NCCC210 Annual Meeting, Orlando, FL

Station Reports

**General Highlights**:

Meeting held April 5, 2019 at the Translational Research Institute for Metabolism and Diabetes

* Attendees arrived by 9 am
* Dr. Lauren Sparks provided in-person attendees with a tour of the Institute
* Opened meeting at 10:30 am
* In-person attendees: Kola Ajuwon, Kim Barnes, Sean Adams, Theo van Kempen, Min Du, Stone Ding, Judy Lin (graduate student with Dr. Ding), and Yuan-Yu Lin (guest faculty)
* Remote attendees (through Zoom): Jim Kinder, Brynn Voy, Werner Bergen, and Sandra Velleman (guest faculty)
* Administrative business:
  + Project renewal – very positive review, a few items for revision, members were asked to provide Kola Ajuwon information on collaborative and outreach efforts
  + Meeting attendance – has been dropping in recent years, especially there has been a reduction in the number of graduate students and post docs attending which has traditionally been a focus of the group – reasons for this (funding, timing of meeting, split of ASN from EB, etc…) were discussed. Also, there has been a general reduction in members of the committee with active appointments as several members have or are nearing retirement – there was a discussion of how to increase interest in the group (expand focus from meat producing animals to more comparative nature, rebranding as metabolic physiology of agri-medical focus, etc…)
  + Meeting location was revisited – sharp drop in attendance the last two years since ASN split from EB, where is the best meeting to pair this with, or should it be stand alone or fully virtual was discussed. It was determined that a survey would be sent to full membership to determine best option for 2020 (Kim Barnes will lead this effort).
  + Discussion about sponsorship potential for the annual meeting – meeting can be challenging to organize based on cost, especially with reduced attendance to share the expenses. Jim Kinder will check on regulations.
  + Is there a way to increase interaction between members more than once a year at the annual meeting?? Sean Adams will look into options.
  + Members were reminded to send Kim Barnes their station reports so she can complete the annual report.
* Station reports from:
  + Purdue University – Kola Ajuwon
  + University of Arkansas – Sean Adams
  + Industry representation – Theo van Kempen
  + Washington State University – Min Du
  + National Taiwan University – Judy Lin, Yuan-Yu Lin, and Stone Ding
  + Auburn University – Werner Bergen
  + University of Tennessee – Brynn Voy
* Adjourned at 4:45 pm

**Station Reports 2018**

1. University of Arkansas

2. Sean Adams

3. Accomplishment:

Project Report: Our laboratory focuses on metabolic physiology, which involves in part the cross-talk of nutrients and hormones across metabolically-important tissues such as fat and muscle. The research also focuses on sub-cellular events that are involved with fuel management including sites that control the fates of fatty acids. At the NCCC210 meeting, recent work was presented that relates to how long-chain fatty acids and derivatives such as long-chain acylcarnitines are trafficked in muscle cells. Specifically, evidence was presented that myoglobin (Mb) avidly binds these lipids and we have hypothesized that Mb binding regulates fatty acid oxidation and lipotoxicity (inordinate build-up of lipids such as acylcarnitines, which can lead to muscle cell stress, myopathy, and insulin resistance). Results were presented from metabolic phenotyping of a mouse genetically engineered to limit Mb binding through two K-to-A mutations in the binding pocket. Longitudinal measures of body weight, body composition, metabolic rate, and insulin sensitivity were conducted ona high fat (45% of calories) diet in males and females. Mb-KA mutant mice displayed increased body fat and weight gain, despite no clear differences in whole-body fat oxidation or energy intake. Males have reduced insulin sensitivity as well. Studies are ongoing to track down what aspects lead to this phenotype, including checking if lower metabolic rate is evident (preliminary data suggest this), or differences in digestible energy and microbiome.

A second line of research was also presented: exploration of the impact of obesity on the temperature-associated shifts in metabolic rate and energy intake. Typically, the latter two factors are closely-matched through as-yet unclear communication networks in the brain, ensuring that as cold temperature sets in there is greater food intake matched to energy expenditure. The preliminary analysis of diet-induced obese mice versus controls indicates that obesity per se does not shift the temperature-energy balance association. However, lean or obese mice exposed to thermoneutrality display hyperphagia—meaning, energy intake regulation deteriorates with warmer temperatures, thus favoring weight gain. Future studies can examine the molecular markers and neuron networks in the hypothalamus and periphery that link ambient temperature with food intake. This knowledge has likely relevance to animal production since changes in temperature-intake-growth associations would have economic impact in an agricultural setting.

All Publications in 2018-2019 time frame:

1. J. Morris, B. Piccolo, K. Shankar, J. Thyfault, **S.H. Adams**. The serum metabolomics signature of Type 2 Diabetes is obscured in Alzheimer’s disease. *Am. J. Physiol. Endocrinology & Metabolism*, 314(6):E584-E596, 2018

2. S. Krishnan, **S.H. Adams**, L.H. Allen, K.D. Laugero, J.W. Newman, C.B. Stephensen, D.J. Burnett, M. Witbracht, L.C. Welch, E.S. Que, N.L. Keim. A randomized controlled-feeding trial based on the Dietary Guidelines for Americans on cardiometabolic health indices. *Am. J. Clin. Nutr.* 108(2):266–278, 2018

3. K.D. Ono-Moore, M.L. Blackburn, **S.H. Adams**\*. Is palmitate truly pro-inflammatory? Experimental confounders and context-specificity. *Am. J. Physiol. Endocrinology & Metabolism* 315: E780–E794, 2018

4. B.D. Piccolo, J.L. Graham, K.L. Stanhope, I. Nookaew, K.E. Mercer, S.V. Chintapalli, U.D. Wankhade, K. Shankar, P.J. Havel, **S.H. Adams**. Diabetes-associated alterations in the cecal microbiome and metabolome are independent of diet or environment in the UC Davis Type 2 Diabetes Mellitus rat model. *Am. J. Physiol. Endocrinology & Metabolism* 315: E961–E972, 2018

5. S.V. Chintapalli, A. Anishkin, **S.H. Adams**. Exploring the entry route of palmitic acid and palmitoylcarnitine into myoglobin. *Arch. Biochem. Biophys.* 655:56-66, 2018

6. S.V. Chintapalli, A. Anishkin, **S.H. Adams**. Binding energies and the entry route of palmitic acid and palmitoylcarnitine into myoglobin. *Data in Brief* 21: 1106–1110, 2018

7. S. Deoni, **S.H. Adams**, X. Li, T.M. Badger, R.T. Pivik, C. Glasier, R. Ramakrishnaiah, X. Ou. C-Section delivery impacts infant brain development. *AJNR Am J Neuroradiol.* 40:169 –77, 2019 [Epub ahead of print 2018 Nov 22. doi: 10.3174/ajnr.A5887]

8. J. Zhang, S. Bhattacharyya, R.C. Hickner, A.R. Light, C.J. Lambert, B.K. Gale, O. Fiehn, **S.H. Adams**\*. Skeletal muscle interstitial fluid metabolomics at rest and associated with an exercise bout: application in rats and humans. *Am. J. Physiol. Endocrinology & Metabolism* 316(1):E43-E532018, 2019 [Epub ahead of print Nov 6. doi: 10.1152/ajpendo.00156.2018]

9. B.L. Zybailov, G.V. Glazko, Y. Rahmatallah, D.S. Andreyev, T. McElroy, O. Karaduta, S.D. Byrum, L. Orr, A.J. Tackett, S.G. Mackintosh, R.D. Edmondson, D.A. Kieffer, R.J. Martin, **S.H. Adams**, N.D. Vaziri, J.M. Arthur. Metaproteomics reveals potential mechanisms by which dietary resistant starch supplementation attenuates chronic kidney disease progression. *PLoS ONE* 14(1): e0199274. <https://doi.org/10.1371/journal.pone.0199274>, 2019

10. C.S. McCoin, T.A. Knotts, J.E. Norman, K.D. Ono-Moore, M.B. Gillingham, J. Vockley, M.L. Blackburn, **S.H. Adams\***. Blood cytokine patterns suggest a modest inflammation phenotype in subjects with long-chain fatty acid acid oxidation disorders. *Physiological Reports* 7 (6): e14037, 2019

1. University of Vermont

2. Eric D. Testroet

3. Accomplishments:

This year to date has been spent on laboratory set up. Activities have included purchasing equipment and planning experiments. In addition, applications for funding have been sent in and will be revised for resubmission. Our primary scientific endeavors are focused on hepatic lipid metabolism of periparturient dairy cattle. To support these endeavors I have hired a full-time laboratory manager and am in the process of recruiting one to two graduate students. Currently we are in the process of establishing an *in vitro* model of bovine hepatic lipidosis. We have successfully isolated and cultured primary bovine hepatocytes and efforts are underway to validate the phenotype of the model (i.e., lipid accumulation, urea production, albumin production, LDH leakage, and cytotoxicity markers). Using this model, we will perform an on-farm experiment using multiparous dairy cattle in which we will either induce hepatic lipidosis or not using established protocols. We will perform liver and adipose biopsies on cattle that are either experience hepatic lipidosis or are not and examine key signaling pathways related to protein kinase A (PKA), AMP-activated protein kinase (AMPK), and phosphodiesterase 4b (PDE4B). It is our hypothesis that dysregulation of PDE4b results in hepatic lipidosis and that ultimately modulation of PDE4b activity can lead to prevention of hepatic lipidosis in the periparturient cow. We plan to have validated our *in vitro* model of hepatic lipidosis and published the results in the Journal of Dairy Science in approximately June 2019 and to begin on-farm trials in Fall 2019. We will use the *in vitro* model to probe metabolic relationships identified in the on-farm trial.

Publications

1. **Testroet**, E. D., K. Chen, J. M. de Avila, D. C. Beitz, and M. Du. 2018. A simple *in vitro* method for primary hepatic mixed cell culture and the study of fatty liver utilizing Holstein heifers from the abattoir. J. Dairy Sci. Submitted – Major Revisions underway
2. Deng, Y., G. Huang, F. Chen, E. D. **Testroet**, H. Li, T. Nong, X. Yang, J. Cui. B. Huang, D. Shi, S. Yang. 2019. Hypoxia enhances proliferation and stemness of buffalo (*bubalus bubalis*) adipose-derived mesenchymal stem cells via HIF-1a interaction with bFGF and VEGF. J Cell. Physiol. In Press.

1. University of Tennessee

2. Brynn Voy

Graduate students: Kamille Piacquadio, Robert Mihelic

Collaborators in NCC210: Woo Kim (UGA)

Other collaborators: Shawn Campagna (UTK), Jeanna Wilson (UGA)

3. Accomplishments:

In 2018 the Voy lab developed a new targeted RNAseq tool for profiling gene expression with high throughput in adipose and other related tissues. The benefit of this tool is that it represents a compromise of sorts between QPCR and genome wide RNAseq in terms of gene coverage and sample size. Rather than focusing on one gene at a time (QPCR) or the whole genome at once (RNAseq), this approach allows us to profile several hundred genes in several hundred samples at once, in one Illumina sequencing lane. Our current panel consists of 171 genes that we selected to broadly cover adipogenesis, lipid and glucose metabolism, stem cell commitment, and other functions relevant to fat accretion and adipocyte biology. This work is done in collaboration with Dr. Kurt Lamour (also of UTK) who developed and patented a novel method for multiplexed sequencing on an Illumina platform.

We initially tested the panel using adipose samples from a recent study (Beckford et al., Sci. Reports, 2017) in which broiler-breeder hens were fed diets containing fish oil or corn oil. Tissue samples were harvested from chicks at 14d after hatch. To test repeatability, each of 6 samples from each diet was reverse transcribed and sequenced in duplicate. Reads from duplicate samples were highly similar to each other. Using these data, we identified ~ 65 genes that were significantly affected at the expression level by maternal fish oil vs. corn oil feeding (unpublished data). These results highlight several pathways that will be further evaluated for effects of maternal programming (e.g., via methylation) in follow-on studies in 2019. Recently, we used the panel to profile expression in three additional studies, collecting reads from ~ 200 RNA samples in one sequencing lane. Analysis of these data are ongoing. This effort specifically targets NCCC210 Objective #2: *Plan to increasingly implement newly emerging high through-put ‘omics-based technologies and experimental methodologies to further refine our understanding of adipose tissue biology and its role in regulation of whole-body metabolism in farm animals, animal models and humans.*

As part of our efforts to use metabolomics to identify novel molecules that regulate energy utilization metabolism in broilers, we worked with our collaborator (Shawn Campagna) and his lab to develop an LC-MS platform to measure a novel class of lipids in chicken serum and tissues. These molecules (N-acyl amino acids) have been shown to influence energy utilization through their ability to uncouple cellular respiration from ATP synthesis. A manuscript describing our experimental approach is currently in review, and a second manuscript in which we describe dietary regulation of these compounds in broilers is in the final stages of preparation. Data and findings from this project were presented at the annual meeting of The Obesity Society, held in Nashville in November. This work also targets NCCC210 Objective #2.

In addition to our research efforts related to NCCC210 in 2018, it is important to note that a collaboration that is now funded by USDA directly arose from discussions between Drs. Voy and Kim (UGA) during the 2018 annual meeting (San Diego, CA). This specifically addresses Objective 4, … “*to develop and submit joint research projects*,” and is a direct result from the work of NCCC210.

**4. SIGNIFICANCE OF FINDINGS**

* We have identified several pathways that can be manipulated through the hen diet to modulate fat accretion in offspring.
* We have established that a novel class of lipid molecules that are implicated in energy utilization are selectively and specifically regulated by feeding status and diet in broilers, and we have developed a platform to measure these compounds with high sensitivity

**5. WORK PLANNED FOR NEXT YEAR**

We will establish methods to profile DNA methylation and determine if developmental programming of fat accretion through the hen diet is mediated through epigenetic mechanisms. We will also screen a library of endogenous N-acyl amino acids in vitro to identify those that influence energy metabolism in broilers.

**6. Publications for 2018**

Journal Articles and Book Chapters

* Barrington, W, P. Wulfridge, A. Wells\*, C. Rojas, S. Howe, A. Perry, K. Hua, M. Pellizon, K. Hansen, B. H. Voy, D. Pomp, and D. W. Threadgill. 2018. Optimizing Metabolic Health Through Precision Dietetics in Mice. Genetics, Jan;208(1):399-417, 2018.
* Beckford, R\*, E. Tague, S. Campagna, and B. H. Voy. 2018. Transcriptomic and Metabolomic Profiling of Chicken Adipose Tissue: Dual Purpose Benefit for Human Obesity and Poultry Production. Current Metabolomics.
* Clemmons, B. A., B. H. Voy, and P. Myer. 2018. Altering the gut microbiome of cattle: Considerations of host-microbiome interactions for persistent microbiome manipulation. Microbial Ecology.
* Cope, E.\*, B. H. Voy, B. Whitlock, M. E. Staton, T. Lane, J. Davitt, and J. T. Mulliniks. 2018. Beta-hydroxybutyrate Infusion Identifies Acute Differentially Expressed Genes Related to Metabolism and Reproduction in the Hypothalamus and Pituitary of Sheep. Physiological Genomics, Jun 1;50(6):468-477. Epub 2018 Apr 6.
* Payton, R. R., L. A. Rispoli, K. A. Nagel, C. Gondro, A. M. Saxton, B. H. Voy, and J. L. Edwards. 2018. Mitochondrial-related consequences of heat stress exposure during bovine oocyte maturation persist in early embryo development. Journal of Reproduction and Development, 64(3):243-251.
* Wells, A.\*, W. Barrington, S. Dearth, A. May, D. Threadgill, S. Campagna, and B. H. Voy. 2018. Tissue Level Diet and Sex-by-Diet Interactions Reveal Unique Metabolite and Clustering Profiles Using Untargeted Liquid Chromatography-Mass Spectrometry on Adipose, Skeletal Muscle, and Liver Tissue in C57BL6/J Mice. Journal of Proteome Research, e-pub Jan 26, 2018.
* Gibson, C., E. Tague, S. Zaver, B. Woodall, E. Torchon\*, H. Berthoud, B. H. Voy, and S. Campagna. 2018. A single UPLC-HRMS method for the profiling of bile acids and N-acyl amino acids in biological matrices: a tool for studying obesity-mediating metabolites and their expression. Metabolomics. (in review)

Conference Abstracts

B. A. Clemmons, C. Martino, M. M. Embree, E. A. Melchior, B. H. Voy, S. R. Campanga, and P. Myer. 2018. Biochemical and Microbial Biomarkers of Feed Efficiency in Black Angus Steers. Journal of Animal Science, 96, (Issue suppl\_2) 237.

C. Gibson, S. Zaver, S. Campagna, and B. H. Voy. 2018. Lipolysis Rapidly Induces the Formation of N-acyl Amino Acids In Vivo. The Obesity Society, T-P-3370; Obesity Week 2018.

Clemmons, B. A., M. T. Henniger, J. B. Powers, E. A. Melchior, S. R. Campagna, B. H. Voy, D. R. Donohoe, and P. Myer. 2018. Comparison of rumen fluid and serum metabolomes in Black Angus cows. ASAS-CSAS Annual Meeting and Trade Show, Vancouver, Canada.

Clemmons, B. A., M. T. Henniger, J. B. Powers, S. R. Campagna, B. H. Voy, D. R. Donohoe, and P. Myer. 2018. Rumen and serum metabolomes differ in Angus cows. UT Beef and Forage Center Graduate Research and Poster Symposium, UT Beef and Forage Center Annual Research and Recommendation Meeting. Knoxville, TN.

Mihelic, R\*, R. Beckford\*, M. Huff, M. E. Staton, S. Das\*, J. Wilson, and B. H. Voy. 2018. Maternal Dietary Fish Oil Influences the Adipose Transcriptome in Offspring. FASEB Journal, Vol. 32, No. 1\_supplement April 2018.

**7. Leveraging and Funding**

*Reducing adiposity and improving body composition through developmental programming by maternal fatty acids*, USDA-AFRI (funding to begin May 1, 2019), PI: Voy, co-PI Kim.

1. West Virginia University

2. Kimberly M. Barnes

3. Accomplishments:

Dr. Barnes is the Coordinator of the Intercollegiate Undergraduate Program in Biochemistry and has served as the Interim Director of the Division of Animal and Nutritional Sciences for much of the past year so no new data has been generated. However, Masters of Science student, Megan Nugent, prepared a manuscript collecting several small pieces of data from a study focused on alterations in gene expression in mice fed either soy or coconut oil and then supplemented or not with conjugated linoleic acid. We anticipate that being submitted for publication in 2019. There also remains data detailing the different effects on lipid metabolism of omega-3 fatty acids coming from fish vs algal sources that is undergoing statistical analysis in order for it to be ready for publication.

1. Ad-hoc member

2. Theo van Kempen

3. Accomplishments:

Publications:

Van Erp, R.J.J., H.M.J. van Hees, R.T. Zijlstra, T.A.T.G. van Kempen, W.J.J. Gerrits (2018) Reduced feed intake, rather than increased energy losses explain variation in growth rate of normal birth weight piglets. J. Nutr. 148:1794-1803.

 Boerboom, G., T. van Kempen, A. Navarro-Villa, and A. Pérez-Bonilla (2018) Unraveling the cause of white striping in broilers using metabolomics. Poultry Sci. 97:3977-3986.

 Van Kempen, T.A.T.G., C. de Bruijn, M.H. Reijersen, and M.G. Traber (2018) Water-soluble all-rac α-tocopheryl-phosphate and fat-soluble all-rac α-tocopheryl-acetate are comparable vitamin E sources for swine. J. Anim. Sci. 96:3330-3336.

Langendijk, P., M. Fleuren, H. van Hees, and T. van Kempen (2018) The course of parturition affects piglet condition at birth and survival and growth through the nursery phase. Animals 8:60

Invited Presentation:

Van Kempen, T. Vitamin Nutrition in the 21st Century. Midwest ASAS Meetings, Omaha, NE. March 2018.

1. Washington State University

2. Min Du

3. Accomplishments:

**Objective 1 and 2:**

During the past year, we are continuing to define mechanisms regulating adipogenesis and fetal adipose tissue development. In mice, we found that exercise during pregnancy can promote fetal brown adipose tissue development, especially when mothers are obese and consuming a high fat diet. In addition, we found that vitamin A supplementation during the pregnancy and lactation enhances fetal intramuscular fat development and overall animal growth, which was confirmed in beef cattle through neonatal vitamin A administration. In the following year, we will further define mechanisms regulating maternal impacts on fetal and neonatal adipose development and subsequent metabolic health of offspring.

**Impacts**:

1. Maternal nutrition has a major impact on fetal and neonatal adipose growth and development.
2. Proper nutritional management of beef cattle during early development improves intramuscular adipose development, beef production efficiency and quality.
3. Adipogenesis during fetal and neonatal development can be effectively altered through altering maternal nutrition and providing other interventions.

**Peer-reviewed Journals:**

1. Son, J., X. Liu, Q. Tian, L. Zhao, Y. Chen, Y. Hu, S. A. Chae, J. M. Deavila, M. J. Zhu, and **M. Du**. (2019). Exercise prevents the adverse effects of maternal obesity on placental vascularization and fetal growth. *Journal of Physiology*, In press.
2. Wei, S., A. Li, L. Zhang, and **M. Du**. (2019). Long noncoding RNAs in adipogenesis and adipose development of meat animals. *Journal of Animal Science*, In press.
3. Han, L., T. Li, **M. Du**, R. Chang, B. Zhan, and X. Mao. (2019). Beneficial effects of Potentilla discolor Bunge water extract on inflammatory cytokines release and gut microbiota in high-fat diet and streptozotocin-induced type 2 diabetic mice. *Nutrients*, 11: E670.
4. Wang, H., X. Mao, and **M. Du**. (2019). Phytanic acid activates PPARa to promote beige adipogenic differentiation of preadipocytes. *Journal of Nutritional Biochemistry*, In press.
5. Zhao, L., B. Wang, N. Gomez, J. Deavila, M. J. Zhu, and **M. Du**. (2019). Even a Low Dose of Tamoxifen Profoundly Induces Adipose Tissue Browning in Female Mice. *International Journal of Obesity*, In press.
6. Son, J.S., S.A. Chae, B.I. Park, **M. Du**, W. Song. (2019). Plasma apelin levels in overweight/obese adults following a single bout of exhaustive exercise: A preliminary cross-sectional study. *Endocrinologia, Diabetes y Nutricion*, 66: 278-290.
7. Gu, H., X. Mao, and **M. Du**. (2019). Prevention of breast cancer by dietary polyphenols: role of cancer stem cells. *Critical Reviews in Food Science and Nutrition*, In press.
8. Zhao, L., **M. Du**, J. Gao, B. Zhan, and X. Mao, (2019). Label-free quantitative proteomic analysis of milk fat globule membrane proteins of yak and cow and identification of proteins associated with glucose and lipid metabolism. *Food Chemistry*, 275: 59-68.
9. Chen, Y., Y. Yang, and **M. Du**. (2018). Beyond brown adipogenesis the inheritance of imprinted H19. *Non-coding RNA Investigation*, 2:64.
10. Wang, B., C. L. Harris, W. Nie, X. Fu, J. M. Deavila, M. J. Zhu, M. Maquivar, S. M. Parish, J. R. Busboom, M. L. Nelson, and **M. Du**. (2018). Neonatal vitamin A injection promotes cattle muscle development and increase oxidative muscle fibers. *Journal of Animal Science and Biotechnology*, 9: 82.
11. Harris, C. L., B. Wang, J. M. Deavila, J. R. Busboom, M. Maquivar, S. M. Parish, B. McCann, M. L. Nelson, and **M. Du**. (2018). Vitamin A administration at birth promotes calf growth and marbling fat development in Angus beef cattle. *Journal of Animal Science and Biotechnology*, 9: 55.
12. Ma, Y.N., B. Wang, Z.X. Wang, N. A. Gomez, M. J. Zhu, and **M. Du**. (2018). Three dimensional spheroid culture of adipose stromal vascular cells for studying adipogenesis in beef cattle. *Animal*, 12: 2123-2129.
13. Zhao, L., T. Zou, N. A. Gomez, B. Wang, M. J. Zhu, and **M. Du**. (2018). Raspberry alleviates obesity-induced inflammation and insulin resistance in skeletal muscle through activation of AMP-activated protein kinase (AMPK) α1. *Nutrition & Diabetes*, 8: 39.
14. Zhang, S., Y. Zhang, X. Zhou, X. Fu, J. Michal, G. Ji, **M. Du**, and Z. Jiang. (2018). Alternative polyadenylation drives genome-to-phenome information detours in the AMPKα1 and AMPKα2 knockout mice. *Scientific Report,* 8: 6462.
15. Li, T., J. Gao, **M. Du**, J. Song, and X. Mao. (2018). Milk fat globule membrane attenuates high-fat diet-induced obesity by inhibiting adipogenesis and increasing uncoupling protein 1 expression in white adipose tissue of mice, *Nutrients*, 10: 331.
16. Zou, T., B. Wang, Q. Yang, J. M. de Avila, M. J. Zhu, J. You, D. Chen, and **M. Du**. (2018). Raspberry promotes brown and beige adipocyte development in mice fed high-fat diet through activation of AMP-activated protein kinase (AMPK) α1. *Journal of Nutritional Biochemistry*, 55: 157.
17. Gao, J., J. Song, **M. Du**, and X. Mao. (2018). Bovine α-lactalbumin hydrolysates (α-LAH) ameliorate adipose insulin resistance and inflammation in high-fat-diet-fed C57BL/6J mice. *Nutrients*, 10: 242.
18. Sun, X., **M. Du**, D. A. Navarre and M. J. Zhu. (2018). Purple potato extract promotes intestinal epithelial differentiation and barrier function by activating AMP-activated protein kinase. *Molecular Nutrition and Food Research*, 62: 1700536.
19. Maricelli, J. A., Y. M. Bishaw, B. Wang, **M. Du**, and B. D. Rodgers. (2018). Systemic SMAD7 gene therapy increases striated muscle mass and enhances exercise capacity in a dose-dependent manner. *Human Gene Therapy*, 29: 390-399.
20. Zhu, M. J., Kang, Y., Y. Xue, X. Liang, M. P. Gonzalez Carcia, D. Rodgers, D. K. Kagel, and **M. Du**. (2018). Red raspberries suppress NLRP3 inflammasome and attenuate metabolic abnormalities in diet-induced obese mice. *Journal of Nutritional Biochemistry*, 53:96-103.
21. Bibi, S., Y. Kang, **M. Du**, and M. J. Zhu. (2018). Dietary red raspberries attenuate dextran sulfate sodium-induced acute colitis. *Journal of Nutritional Biochemistry*, 51:40-46.
22. Xing, T., Y. Kang, X. Xu, B. Wang, **M. Du**, and M. J. Zhu. (2018). Raspberry supplementation improves insulin signaling and promotes brown-like adipocyte development in white adipose tissue of obese mice. *Molecular Nutrition and Food Research*, 2018, 62:1701035.
23. Son, J. S., S. A. Chae, E. D. Testroet, **M. Du**, and H. Jun. (2018). Exercise-induced myokines: a brief review of controversial issues of this decade. *Expert Review of Endocrinology & Metabolism*, 13: 51-58.

**Major Federal Funding**

1. NIH (R01HD067449). Maternal obesity, AMPK and fetal brown adipogenesis. $ 1,561,745 (8/1/2017-7/31/2022). Du, M. (PI), and M. J. Zhu.
2. NIH (R21AG049976). Zfp423 and progenitor adipogenesis during aging. $404,777 (4/1/2016-3/31/2019, one year non-cost extension). Du, M. (PI).
3. NIH (R15AA024284). Mechanism of chronic alcohol consumption-induced cancer associated cachexia. $456,000. (01/01/2017-12/31/2020). Zhang, H., and M. Du (Co-PI).
4. USDA-NIFA (2016-68006-24634), High quality beef – a niche market for small and medium sized farms. $479,995 (1/1/2016-12/31/2019). Du, M. (PI), J. S. Neibergs, D. A. Llewellyn, J. R. Busboom, and M. L. Nelson.
5. USDA-NIFA (2016-67015-24470), Genome wide mapping of alternative polyadenylation sites in cattle. $470,000 (1/1/2016-12/31/2019, one year non-cost extension). Jiang Z., M. Du (Co-PI), L. K. Fox, and M. Maquivar.
6. USDA-NIFA (2015-67015-23219). Vitamin A, Zfp423 and intramuscular adipogenesis in beef cattle. $500,000 (4/1/2015-3/31/2020, one year non-cost extension). Du, M. (PI), J. R. Busboom, and M. L. Nelson.

1. Auburn University/AAES

2. Werner Bergen and Terry Brandebourg

3. Accomplishments:

The Bergen laboratory has continued some work on the effect of flax seed/meal on fatty acid profile and gene expression in porcine adipose tissue and skeletal muscle.

The Brandebourg laboratory has concentrated of developing primary cells from AT of very obese pigs for future biochemical; experiments.

Citations

Hausman GJ, Bergen WG, Etherton TD, Smith SB.

The history of adipocyte and adipose tissue research in meat animals.

J Anim Sci. 2018 Mar 6;96(2):473-486. doi: 10.1093/jas/skx050.

Erin M Forte; Mary Kimberly Mullenix; Jennifer J Tucker; Joshua B Elmore; Werner G Bergen. Conserved forage-based systems for backgrounding weaned beef calves. Translational Animal Science, Volume 2, Issue 3, 25 July 2018, Pages 272–279,

Chunxi Huang, Lee Chiba, Whitney Magee, Yingfeng Wang, Derrick Griffing, Indira Torres, Soren Rodning, Christy Bratcher, Werner Bergen, Elizabeth Spangler. Effect of flaxseed oil, animal fat, and vitamin E supplementation on growth performance, serum metabolites, and carcass characteristics of finisher pigs, and physical characteristics of pork. Livestock Science https://doi.org/10.1093/tas/txy063 LIVSCI\_2018\_105\_R1

Phillips KM, Read CC, Kriese-Anderson LA, Rodning SP, Brandebourg TD, Biase FH, Marks ML, Elmore JB, Stanford MK, Dyce PW. 2018. Plasma metabolomic profiles differ at the time of artificial insemination based on pregnancy outcome, in Bos taurus beef heifers. Sci Rep. 2018 8(1):13196. doi: 10.1038/s41598-018-31605-0.

Meloche, K.J., Dozier, W.A., Brandebourg, T.D. and J.D. Starkey. 2018. Skeletal muscle growth characteristics and myogenic stem cell activity in broiler chickens affected by wooden breast. Poultry Sci. 2018 Jul 5. doi: 10.3382/ps/pey287.

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1. The Ohio State University

2. Kichoon Lee

3. Accomplishments:

Discovery of novel adipose-specific genes and consolidation of obesity loci.

Discovery of each adipose-specific gene (Leptin, Adiponectin, PPAR, FABP4, ATGL, G0S2 etc.) has profoundly contributed to our understanding of adipocyte biology and their etiologic implications for obesity and obesity-related diseases. Although an average of about 200 tissue-specific genes are estimated in each tissue, more adipose-specific genes in humans and animals need to be identified to understand their roles in adipose development and the development of obesity. To identify additional adipose-specific genes in humans, the most recent Genotype-Tissue Expression (GTEx) data v7 obtained from more than 400 individuals and 46 tissues were used for analysis. In addition, data from Gene Expression Omnibus and genome-wide association studies (GWASs) were also analyzed for this project. According to our analysis, 38 adipose-specific genes were identified. These genes were further analyzed for expression patterns at different developmental stages of adipogenesis and obesity conditions. In addition, 414 differentially expressed genes between subcutaneous and omental adipose depots were identified. Furthermore, some of the depot-specific genes (subcutaneous versus omental depots) were perfectly matched with particular GWAS loci for hip circumferences, waist circumferences and waist-to-hip ratio, consolidating association of these genes with the regional fat distribution. These results were published in Scientific Reports. Because genetic networks regulating adipose development and fat accretion are conserved in mammalian and avian species, the novel adipose-specific genes will be further studied to understand their roles in development of obesity and fat accretion in food animals.

Papers published:

1. Ahn J, Woodfint R, Lee J, Wu H, Ma J, Suh Y, Hwang S, Cressman M, Lee K. 2019. Comparative identification and nutritional and physiological regulation of chicken liver-specific genes. Poultry Science DOI:10.3382/ps/pez057.

2. Lee B, Lee BJ, Lee YK, Hur SW, Kim KD, Kim KW, Han HS, Shin S, Choe JH, Lee K, Choi YM. 2019. Muscle fiber growth in olive flounder, Paralichthys olivaceus: Fiber hyperplasia at a specific body weight period and continuous hypertrophy. Journal of the World Aquaculture Society DOI: 10.1111/jwas.12580.

3. Ahn J, Wu H, Lee K. 2019. Integrative Analysis Revealing Human Adipose-Specific Genes and Consolidating Obesity Loci. Scientific Reports 9(1):3087.

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5. Woodfint R, Hanmlin E, Lee K. 2018. Avian Bioreactor Systems: A Review. Molecular Biotechnology 60(12):975-983.

6. Ahn J, Kim DH, Suh Y, Lee JW, Lee K. 2018. Adipose-specific expression of mouse Rbp7 gene and its developmental and metabolic changes. Gene 670:38-45.

7. Biswas A, Lee SS, Mamuad L, Kim SH, Choi YJ, Lee C, Lee K, Bae GS, Lee S. 2018. Effects of illite supplementation on in vitro and in vivo rumen fermentation, microbial population and methane emission of Hanwoo steers fed high concentrate diets. Animal Science Journal 89(1):114-121.

1. Purdue University

2. Kola Ajuwon

3. Accomplishments:

Our focus in 2018 was understanding the mechanism involved in the regulation of adipose and intestinal tissue development and function. We continue to conduct research in the area of effects of fiber and fiber products on metabolism and function of intestinal tissue. A major finding in 2018 was on the role of 18C fatty acids with different degrees of saturation in the regulation of metabolism. We also investigated the response of adipose tissue to heat stress in pigs. This response was in favor of increased adipose tissue triglyceride storage. We determined the phosphoenolpyruvate carboxy kinase (PEPCK) played a major role in triglyceride storage in adipose tissue during heat stress. We also determined the identity of metabolites that might be involved in the response to heat stress in adipose tissue using metabolomics.

Publications:

1. Qu. H., and K.M. 2018. Adipose tissue specific responses reveal an important role of lipogenesis during heat stress adaptation in pigs. J. Anim. Sci. 96:975-989. doi: 10.1093/jas/sky022.

2. Shin, S. and K.M. Ajuwon. 2018. Divergent response of murine and porcine adipocytes to stimulation of browning genes by 18-carbon polyunsaturated fatty acids and beta-adrenergic receptor agonists. Lipids. 53:65-75. doi: 10.1002/lipd.12010.

3. Shin, S. and K.M. Ajuwon. 2018. Effects of diets differing in composition of 18-C fatty acids on adipose tissue thermogenic gene expression in mice fed high-fat diets. Nutrients. 10(2). pii: E256. doi: 10.3390/nu10020256.

4. Almeida, V.V., H. Yan, C. H. Nakatsu and K. M. Ajuwon. 2018. Investigation of carry-over effect of prior fiber consumption on diet-induced obesity susceptibility and metabolic health indicators in Ossabaw pigs. J. Anim. Physiol. Anim. Nutr. (Berl). 102:1053-1061. doi: 10.1111/jpn.12900. Contribution: Almeida was Ajuwon’s postdoctoral scholar.

5. Qu. H., and K.M. 2018. Cytosolic phosphoenolpyruvate is a response gene involved in porcine adipocyte adaptation to heat stress. J. Anim. Sci. 96:1724-1735. doi: 10.1093/jas/sky126.

6. Qu. H., and K.M. Ajuwon. 2018. Metabolomics of heat stress response in pig adipose tissue reveals alteration of phospholipid and fatty acid composition during heat stress. J. Anim. Sci. 96:3184-3195. doi: 10.1093/jas/sky127.

7. Shin, S. and K.M. Ajuwon. 2018. Lipopolysaccharide Alters Thermogenic and Inflammatory Genes in White Adipose Tissue in Mice Fed Diets with Distinct 18-Carbon Fatty-Acid Composition. Lipids. 53:885-896. doi: 10.1002/lipd.12101.