12, 24, and 48 h postnatally. Data were analyzed for effects of parity using a mixed model. Hour and hour x parity were included for neonatal metabolites; hour was a repeated measure. **Results:** We previously reported that multiparous dams had a greater increase in ipsilateral uterine artery blood flow during late pregnancy, although total uterine artery blood flow was unaffected by parity. Calf birth weight was unaffected by parity ($P = 0.72$) but length was greater ($P = 0.03$) for calves born to primiparous dams, leading to decreased ponderal index ($P = 0.02$). Intercotyledonary dry mass and average cotyledonary mass were greater ($P \leq 0.06$) for placentas from multiparous dams. Calves born to multiparous dams had greater vigor score at 20 min of age ($P = 0.02$) and decreased time to stand ($P = 0.04$). Plasma glucose was greater ($P = 0.04$) for calves born to multiparous dams. Additionally, calves born to multiparous dams had greater ($P < 0.008$) plasma triglycerides at 48 h and greater ($P < 0.10$) serum urea nitrogen at 0, 12, and 24 h of age. **Conclusions:** Impaired placental growth and uterine blood flow may lead to altered perinatal nutrient availability and decreased vigor in calves born to primiparous dams, even when birth weight is unaffected and metabolic demands of cold stress are not experienced.

II-XVIII Maternal western-style diet persistently alters liver physiology and bone marrow derived immune cell development and function in a non-human primate model

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Objectives: Poor maternal diet and obesity predispose offspring to metabolic diseases such as non-alcoholic fatty liver disease (NAFLD). Macrophage dysfunction is a key aspect of obesity and NAFLD. During development, macrophages arise from hematopoietic stem cells (HSC) that develop first in the liver before migrating to the bone marrow during late gestation. Our objective was to identify the impact of maternal western-style diet (MWSD) on liver physiology, macrophage function, and HSC development in offspring. **Methods:** We used a Non-Human Primate model to examine livers and bone marrow in early third trimester fetuses exposed to MWSD and in 3-year-old (3yo) offspring that were maintained with MWSD mothers until weaning then switched to chow diet for the remaining 2.5 years. We utilized *in vitro* colony forming unit assays from plated bone marrow, complete blood counts, qPCR, second harmonic generation microscopy, and liver triglyceride quantification. **Results:** Colony-forming assays of fetal bone marrow cells showed a 34.5% increase in myeloid cells at the expense of erythroid (-78.9%) and multilineage (-53.8%) progenitors, and a decrease in total colony types. In 3yo, we find similar phenotypes and decreased RBC count but increased mean RBC volume. Liver and bone marrow derived macrophages from MWSD fetuses showed significantly lower LPS induced *IL1B* cytokine expression, suggesting decreased inflammatory response, whereas in liver macrophage from 3yo, *IL10* and *TNFA* expression were increased. We also find increased blood vessel collagen area and periportal fibrosis in livers from fetuses and 3yo exposed to MWSD. Finally, livers from MWSD 3yo have increased triglyceride content and fatty acid synthase gene expression. **Conclusions:** Our findings suggest that exposure to MWSD has long-term effects on HSC and macrophage function which may not resolve despite dietary intervention later in life, and which may play an important role in inflammation and fibrosis, characteristic of NAFLD. [Funding sources: (NIH R24-DK102766-06, P50HD071836, P51OD011092)]

II-XIX Impaired mitochondrial function in growth restricted ovine fetuses with placental insufficiency

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Objectives: Placental insufficiency-induced intrauterine growth restriction (IUGR) fetuses have reduced muscle mass and lower hind-limb protein accretion rates. Weight-specific oxygen uptake was lower in IUGR fetal hind-limb, indicating that muscle growth and metabolism are conserved due decreased mitochondrial function. Our objective was to evaluate mitochondrial oxygen consumption rate (OCR), and Complex 1 activity and expression to determine whether skeletal muscle mitochondrial function is lower in IUGR fetuses. **Methods**: Ewes were randomly assigned to either a control (CON; n = 5) or IUGR (n = 4) groups. IUGR fetuses were created by exposing pregnant ewes to elevated ambient temperatures (40° C for 12 h; 35° C for 12 h) in mid-gestation. At gestation day133±1, fetuses were necropsied and biceps femoris muscle was collected for mitochondrial isolation. State 2 (+ 150mM ADP/no substrates) and State 3 (+150mM ADP/+5mM substrates) OCRs were determined using respiratory substrates (glutamate/malate, +/- ADP) or inhibitors in a NeoFox system. Complex 1 activity was measured with a colorimetric assay, and NDUFB8 (Complex 1) expression was determined via immunoblot. Measurements were analyzed by ANOVA and LSD test. **Results**: There were no significant differences in State 2 respiration rates between IUGR or CON mitochondria (0.67±0.07 vs 0.99±0.23 nmol O_2/min/mg); however, IUGR mitochondria had lower ($P < 0.05$) State 3 respiration rates relative to CON (5.4±1.2 vs 12.0±1.5 nmol O_2/min/mg). There were no differences in mitochondrial OCRs between groups upon the addition of Oligomycin A, Rotenone, or cytochrome C. Complex 1 activity was lower ($P < 0.01$) in PI-IUGR muscle relative to CON (26±1.8 vs 31±3.6 mOD/min/mg). NDUFB8 expression was lower in PI-IUGR ($P < 0.05$) compared to CON. **Conclusions**: State 3 mitochondrial OCRs were depressed in IUGR fetal skeletal muscle due to decreased Complex 1 activity. Lower Complex 1 activity may decrease oxidative phosphorylation in IUGR skeletal muscle, thus stifling hind-limb growth. This adaptation may be advantageous to IUGR fetuses as it may lower metabolic homeostasis conserving energy for vital tissues. (Supported by NIH RO1 DK084842 and T32 HL007249)

II-XX Effect of placental parameters on dairy calf performance

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Objectives and Methods: Specific morphological characteristics of cotyledonary placentae are indicative of placental function. To determine the effects of various selected placental characteristics on calf growth, placentae were collected (n = 33) at expulsion from dairy cows that were randomly assigned to two treatments during the final 46d pre-calving and experienced heat abatement (CL n = 14) or heat stress (HT n = 18). Data for a number of placental measures was recorded. These included cotyledonary total weight, total volume, total surface area, total placental weight, total cotyledon number, umbilical insertion site, and all placental abnormalities. In addition, several potential estimates of placental efficiency were calculated, including placental weight:calf birth weight, cotyledonary weight:placental weight and cotyledonary weight:calf weight to determine if these measures affected postnatal calf performance. Calves at birth were also assigned to heat abatement (CL n = 14) or heat stress (HT n = 14); calves were then classified for analyses based on the treatment they received *in utero* as well as the postnatal treatment: HTHT, HTCL, CLHT, CLCL. Calves were observed for 56 d following birth and several performance parameters were collected, including average daily gain, hip height change, and hip width change. All data were analyzed using PROC MIXED and associations between parameters were determined by calculating Pearson Correlation Coefficients using SAS. **Results**: Incidence of teratomas and a higher cotyledonary weight/placental weight ratio both significantly reduced calf birth weight ($P < 0.05$). In addition, higher placental weight, cotyledonary weight, cotyledonary surface area, cotyledonary number, and membrane weight significantly reduced calf birth weight ($P < 0.05$). A higher incidence of color abnormalities in cotyledons and a higher cotyledonary volume tended to reduce calf birth weight ($P < 0.10$). Heat stress, higher placental weight, cotyledonary surface area, cotyledonary volume, and increased teratomal mass reduced average daily gain ($P < 0.05$). A higher placental weight:calf birth weight ratio significantly increased average daily gain ($P < 0.05$). **Conclusions**: This data demonstrates that heavier placentae and cotyledons with increased surface area produce smaller calves with reduced postnatal growth rates.

II-XXI Fetal exosomes are important for parturition

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Objectives: The present study focused on contributions of fetal-specific factors to inform and regulate maternal physiology related to the parturition process. The initial aim tested the hypothesis that paracrine signaling by exosomes are key regulators of parturition. The second goal determined whether fetal exosome traffic to reproductive tissues responsible for delivery. **Methods:** Exosomes were characterized from maternal plasma of pregnant CD-1 mice on d18 or 9 postbreeding. On E15, mice were injected (i.p. 4x over 24h) with E18 or E9 exosomes or PBS (control). On E17, cervix and uterus were assessed by western blot for NF-kB activation (Rel A phosphorylation), connexin (CX)-43, and COX-2 expression or by immunoassay for IL-6 and TNF-⍰. The cervix from other mice were fixed, sectioned and stained for resident F4/80 macrophages. For the second aim, fetal exosomes derived from amnion epithelial cells were labeled with the lipophilic dye DiR and injected intra-amniotically into pregnant mice on E17. Maternal tissues were collected 24h post-injection and imaged to assess for fluorescent exosomes. **Results:** Maternal exosome shape and size remained constant throughout gestation. However, exosomes carrying inflammatory mediators progressively increased from E5-19 (day of birth). Although, intraperitoneal injections of exosomes localized in the maternal reproductive tract and intrauterine fetal compartments, E18, but neither E9 exosomes nor PBS induced cervix inflammation, ripening, and preterm birth within 48h. For the uterus, only CX-43 expression increased after E18 exosome treatments, other inflammatory markers were unchanged. In addition, fluorescence was evident in maternal uterus, kidney, and placenta after intra-amniotic injection of fetal exosomes. **Conclusions:** Findings support the possibility that fetal exosomes in maternal circulation may directly signal maternal reproductive tissues to regulate the progression of pregnancy and processes that open the gate for birth. (Supported by NIEHS T32ES007254 and NIH Grant HD954931).

II-XXII Insulin regulates fatty acid storage in primary human trophoblast cells

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Objectives: Normal fetal development and growth are critically dependent on the placental supply of fatty acids (FA) and many placental functions are regulated by insulin. The role of insulin in regulating trophoblast FA transport and metabolism is largely unknown. We tested the hypothesis that insulin stimulates FA uptake in primary human trophoblast (PHT) cells. **Methods:** Placentas were collected from term pregnancies (n = 5) and PHT cells were isolated using standard techniques. After 88.5 hours of culture, cells were treated with insulin (1 nM) for either 0.5 or 1 hour. After insulin treatment, PHT were incubated with a mixture of ^{13}C labeled FA [palmitic acid (PA, 95μM), oleic acid (95μM), linoleic acid (95μM) and docosahexaenoic acid (DHA, 15μM)] for 30 minutes. At the end of treatment, PHT cells were collected to determine cellular ^{13}C-FA uptake as well as unlabeled FA levels by GC/MS. We also determined PHT cell palmitic acid oxidation in response to insulin using an Agilent Seahorse XFe96 Analyzer. Data were analyzed by ONE-WAY ANOVA. **Results:** Insulin had no significant effect on PHT cell ^{13}C-FA uptake. In contrast, both 0.5 and 1 hour of insulin treatment significantly increased unlabeled DHA levels in PHT cells (+65% and +57%, respectively, $P = 0.02$). Insulin also tended to increase the levels of unlabeled PA ($P = 0.09$). In preliminary studies, insulin tended to decrease mitochondrial beta-oxidation, (-36%, n = 3, $P = 0.1$). **Conclusions:** Insulin promoted accumulation of trophoblast cellular DHA and reduced oxidation of PA, without a change in uptake. This suggests that maternal insulin may affect placental lipid storage and utilization. One implication of our findings is that maternal hyperinsulinemia may lead to placental DHA accumulation and compromise lipid transfer to the fetus. Reduced placental DHA transfer has been found in clinical conditions associated with elevated insulin, in particular obesity and gestational diabetes (Clin Nutr 2017,36:513).

II-XXIII The effects of maternal nutrient restriction followed by re-alimentation on offspring metabolism in sheep

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Objectives and Methods: To determine the effects of maternal nutrient restriction and re-alimentation on offspring growth and metabolism, 48 primiparous ewes, pregnant with singletons, were fed a control diet [100% National Research Council (NRC) requirements (CON)] starting at the beginning of gestation. On day 50 of gestation, ewes (n = 7) were euthanized and fetal liver, muscle, and blood samples were collected. The remaining animals were fed either CON or 60% NRC requirements (RES), euthanized at day 90 of gestation (n = 7/treatment), and fetal samples obtained. Remaining ewes were maintained on the current diet (CON-CON, n = 6; RES-RES, n = 7) or switched to alternative diet (CON-RES, RES-CON; n = 7/treatment). On day 130 of gestation, remaining ewes were euthanized, and fetal samples collected. Fetal liver, longissimus dorsi, and blood metabolites were analyzed by LC-MS/MS at Metabolon Inc. **Results**: Fetal liver weights decreased in RES-RES compared with CON-CON at day 130 ($P = 0.05$), but were not different at day 90 ($P = 0.7$). There was a tendency for decreased semitendinosus weight in RES compared with CON at day 90 ($P = 0.06$). Fourteen pentose phosphate pathway metabolites decreased in CON-RES, RES-CON, and RES-RES compared with CON-CON in the liver at day 130 ($P \leq 0.05$). In the liver and muscle, two metabolites in the β-oxidation pathway increased in RES at day 90. At day 130, 13 metabolites in the β-oxidation pathway increased in CON-RES compared with CON-CON ($P \leq 0.05$). In RES-RES vs. RES-CON groups, 67, 45, and 45 metabolites were altered in liver, muscle, and blood, respectively ($P \leq 0.05$). **Conclusions**: Maternal nutrient restriction and re-alimentation alter key metabolic pathways in liver and muscle, which may contribute to altered metabolism in offspring. (Supported by USDA-AFRI grant 2016-67016-24884).

II-XXIV Rewiring of the placenta immune landscape with pregravid obesity

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Objectives: The immunological landscape of the placenta undergoes a compositional and functional transformation over the course of gestation. Evidence from epidemiological studies and experimental models strongly suggest that pregravid obesity disrupts these adaptations by upregulating inflammatory macrophage markers and alter function of NK cells in early deciduas. However, our understanding of the placental immune landscape at term and the disruptions induced by obesity remains incomplete. **Methods:** We profiled CD45+ cells isolated from human term deciduas from lean and obese pregnant women stratified by pregravid BMI following cesarean using droplet-based single-cell RNA sequencing. **Results:** Clustering analyses of single cell transcriptomes revealed T cells, NK cells, and macrophages as major components of term placentas. As described for the early gestational decidua, we describe three NK cell subsets with distinct transcriptional signatures. Additionally, we observed equal proportions of CD4+ and CD8+ T cells, and a smaller subset of regulatory T cells. Interestingly, t-SNE analysis of the clusters identified three populations of macrophages a) a population of pro-inflammatory macrophages expressing high levels of S100 proteins, *IL1B* and *ITGAX* (FDR<0.05); b) a second population of hybrid macrophages expressing high HLA molecules and canonical M2 macrophage like markers such as *MSR1* and *VCAN*; and finally c) a minor population of regulatory macrophages expressing high levels of *CD163* and *IGF1*. Pregravid obesity was associated with a dramatic drop in all T cell subsets, and an expansion of all three sub-populations of macrophages. Moreover, macrophages from obese placentas expressed higher levels of *NFKB1* and *REL*, suggestive of *in vivo* activation. **Conclusions:** These findings strongly support the concept of immune cell rewiring as a significant source of obesity associated inflammation in the decidua. Identification of shifts in polarized macrophage states and integration with matched fetal placental immune cells will reveal the immunological adaptations at term, and their aberrations with pregravid obesity. (Supported by NIH 1R01AI142841).

II-XXV Prenatal supplementation with choline programs the whole blood transcriptome of the newborn dairy calf

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Objectives: Supplementation with rumen-protected choline (RPC; ReaShure, Balchem Corp., New Hampton, NY) during late-pregnancy in multiparous Holstein cows improves development of the offspring's immune system and growth. The objective was to evaluate if maternal RPC intake concurrently altered the whole-blood transcriptome of newborn calves. **Methods**: Twenty-four Holstein heifers born to cows fed a basal diet [1.59 Mcal/kg DM, 15.8% CP, 2.9% methionine (% MP) and a lysine to methionine ratio of 2.6] without (control) or with RPC (last 21 d of gestation at a rate of 60 g/d) were used. Immediately after birth, whole blood samples were taken and stored at -20°C until mRNA extraction. Constructed stranded-specific cDNA libraries were sequenced with the Illumina HiSeq 3000 platform 2x100pb. Resulting sequence reads were aligned to the bovine reference genome (bosTau8) and counted at gene level to determine differentially expressed genes (DEG) between groups, using the R environment. **Results**: There were 657 DEG ($P < 0.05$), with 469 upregulated and 188 downregulated DEG by prenatal RPC supplementation. Correction for a FDR of ≤ 0.1 resulted in 41 DEG, with 34 upregulated and 7 downregulated DEG by prenatal RPC supplementation. Functional analysis using the DAVID database revealed that genes upregulated by RPC supplementation are strongly enriched in development of the nervous system, including substantia nigra development, and synaptic transmission; whereas, genes downregulated by RPC supplementation are enriched in key pathways involved in cellular growth including regulation of PI3K signaling and of insulin secretion, as well as pathways involved in immune response such as regulation of NF-kappa B transcription factor activity and cellular response to interferon-gamma. **Conclusions**: Overall, these results suggest that maternal supplementation with RPC during late-gestation changes the whole-blood transcriptome of the offspring, which is likely to be involved in the positive effect of prenatal RPC supplementation on neonatal heifer growth and immune responses.

II-XXVI Chronic IGF1 infusions increase pancreatic insulin concentrations but not beta-cell mass in fetal sheep

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Objectives: To evaluate the extent to which increased circulating concentrations of IGF1 impact fetal growth, islet development, and pancreatic insulin content, we chronically infused an IGF1 derivative into late gestation fetal sheep circulation and determined changes in β-cell mass, pancreatic insulin content and vascularity, paracrine growth factor levels, and fetal arterial oxygen, glucose, and insulin content. **Methods:** Late gestation fetal sheep were infused for one week with either 6.6 μg/kg/hr of IGF1 Long R3 (LR3, n = 8) or saline control (CON, n = 10). On the last day of infusions (133±0 d gestation; term=148 d), arterial oxygen, glucose, and insulin were measured. The splenic portion of the pancreas was fixed in paraformaldehyde, and the hepatic portion was snap frozen. Four pancreas sections were immunostained with anti-insulin antibody and two sections were stained with GS1 agglutinin to determine β-cell area and vascularity, respectively. β-cell mass was calculated as the product of β-cell area and pancreatic mass. Pancreatic insulin was measured by ELISA and mRNA by real-time quantitative PCR. **Results:** Pancreatic insulin concentrations were 80% higher in IGF1 fetuses ($P < 0.05$, *Student's t-test)*, but there were no differences in β-cell area, β-cells mass, or pancreatic vascularity. Pancreatic expression of IGF1, IGF2, VEGFA, and HGF mRNA were 70-90% higher in IGF1 fetuses ($P < 0.05$, *Student's t-test*). Oxygen, glucose, and insulin concentrations were 25%, 22%, and 84% lower in IGF1 fetuses, respectively ($P < 0.05$, *Student's t-test*). **Discussion:** Fetal infusion of IGF1 LR3 for one week late in gestation increases pancreatic insulin concentrations and expression of several paracrine growth factors but does not impact pancreatic vascularity or β-cell mass. Furthermore, IGF1 LR3 infusions lower fetal plasma insulin concentrations. The previously described role for IGF1 as a β-cell growth factor may be more relevant for local paracrine action in the pancreas compared to circulating endocrine actions. (Supported by NIDDK R01DK088139; PJR, PI).

II-XXVII *In-utero* inflammatory challenge activates the early hepatic innate immune response in late gestation fetal sheep

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Introduction: Chorioamnionitis is a common cause for high neonatal mortality. Reports have shown that chorioamnionitis induces an inflammatory signaling in the fetal lung and amniotic fluid, but the source of this response remains unknown. We hypothesized that an *in-utero* inflammatory challenge produces an early activation of the fetal hepatic innate immune response through the NFκB signaling. Methods: 12 late gestation fetal sheep (1hr LPS=5; 5 hrs LPS=7) were surgically catheterized in the hepatic vein and abdominal aorta. At 7 d post-surgery, intraamniotic lipopolysaccharide (IA LPS) was administered, and fetal blood samples were collected (baseline, 1 and 5 hrs) for blood gas, endocrine and TNF-α measurements. After experiment, fetal livers were collected and we performed RT-qPCR for pro-inflammatory cytokines (IL1A, IL1B, TNF, IL6, IL8), and western blot (WB) for NFκB subunits (p50/p65) and inhibitory protein (IκBα). We also isolated control hepatic macrophages, exposed them to LPS (100 ng/mL), and performed RT-qPCR for the same pro-inflammatory markers. Data were analyzed as 1-way ANOVA (blood chemistry and ELISA) or Mann Whitney test (RT-qPCR, WB, and cell culture) with significance declared at $P < 0.05$. **Results:** IA LPS induced fetal metabolic acidosis and increased norepinephrine and cortisol levels at 5 hrs post exposure. At the transcript level, IA LPS produced an upregulation of hepatic pro-inflammatory cytokines 1 and 5 hrs after exposure. Similar results were observed *in-vitro* with LPS-exposed hepatic macrophages. Nuclear p50 and p65 were higher and cytosolic IκBα levels were reduced at 1 hr post IA LPS. Systemically, TNF-α values tended to increase ($P = 0.08$) in the hepatic vein at 1 hr and returned to basal values after 5 hrs. **Conclusion:** *In-utero* LPS inflammatory challenge produced an early activation of NFκB-mediated fetal hepatic innate immune response and metabolic acidosis. This may represent a paradigm shift by linking a sustained pro-inflammatory innate immune response to metabolic disturbances and subsequent abnormal development. (Supported by NIH Grant HL132941-02S1).

II-XXVIII Identification of four nutrient transporters in the fetal membranes of the bovine placenta at parturition

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Objective: In order to elucidate the potential influence of the placental microbiome on the development of the rumen microbiome, our objective was to identify three amino acid transporters and one glucose transporter in the fetal membranes of the bovine placenta, which are reported to be present in the human placenta, including CAT1, y^+LAT-1, y^+LAT-2, and GLUT5. **Methods**: The placentas of University of Wyoming multiparous beef cows (n = 10) were collected at parturition, where the microvillous membrane (MVM) and allantois (AL) were washed in 1x PBS, and snap frozen until processing. Real time RT-PCR was performed to determine placental mRNA expression for each of the identified transporters. Data was analyzed as a mixed model with effects of tissue type, sex, and their interaction using an alpha of 0.05. **Results**: The tissue type by sex interaction was significant ($P = 0.03$) for y^+LAT-1 where heifer AL expression was greater ($P \leq 0.005$) than all other tissue by sex interactions. The tissue type by sex interaction was not different ($P \geq 0.14$) for CAT1, y^+LAT-2, or GLUT5. Tissue type was significantly different ($P \leq 0.04$) for CAT1, y^+LAT-2, and GLUT5 where AL expression was greater than in the MVM. Sex was not different ($P \geq 0.22$) for CAT1, y^+LAT-2, or GLUT5. **Conclusion**: These data suggest that tissue type has a strong influence on expression of these nutrient transporters and is most likely due to differences in membrane physiology between the two tissues and their relationship to the fetus. This also suggests a possible pathway for microbes to utilize and recycle substrates within the placenta prior to the inoculation of the fetal microbiome, providing an ecological niche for the presence of these microbes *in utero*.