

Accomplishments Report

Project/Activity Number: NC1184

Project/Activity Title: Molecular Mechanisms Regulating Skeletal Muscle Growth and Differentiation

Period Covered: October 1st, 2023 to September 30th, 2024

Date of This Report: December 17th, 2024

Annual Meeting Date(s): November 20th and 21st, 2024

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Brief summary of minutes of annual meeting:

The NC1184 annual meeting was held on November 20th and 21st, 2024 at Louisiana State University (LSU) in a hybrid format. Dr. Xing Fu of the LSU School of Animal Sciences was the host of the meeting. On November 20th, the group was welcomed by Dr. Michael Salassi, Executive Associate Vice President of LSU AgCenter, and Dr. Philip Elzer, Director of the LSU School of Animal Sciences. Following the welcome, Drs. Mark Mirando and Amber Campbell of USDA-NIFA joined the meeting via zoom. They provided an update on NIFA, an overview of the NIFA budget, current and future planned RFAs, and current funding statistics. Following the meeting, the group shared their oral station reports. On November 21st, the group finished the remaining station reports and worked on the rewrite for the NC1184 group.

The group voted to hold the 2026 meeting at the University of Arkansas, hosted by Dr. Jamie Baum.

The 2025 meeting will be at the University of Hawaii, hosted by Dr. Caleb Reichhardt.

Accomplishments:

Objective 1: Characterize the signal transduction pathway that regulates skeletal muscle growth and metabolism including the influence of endogenous growth factors and various production practices.

Utah Station – 2024

- Learned more about the mechanism through which anabolic implants improve growth of skeletal muscle in beef cattle.
- Conducted research to determine whether there was an interaction between supplemental trace mineral concentration and presence of the steroids found in anabolic implants in a bovine muscle cell culture model.
- Determined differences in skeletal muscle growth, production performance, and meat quality of cattle of different breed types.

Texas Station - 2024

- Trained undergraduate and graduate researchers in methods for characterizing development of muscle quality traits and evaluating muscle and intramuscular fat content in harvested muscle samples

Hawaii Station - 2024

- Conducted research evaluating the effects of vitamin dosage on proliferation and protein synthesis rates of primary ovine satellite cells
- Found that an RXR agonist increases proliferation rates of primary ovine satellite cells

Louisiana Station – 2024

- Single-nucleus RNAseq and ATACseq multiomic analysis of bovine skeletal muscle and adipose tissue was performed.
- Significant differences in cell composition were identified between muscle and adipose tissue. Multiple subtypes of fibro/adipogenic progenitors (FAPs) were identified in bovine muscle and adipose tissue, many showing clear tissue specificity or preference, which may explain the lower adipogenic activity of the intramuscular adipose depot.

Wisconsin Station – 2024

- Through collaboration with Dr. Tom Crenshaw, an animal nutritionist at the University of Wisconsin-Madison, we developed an economically efficient pig model to mitigate growth by feeding diets containing 2% ammonium chloride. This approach was designed as a crisis management strategy to temporarily halt growth at various stages. Remarkably, pigs subjected to this diet demonstrated robust compensatory growth during a refeeding period following four weeks of growth attenuation. Although market weight was delayed by approximately two weeks, this method proved to be more cost-effective than rearing control pigs without growth attenuation. Using this model, we observed significant alterations in the RBM20-titin pathway during compensatory growth, suggesting a novel regulatory mechanism driving this process.

Iowa Station – 2024

- In collaboration with Dr. Rhoads (Virginia Tech) and Dr. White (TAMU), we are working to better understand metabolic dysregulation and muscle injury caused by heat stress. We have expanded our investigations to explore the role of heat stress on the myocardium and kidney as we are considering more holistically the impact of heat stress on an organism with the underlying premise that total health needs to be optimized to maximize animal production efficiency. To that end, we have determined that heat stress negatively impacts the myocardium, and importantly, impacts the right and left ventricles differently.
- In conjunction with Dr. Rhoads (Virginia Tech) and Dr. White (TAMU), we have made further inroads into the role of biological sex on the muscular response to heat stress. We are continuing to work through analysis of phenotypical outcomes and biochemical and histological measures. Most recently, we discovered that muscle proteostasis appears to be shifting toward loss due to impaired synthesis rather than increased proteolysis. Moreover, skeletal muscle appears to retain amino acids with the exception of ketogenic amino acids, which may provide clues about heat stress-mediated changes in systemic metabolism.

New Jersey Station – 2024

- Found that amino acid transport in skeletal muscle and adipose tissue is regulated by acute cold and is necessary for survival

Indiana Station – 2024

- Found that ANXA1/FPR2 signalling promotes tissue repair in Duchenne muscular dystrophy
- Found that Molecular signatures of *longissimus dorsi* differ between dairy cattle based on

- prepartum muscle reserves and branched-chain volatile fatty acid supplementation
- Found that Maresin 1 repletion improves muscle regeneration after volumetric muscle loss

Virginia Station – 2024

- The **Virginia** station showed that reducing feed inputs from intensive feeding regimes to maintenance diets of forage or grain up to 60 d had minimal effect on metabolic properties of muscle, thus preserving quality and yield.
 - Muscle metabolism remained largely stagnated, as indicated by lack of significance in oxidative and glycolytic proteins such as succinate dehydrogenase, citrate synthase, lactate dehydrogenase, and phosphofructokinase-1
- The **Virginia** and **Florida** stations wrote a review to assess the potential of exploiting *Bos indicus* cattle in tropical production systems to produce beef that fulfills the growing demand for high-quality meat worldwide.
- The **Virginia** station has identified a phytochemical formula that was highly effective at increasing muscle cell proliferation, differentiation, and fatty acid oxidation *in vitro*.
- The **Virginia** station demonstrated that early metabolic perturbations, such as those induced by MCFA feeding, can fundamentally alter muscle growth trajectories.

Objective 2: Characterize the cellular and molecular basis of myogenesis.

Washington Station – 2024

- As the obesity rates in women at reproductive age continue to increase, it is important to understand the impacts of maternal obesity on fetal development. In recent years, the Washington Station studied early myogenesis affected by maternal obesity using mice as an experimental model. Using single-cell RNA-sequencing, they found that maternal obesity and high fat diet suppress myogenesis during embryonic and fetal development. They also found that AMP-activated protein (AMPK) activation can promote embryonic myogenesis and fetal skeletal muscle development.

Utah Station – 2024

- Gained insight into which genes are actively being transcribed during the process of myogenesis in growing satellite cells

Kansas Station – 2024

- Changes in mitochondrial metabolite utilization can occur independent of measures commonly used to characterize fiber type shifts.
- Overexpression of ATP citrate lyase alters glucose utilization in myoblasts.

Virginia Station – 2024

- The **Virginia**, **Missouri** and **Utah** stations investigated the effects of ATP and pH on phosphofructokinase (PFK) using the conventional initial-velocity method and a new method by kinetic modeling
 - A kinetic model was developed to describe the underlying enzymatic reactions, and PFK activity and inhibitory effects were quantitatively evaluated.
 - Analysis based on the model was performed to provide insights into the mechanisms involved in the regulation of PFK activity.

- The porcine growth promotant, Paylean™ (PL), is a beta-adrenergic agonist that appears to ‘push’ or ‘pull’ fiber type composition in growing pigs to a faster-contracting, whiter muscle phenotype.
 - The **Virginia** and **Kansas** stations fed (Paylean™) PL to pigs to investigate changes in myosin heavy chain (MyHC) isoforms and metabolic enzymes as well as mitochondrial utilization of pyruvate, the glycolytic end product.
 - Findings suggest mitochondria with inherent metabolic differences exhibit unique responses to PL supplementation.
- The **Iowa**, **Virginia** and **Texas** stations have made strides in determining the cellular dysfunctions caused by heat stress
 - Emerging and compelling data indicate there is a sex effect of environmental hyperthermia such that gilts are more susceptible and barrows are less sensitive to heat stress
 - This work indicates that in muscle and primary myoblasts collected from gilts (female), heat stress causes mitochondrial injury and a failure to remove these damaged mitochondria, which contribute to metabolic dysfunction and oxidative stress.
- The **Virginia** station demonstrated that feeding medium-chain fatty acids to neonatal pigs upregulates key cholesterol and lipid homeostatic genes in skeletal muscle, including ABCA1, GRAMD1B, INSIG1, and LDLR, suggesting a novel metabolic crosstalk between liver and muscle tissues.

Objective 3: Characterize mechanism of protein assembly and degradation in skeletal muscle

Utah Station -2024

- Gained insight into how mitochondria modulate the rate of postmortem pH decline and, ultimately, fresh pork quality.

Georgia Station -2024

- Established muscle fascicle fracturing (**MFF**) was not related to two commercial genetic lines.
- Established MFF was not affected by intramuscular location.
- Established extreme MFF had loins had type I and IIB fibers that were 34% larger in cross-sectional area than non-affected loins. Additionally, average muscle fiber cross-sectional area was greater by 42% for extreme MFF-affected loins.
- Established extremely affected MFF loins had 28% more fibers per bundle than non-affected loins.
- Established MFF-loins with score of 2 had between 10 and 14% more bundles per fiber when compared to loins scored 3 to 5 on a 5-point scale.

Kansas Station – 2024

- Kinase activity of the conserved S/T NUAK is required to prevent muscle degeneration
- The chaperone alpha-crystallin B chain/CryAB is phosphorylated by NUAK
- The Striatin-Interacting Phosphatase and Kinase (STRIPAK) complex functions with NUAK to maintain autophagic flux by regulating autophagosome-lysosome fusion

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2. Mayorga-Lonazo EJ, Horst E, Freestone A, Rhoads RP, Selsby JT, Baumgard LH. Therapeutic effects of mitoquinol during an acute heat stress challenge in growing barrows. *Journal of Animal Science*. 102:skae161, 2024.
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13. Giotto, F.M, H. Nadini. G. Franco, D.E. Gerrard, M.A. Fonseca and A.S. de Mello. 2024. Effects of liquid-based diets with breweries grains enriched with isolated starch and fish oil on veal quality. *Meat Science* 216: <https://doi.org/10.1016/j.meatsci.2024.109592>.
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15. Opgenorth, J., M.A. Abeyta, B.M. Goetz, S. Rodriguez-Jimenez, A.D. Freestone, R.P. Rhoads, R.P. McMillan, J.L. McGill, and L.H. Baumgard. 2024. Intramammary lipopolysaccharide challenge in early versus mid-lactation dairy cattle: immune, production, and metabolic responses. *J Dairy Sci*. doi: 10.3168/jds.2023-24488.
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22. Wang, C., M. Taylor, C. Stafford, D. Dang, S. Matarneh, D.E. Gerrard and J. Tan. 2024. Analysis of phosphofructokinase activity as affected by pH and ATP concentration *Sci Rep*. 14(1):21192. doi: 10.1038/s41598-024-72028-4.
23. Wicks, J. C., Wivell, A. L., Beline, M., Zumbaugh, M. D., Bodmer, J. S., Yen, C. N., Johnson-Schuster, C., Wilson, T. B., Greiner, S. P., Johnson, S. E., Shi, T. H., Silva, S. L., & D.E. Gerrard. 2024. Determining muscle plasticity and meat quality development of low-input extended fed market-ready steers. *Translational Animal Science*, 8, txae064.

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25. Yadav R, Gerrard SD, Lima MRM, Southard TL, Sunny NE, El-Kadi SW. The Onset of Steatosis Occurs as Early as Seven Days and Progresses to Nonalcoholic Steatohepatitis in a Pediatric Pig Model of Nonalcoholic Fatty Liver Disease. *The Journal of Nutrition.* 2024 doi.org/10.1016/j.tjnut.2024.11.009.
26. Yen, C-N., J. Bodmer, J. Wicks, M. Zumbaugh, H. Shi and D.E. Gerrard. Mitochondrial abundance and function differ across muscle within species *Metabolites.* 2024 Oct 16;14(10):553. doi: 10.3390/metabo14100553.

Thesis/Dissertations:

1. Lexie Seligman, “The Effect of Phytonutrient Supplementation on Pig Growth” (M.S. degree conferred August 2024).
2. Samuel Gerrard, “Hepatic Lipid metabolism in Neonatal Pigs” (Ph.D. degree conferred December 2024).

Abstracts, Posters, and Professional Presentations:

1. K.A. Shira, G.M. Becker, B.M. Murdoch, K.J. Thornton, G.E. Chibisa, G.K. Murdoch. Myokine expression by cultured bovine satellite cells from 3 and 11 month old steers. Annual Meeting of the American Society for Animal Science. July 16-20, 2023. Albuquerque, NM.
2. Wesolowski, LT, JJ Kelly, PL Semanchik, M Roths, TE Rudolph, **RP Rhoads**, LH Baumgard, **JT Selsby**, and **SH White-Springer**. 2024. Thyroid hormone does not protect skeletal muscle mitochondrial function from heat stress in pigs. *Journal of Animal Science.* 102(Suppl 3):547-548. doi: 10.1093/jas/skae234.614. ASAS Meeting in Calgary, Canada. *Poster.*
3. Kwiatkowski, Z., D. Hagen, P. Riggs. 2024. RNA SEQ Analysis of skeletal muscle from dark cutting carcasses. AMSA Reciprocal Meat Conference, Poster 75, Oklahoma City, June 16-19.
4. Kelly JJ, Wesolowski LT, Semanchik PL, Roths M, Rudolph TE, Rhoads RP, Baumgard LH, **Selsby JT**, and White-Springer SH. Thyroid hormone does not protect skeletal muscle mitochondrial function from heat stress in pigs. American Society of Animal Scientists Annual Meeting, Calgary, Canada, July 22-25, 2024.
5. Munk S. A., L.A. Rimmer, E.S. Beyer, J.L. Vipham, M.D. Chao, J.C. Woodworth, T.G. O’Quinn, D.E. Gerrard and M. D. Zumbaugh. Beta-adrenergic agonists alter mitochondrial metabolite utilization independent of a fiber type shift. APS.
6. Yadav R, Gerrard SD, Sunny NE, El-Kadi SW. Medium-Chain Fatty Acid Rich Formula Causes Hepatic Steatosis by 7 Days and Progresses to Nonalcoholic Steatohepatitis by 14 Days in Neonatal Pigs. *Nutrition* 2024.
7. Tiwari, P. and Geisbrecht E.R. Role of NUAKE in sarcomere formation and actin filament assembly. K-INBRE Symposium, Manhattan, KS. Jan 2024.
8. Feist, D. Green N., and Geisbrecht E.R. Fine-tuning of Cell-ECM Assembly by

Transglutaminase. K-INBRE Symposium, Manhattan, KS. Jan 2024.

9. Feist, D. Green N., and Geisbrecht E.R. Fine-tuning of Cell-ECM Assembly by Transglutaminase. The Allied Genetics Conference, Washington D.C. March 2024.
10. Guo, Y., Brooks, D., and Geisbrecht E.R. Interweaving Autophagy and Exosome Functions: Unraveling CryAB. The Allied Genetics Conference, Washington D.C. March 2024.
11. Zhao, Z., Brooks, D., Guo, Y., and Geisbrecht E.R. Pavarotti and Tumbleweed function in maintaining mitochondrial integrity in post-mitotic muscle tissue. The Allied Genetics Conference, Washington D.C. March 2024.
12. Feist, D. Green N., and Geisbrecht E.R. Fine-tuning of Cell-ECM Assembly by Transglutaminase. KU Center for Genomics Annual Research Symposium, Lawrence, KS. May 2024
13. Feist, D. Green N., and Geisbrecht E.R. Fine-tuning of Cell-ECM Assembly by Transglutaminase. National K-INBRE Symposium, Washington D.C. June 2024

Other Activities:

1. Tracy Anthony, New Jersey Station, served as a Special Issue Editor with Dr. Jamie I. Baum, Arkansas Station on the topic of “Protein, Amino Acids, and Healthspan” in the scientific journal *Nutrients*.

Authorization: Submission by an AES or CES director or administrative advisor through NIMSS constitutes signature authority for this information.