

Project/Activity Number: Multistate Research Project NC1184  
Project/Activity Title: **Molecular Mechanisms Regulating Skeletal Muscle Growth and Differentiation**  
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**Station Participants:**

Duane Keisler (Missouri; Host) - [keislerd@missouri.edu](mailto:keislerd@missouri.edu)  
John Michael Gonzalez (Kansas; Secretary) - [johngonz@ksu.edu](mailto:johngonz@ksu.edu)  
Ron Allen (Arizona) - [rallen@ag.arizona.edu](mailto:rallen@ag.arizona.edu)  
Jamie Baum (Arkansas) - [baum@uark.edu](mailto:baum@uark.edu)  
Derris Burnett (Mississippi) - [ddb362@msstate.edu](mailto:ddb362@msstate.edu)  
William Dayton (Minnesota) - [wdayton@umn.edu](mailto:wdayton@umn.edu)  
Samer El-Kadi (Virginia Tech) - [elkadi@vt.edu](mailto:elkadi@vt.edu)  
David Gerrard (Virginia Tech) - [dgerrard@vt.edu](mailto:dgerrard@vt.edu)  
Wei Gou (Wyoming) - [wguo3@uwyo.edu](mailto:wguo3@uwyo.edu)  
Yan Huang (Arkansas) - [yxh010@uark.edu](mailto:yxh010@uark.edu)  
Bradley Johnson (Texas Tech) - [bradley.johnson@ttu.edu](mailto:bradley.johnson@ttu.edu)  
Sally Johnson (Virginia Tech) - [sealy@vt.edu](mailto:sealy@vt.edu)  
Sarah Reed (UConn) - [sarah.reed@uconn.edu](mailto:sarah.reed@uconn.edu)  
Kara Thornton-Kurth (Utah) - [kara.thornton@usu.edu](mailto:kara.thornton@usu.edu)  
Mathew Vaughn (Grad Student/Kansas) - [mvaughn@ksu.edu](mailto:mvaughn@ksu.edu)  
Sandra G. Velleman (Ohio) - [velleman.1@osu.edu](mailto:velleman.1@osu.edu)

**Summary of Minutes of Annual Meeting:**

The annual NC1184 technical committee meeting was held in the S119 room of the Animal Science Research Center at the University of Missouri on October 16, 2014, and was hosted by Dr. Duane Keisler from the Division of Animal Sciences, University of Missouri. On October 16<sup>th</sup> the group was welcomed by Dr. Tom McFadden, Director of the Division of Animal Sciences. Dr. McFadden shared his welcome with the group and shared some information about the University of Missouri and the significance and role of the Division of Animal Sciences within the university. Following Dr. McFadden, Dr. Randy Prather spoke about his role as the director of the National Swine Resource and Research Center. Dr. Prather informed the group what type of models are available for use in their work and the means through which they may secure pigs from his program. Following a question and answer session, the group then began with oral station reports. A lunch break was then provided by Dr. Keisler and Animal Sciences graduate students. After lunch, the group continued with more station reports. The group took a break and then held a Skype conference call with Dr. Mark Mirando, USDA, NIFA, who outlined the current funding situation and gave some statistics on the number of proposals submitted annually and funding rates. Thereafter, a question and answer session was held with Dr. Mirando. The remainder of the day was filled with the final oral station reports summarizing each station's contributions to the objectives of the NC1184 project. Prior to conclusion of the meeting, the decided the 2016 meeting of the NC1184 committee will be hosted by Dr. John Gonzalez at Kansas State University in Manhattan, KS. The group also voted to hold the 2017 meeting of the NC1184 committee at the University of Florida, which will hosted by Dr. Tracy Scheffler. The meeting adjourned and the group met for a dinner and social at the Jefferson Farm & Garden. At the end of the social, it was

decided that the meeting officially be adjourned for the year.

### **Accomplishments:**

***Objective 1: Characterize the mechanisms of skeletal muscle protein turnover.***

#### **Hawaii Station:**

1. The administration of rapamycin (RAP), a mTOR pathway blocker, suppresses muscle hypertrophy induced by myostatin inhibition in mice.
  - a. Real time quantitative PCR analysis showed that myogenic regulatory factors including MyoD and myogenin were not affected either by genotype or RAP. Myf5 was down-regulated by RAP, but not affected by genotype. Also, Mrf4 was down-regulated by both RAP and genotype
  - b. RAP suppressed the muscle mass increase and skeletal muscle expression of genes in the Akt/mTOR pathway in transgenic animals whose myostatin (MSTN) activity was genetically suppressed, thus supporting that MSTN suppresses skeletal muscle mass by suppression of the Akt/mTOR pathway.

#### **Illinois Station**

1. Satellite Cell Activation and Amino Acid Transporter Expression:
  - a. We have collected and prepared all human muscle biopsies for immunofluorescence analyses.
  - b. We have completed preliminary in vitro experiments examining the protein content and gene expression of various amino acid transporters across the lifespan of myoblasts.
  - c. Preliminary experiments indicate that gene expression of amino acid transporters decreases during myoblast differentiation; however, protein content is increased.

#### **Iowa Station:**

1. We have completed data analysis for in vivo respiratory function measures from dystrophic mice treated for 12 months with either a control or quercetin enriched diet. We found that the addition of quercetin to the diet temporarily protected respiratory function.
2. Our preliminary data indicate that in the diaphragm the pathway we predict is activated by quercetin was no longer activated indicating a quercetin insensitivity. Our next step will be to measure pathway activity in the soleus, which did have some quercetin mediated protection.

#### **Missouri Station:**

1. Development of a novel immunoassay for simultaneous quantification of endocrine parameters
  - a. Able to establish an assay for leptin hormone (LH) on the Luminex platform, but were unable to develop an analyte detection assay on the Illumina platform.
  - b. Demonstrated that the iPCR methodology could detect unlabeled biotin across three orders of magnitude.

- c. Observations suggest that immuno-PCR has the potential to improve detection capabilities of current hormonal assays with three or more orders of magnitude in sensitivity, and ultimately provide multiplex capabilities, with the conjugated oligonucleotide serving as both a quantitative detection label and as a barcode for later identification of analyte.

**Texas Tech:**

2. Protected amino acids and essential trace elements alter skeletal muscle hypertrophy in finishing cattle. Calf-fed Holstein steers were supplemented with a Zn methionine supplement (ZnMet; ZINPRO®; Zinpro Corporation, Eden Prairie, MN) for 115±5 d prior to harvest along with zilpaterol hydrochloride (ZH; Zilmax®; Merck Animal Health, Summit, NJ) for the last 20 d with a 3 d withdrawal to evaluate the effects on growth and carcass performance together with gene and protein expression of skeletal muscle, adipose tissue and fatty acid composition of polar and neutral lipid depots.
  - a. The ZnMet-fed cattle had reduced ( $P<0.05$ ) abundance of myosin heavy chain (MHC)-IIX,  $\beta$ 1-adrenergic receptor ( $\beta$ AR), peroxisome proliferator-activated receptor gamma and stearyl-CoA desaturase mRNA in skeletal muscle tissue.
  - b. The ZnMet cattle had greater ( $P<0.05$ ) abundance of MHC-II protein, increased MHC-IIA and IIX cross-sectional areas ( $P<0.05$ ), an increased percentage of MHC-I fibers ( $P<0.05$ ) and a decreased percentage of MHC-IIX fibers ( $P<0.05$ ).

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

**Arkansas Station:**

1. Nutrient modulation of the mammalian target of rapamycin (mTOR) to improve muscle function and growth
  - a. Preliminary studies were conducted using a murine in vitro muscle cell model (C2C12 cells) to identify the primary essential nutrients for regulating muscle growth (via molecular markers of protein synthesis) under conditions of metabolic stress.
  - b. Leucine and omega-3 fatty acids were identified as key nutrients for stimulation of translation initiation in muscle that has undergone metabolic stress. In addition, leucine and omega-3 fatty acids have a synergistic effect on muscle protein synthesis.
  - c. Both nutrients are acting via the mammalian target of rapamycin (mTOR).
  - d. Traditionally, it has been thought that leucine (and other essential amino acids), alone, has the ability to stimulate muscle protein synthesis. However, this study demonstrated that omega-3 fatty acids act via the same mechanism.

**Connecticut Station:**

1. Effects of inflammatory cytokines and growth factors on equine satellite cell proliferation and differentiation
  - a. Interleukin-6 and TNF- $\alpha$  decreased satellite cell proliferation ( $P < 0.05$ ).

Interleukin-6 increased fusion, whereas TNF- $\alpha$  decreased fusion compared with control cells ( $P < 0.05$ ).

- b. Interleukin-1 $\beta$  had no effect on proliferation but tended to decrease fusion ( $P < 0.10$ ).
  - c. Satellite cell proliferation was increased by IGF-I and FGF-2. Differentiation was decreased in the presence of FGF-2, but increased in the presence of IGF-I ( $P < 0.05$ ).
2. Effects of poor maternal nutrition during gestation on fetal muscle development
- a. Completed sample collection on study investigating the effects of poor maternal nutrition during gestation on muscle development in sheep.
    - i. Diet had no effect on the muscle weight as a percent of body weight at any time point.
    - ii. Preliminary data indicates differences in muscle fiber cross sectional area (CSA) in a subset of muscles ( $n = 3-6$  per treatment per time point).
    - iii. Blood samples collected and RNA isolated for analysis of systemic markers of inflammation in ewes throughout gestation and in the offspring at d 135 of gestation and within 24 h of birth.

### **Illinois Station:**

1. MSC Quantity and Paracrine Factor Secretion:
  - a. Protocols for isolation of MSCs from fresh human muscle biopsies have been optimized.
  - b. All human muscle biopsies have been collected from healthy weight, overweight, and obese individuals.
  - c. Protocols for immunofluorescence detection of MSCs in muscle cross-section have been optimized.
  - d. Preliminary data indicate that MSCs have higher levels of expression of inflammatory factors (IL-6), growth factors (IGF-1), and extracellular matrix proteins (Collagen 1) than myoblasts.
2. Interaction of IGF2 and Myostatin in the Regulation of Muscle Growth and Development
  - a. Using zinc-finger nuclease technology, we have engineered mutant myostatin pigs lacking one nucleotide in exon 3 of the myostatin gene. This mutation results in a premature stop codon and is predicted to result in pigs lacking functional myostatin. Cloned gilts heterozygous this mutation were bred and have successfully farrowed.
  - b. Pigs heterozygous for this myostatin mutation with either paternal A or paternal G IGF2 alleles are viable, fertile and produce viable offspring.
  - c. Segregation ratios of the myostatin mutation are consistent with the expected inheritance pattern.
  - d. Initial evaluations of piglets with homozygous mutations of myostatin suggest that muscle mass, expressed as a percentage of body weight, is increased.

- e. To further explore the interaction between IGF2 and myostatin, transcription activator-like effector nucleases (TALEN) with oligodeoxynucleotides templates intended to disrupt the ZBED6 binding site mimicking the G>A substitution that occurs in pigs were used to create mouse models. This resulted in 3 mutant lines with mutations within the ZBED6 binding site.
- f. Founders have been bred to produce experimental animals to characterize gene expression, muscle growth and body composition.

### **Indiana Station:**

1. Heterogeneous activation of Myh7 in proliferating myoblasts and differentiated single myofibers
  - a. Lineage tracing indicates that during development all muscles have activated the fast myosin gene Myl1, but not the slow myosin gene Myh7, which is activated in all slow but a subset of fast myofibers. Similarly, most nascent myofibers do not activate Myh7 during fast muscle regeneration, but the ratio and pattern of fast and slow myofibers are restored at the completion of regeneration.
  - b. When induced to differentiate, the Myh7-activated myoblasts differentiate more readily than the non-activated myoblasts, and have a higher tendency, but not restricted, to become slow myotubes.
  - c. Data reveal significant nuclear heterogeneity within a single myofiber, and challenge the conventional view that myosin genes are only expressed after myogenic differentiation.
2. mTOR is necessary for proper satellite cell activity and skeletal muscle regeneration
  - a. Established a satellite cell specific Mtor conditional knockout (cKO) mouse model by crossing Pax7(CreER) and Mtor(flox/flox) mice.
  - b. Skeletal muscle regeneration after injury was severely compromised in the absence of Mtor.
  - c. Mtor cKO myoblasts exhibited defective proliferation and differentiation kinetics when compared to myoblasts derived from WT littermates.

### **Kansas Station:**

1. Fetal myoblasts and neonatal satellite cells exhibit divergent cellular kinetics when treated with a porcine plasma product *in vitro*.
  - a. Myoblasts harvested from 60-d of gestation fetuses treated with a plasma product *in vitro* exhibited increased proliferation rate, a transcriptional profile similar to a high serum control, and increased nuclear size.
  - b. Satellite cells from neonatal piglets treated with a plasma product *in vitro* exhibited decreased proliferation rate, a transcriptional profile similar to the low serum control, and increased nuclear size.

### **Minnesota Station:**

1. Trenbolone Acetate mediated increases in protein synthesis and decreases in protein

degradation in fused bovine satellite cell are modulated through the AKT pathway, G protein-coupled receptors (GPCR), matrix metalloproteinases 2/9 (MMP2/9), heparin binding epidermal growth factor (hbEGF), epidermal growth factor receptor (EGFR), erbB2, and insulin-like growth factor 1 receptor (IGF-1R).

2. Role of the G protein-coupled receptor-1, matrix metalloproteinases 2 and 9 and heparin binding epidermal growth factor-like growth factor in Estradiol-17 $\beta$  -induced alterations in protein synthesis and protein degradation rates in fused bovine satellite cell cultures.

#### **North Carolina Station:**

1. Studies have been initiated to further understand embryonic muscle development and the contribution of satellite cells/myogenic stem cells to embryonic development.

#### **Ohio Station:**

1. Effect of Thermal Stress and Growth Selection on Satellite Cell Proliferation and Differentiation in Turkeys
  - a. Initial studies have begun on determining the effect of thermal stress both hot and cold on turkey satellite cell proliferation and differentiation. These studies are using satellite cells isolated from a randombred control line 2 (RBC2) turkey that has been maintained without selection for any trait and a line F which was selected from the RBC2 line for 16-wk body weight to avoid line differences.
  - b. Satellite cells are precursors to skeletal muscle and mediate all posthatch muscle growth. Their physiological functions are affected by temperature.
  - c. Pectoralis major muscle satellite cells were thermally challenged by culturing between 33°C and 43°C to analyze the effects of cold and heat on proliferation and differentiation as compared to control temperature of 38 °C.
  - d. Expression levels of myogenic regulatory factors: *myogenic differentiation factor 1 (MYOD1)* and *myogenin (MYOG)* were quantified by quantitative polymerase chain reaction (qPCR). Proliferation rates increased ( $P < 0.05$ ) in both lines at elevated temperatures (41 and 43 °C) and decreased ( $P < 0.05$ ) at reduced temperatures (33, 35, and 37 °C) compared to 38 °C. Differentiation rates increased ( $P < 0.05$ ) at elevated temperatures (39 and 41 °C) and decreased ( $P < 0.05$ ) at reduced temperatures (33 and 35 °C).
  - e. Satellite cells isolated from F line turkeys were more sensitive to both hot and cold temperatures as proliferation and differentiation rates increased to a greater extent across temperature (33 to 43 °C) when compared with the RBC2 line. Expression of *MYOD1* and *MYOG* increased at elevated temperatures and decreased at reduced temperatures compared to 38° C for both lines.
  - f. These results demonstrate that satellite cell function is sensitive to both cold and hot temperatures and that p. major muscle satellite cells from F line turkeys are more sensitive to temperature extremes than RBC2 satellite cells.

- g. Changes in the physiological functions of satellite cells not only have long-term implications on skeletal muscle growth, but will likely impact intramuscular fat accumulation and the incidence of skeletal muscle myopathies.

#### **Virginia Station:**

1. Calves fed a low plane of nutrition (LPN) for 8 wks have smaller longissimus muscle mass and fiber sizes. The intracellular signals that underlie the smaller size are related to lower amounts of Peroxisome Proliferator-Activated Receptor Gamma, Coactivator 1 Alpha 4 (PGC1a4) protein by comparison to calves fed a HPN.
2. Calves fed LPN contained lower amounts of IGF-1 mRNA; MSTN was not different between the groups.
3. These results indicate that LPN causes a reduction in PGC1a4 and IGF-1, both critical mediators of muscle growth.

#### ***Objective 3. Characterize the signaling networks regulating skeletal muscle structure, function and metabolism.***

#### **Arkansas Station:**

1. Defining the role of leucine in skeletal muscle energy metabolism
  - a. This study demonstrated that leucine regulates skeletal muscle bioenergetics via the mammalian target of rapamycin (mTOR) under conditions of metabolic stress in a murine in vitro muscle cell model (C2C12 cells).

#### **New Jersey Station:**

1. Regulation of Mechanistic Target of Rapamycin Complex 1 (mTORC1) Signaling in the Skeletal Muscle and Liver of Rats by 20-Hydroxyecdysone (20HE)
  - a. Phytoecdysteroids such as 20HE are nutritional supplements marketed as enhancers of lean body mass. In a series of three experiments, we studied the impact of 20HE ingestion on protein kinase B/Akt-mTORC1 signaling pathway in the skeletal muscle and liver of male rats. In all experimental designs conducted (20HE dose-response, 20HE time course, 20HE in combination with leucine) the impact on mTORC1 signaling in skeletal muscle and liver was found to be limited.
  - b. Bioavailability of 20HE, whether consumed alone or with leucine, remained low at all doses ingested.
2. Dietary Methionine Restriction and Body Composition, Metabolic Health
  - a. Dietary methionine restriction (MR) produces a series of physiological responses associated with increased health span such as increased energy intake and expenditure, decreased adiposity, and increased insulin sensitivity.
  - b. Reduced amino acid supply is sensed by the eukaryotic initiation factor 2 (eIF2) kinase called GCN2 which functions to promote cytoprotection and disease resistance.
  - c. We found that the absence of GCN2 had no effect on the ability of MR to reduce body weight or adiposity, increase energy intake and expenditure, increase hepatic

transcription and release of fibroblast growth factor 21 (FGF21), or improve insulin sensitivity in mice.

- d. Instead, we discovered that MR activates a different eIF2 kinase called PKR-like endoplasmic reticulum kinase (PERK) in the livers of both intact and GCN2 null mice. PERK activation corresponded with induction of the NRF2 antioxidant program but not ER stress in liver. These data suggest a novel mechanism involving PERK linking dietary MR to its metabolic phenotype.

### **Virginia Station:**

1. Calves fed a low plane of nutrition (LPN) for 8 wks results in stagnant muscle growth as indicated by a smaller muscle mass and fiber diameters than controls maintained on a high plane of nutrition (HPN).
2. No differences in the numbers of satellite cells per fiber are evident between the groups.
3. HPN SCs have a greater mitotic index during log-phase proliferation than LPN SCs after 2 wks suggesting that the rapid muscle growth in HPN is supported, in part, by increased myogenic capacity of the SCs.

### **Washington Station:**

1. Muscle regeneration and epigenetic regulation of early adipogenic commitment, focusing on the role of AMP-activated protein kinase in these processes.
  - a. We found that a non-canonical Sonic Hedgehog (Shh) pathway is rapidly activated in response to muscle injury, which activates AMPK and induces a Warburg-like glycolysis in satellite cells.
  - b. AMPK $\alpha$ 1 deficiency in satellite cells impairs their activation and myogenic differentiation during muscle regeneration.
  - c. Drugs activating non-canonical Shh promote proliferation of satellite cells, which is abolished due to satellite cell-specific AMPK $\alpha$ 1 knockout.
  - d. Found that obesity inhibits AMPK activity in regenerating muscle, which was associated with impeded satellite cell activation, and impaired muscle regeneration.
  - e. Transplanted satellite cells with AMPK $\alpha$ 1 deficiency had severely impaired myogenic capacity in regenerating muscle fibers.
  - f. Attenuated muscle regeneration in obese mice was rescued by AICAR, a drug specifically activating AMPK.

### **Impact Statements**

#### **Arkansas Station:**

1. Protein (as well as essential amino acid/leucine) intake greater than the amount required can reduce rapid loss of muscle mass associated with metabolic stress. Benefits of increased protein intake include improved muscle function and improved ability to recover from disease and trauma, which could result in reduce animal production cost.
2. Leucine and omega-3 fatty acids are able to work synergistically to increase muscle protein



synthesis in vitro. This could mean that when taken together they could increase skeletal muscle mass. In addition, both leucine and omega-3 fatty acids increase cellular bioenergetics in isolated muscle cells. This is a biomarker for increased mitochondrial biogenesis and improved muscle function at the cellular level.

#### **Connecticut Station:**

1. Growth factors and pro-inflammatory cytokines alter the proliferation and differentiation of satellite cells isolated from young horses. Prolonged exposures to negative factors may decrease muscle growth in young horses.
2. Poor maternal nutrition (over- and restricted-feeding) during gestation inhibits muscle fiber growth in developing offspring.

#### **Hawaii Station:**

1. Results show that MSTN suppresses skeletal muscle mass by suppression of the Akt/mTOR pathway, supporting our current understanding of the underlying mechanisms of MSTN's regulation of skeletal muscle hypertrophy.

#### **Illinois Station:**

1. The paternal A allele of IGF2, most common in commercial swine, does not preclude the presence of mutations in myostatin. This suggests that the combination of increased IGF2 expression (from the paternal A allele) and reduced myostatin expression due to our engineered mutation may be an avenue to enhance muscle growth and therefore meat yield in pigs.
2. These data will be the first to identify the potential direct regulation of myoblasts by amino acid supplementation. Additionally, they will be the first to characterize various stem cell populations in muscle in obesity. These data will provide key insights into the regulation of muscle mass, and could provide novel opportunities for increasing muscle mass in animals and humans.

#### **Indiana Station:**

2. Study provides new findings regarding how the slow and fast myosin genes are activated during development.
3. Knowledge gained from these studies may lead to promising strategies to regulate meat quality and treat some muscle related diseases.

#### **Iowa Station:**

1. Oral quercetin administration provides cardioprotection to the dystrophic myocardium.
2. This degree of protection is greater than conventional medications to treat the cardiomyopathy associated with muscular dystrophy.
3. Quercetin provides some protection to dystrophic skeletal muscle.

#### **Kansas Station:**

1. These data are the first to demonstrate the divergent mechanisms by which porcine plasma affects fetal myoblast activity and postnatal satellite cell activity.
2. Smaller fetal myoblasts are more proliferative and more commonly express Pax7.

**Minnesota Station:**

1. Treatment with E2 stimulates proliferation in proliferating bovine satellite cell (**BSC**) cultures. In fused BSC cultures, E2 increases protein synthesis rate and suppresses protein degradation rate.
2. In fused BSC cultures binding of E2 to G protein-coupled estrogen receptor (GPER)-1 results in activation of matrix metalloproteinases 2 and 9 (MMP2/9) resulting in proteolytic release of heparin binding epidermal growth factor-like growth factor (hbEGF) from the cell surface. Released hbEGF binds to and activates the epidermal growth factor receptor (EGFR) resulting in increased protein synthesis rate. In proliferating BSC cultures E2 acts via this mechanism to increase proliferation rate. This mechanism does not appear to be involved in the ability of E2 to suppress protein degradation rate in BSC cultures.
3. Treatment with trenbolone acetate (TBA) (a testosterone analog) stimulates proliferation in proliferating BSC cultures. In fused BSC cultures, TBA increases protein synthesis rate and suppresses protein degradation rate.
4. In fused BSC cultures TBA increases protein synthesis rate through a non-genomic mechanism involving G protein-coupled receptors (GPCR), matrix metalloproteinases (MMP), heparin binding epidermal growth factor (hbEGF), the epidermal growth factor receptor (EGFR), erbB2 and the insulin-like growth factor 1 receptor (IGF-1R). In proliferating BSC cultures TBA acts via this mechanism to increase proliferation rate. This mechanism does not appear to be involved in the ability of TBA to suppress protein degradation rate in BSC cultures.
5. Treatment of fused BSC cultures with either TBA or E2 increases the levels of pAKT, an intracellular signaling factor that has been shown to stimulate hypertrophy in skeletal muscle.

**Missouri Station:**

1. Our observations suggest that immuno-PCR has the potential to improve detection capabilities of current hormonal assays with three or more orders of magnitude in sensitivity, and ultimately provide multiplex capabilities, with the conjugated oligonucleotide serving as both a quantitative detection label and as a barcode for later identification of analyte.
2. The technological leap in capabilities provided by successfully multiplexing can greatly aid in our efforts to understand the complex interaction of endocrine and metabolic signals in the dynamically changing animal and greatly reduce sample throughput investments.

**New Jersey Station:**

1. The addition of 20HE to feedstuffs for the purpose of improving lean body mass in livestock is not indicated.
2. Feeding diets restricted in the amino acid methionine improves metabolism and oxidative defenses. Identifying PERK as an initial sensor of these responses may lead to new treatments or dietary regimens to improve the health of livestock while maintaining lean mass.

### **North Carolina Station:**

1. Understanding the mechanisms governing muscle cell size and the environmental cues directing cell fate will lead to new incubation strategies or cell-based strategies to augment or optimize skeletal muscle growth.

### **Ohio Station:**

1. Thermal stress effects both the proliferation and differentiation of satellite cells which will alter muscle fiber formation and muscle mass accumulation.
2. Thermal stress may have long-term implications on meat quality through changes to muscle muscle growth potential and the morphological structure of the breast muscle.
3. The regulation of muscle growth especially the breast which is the most economically valuable part of the bird carcass is of importance to the poultry industry. For the turkey industry a 1% increase in breast muscle yield from a 40 lb bird per million birds processed results in an increase in revenues estimated to be over \$700,000 not including improved feed conversion in the calculation.

### **Virginia Station:**

1. Nutrition alters satellite cell activity and may be a useful means of modifying long-term skeletal muscle growth through creation of an autocrine PGC1 $\alpha$ /IGF-1 loop.

### **Washington Station:**

2. AMPK $\alpha$ 1 is a critical mediator linking non-canonical Shh pathway to Warburg-like glycolysis in satellite cells, which is required for satellite activation and muscle regeneration.
3. Demonstrated the importance of AMPK $\alpha$ 1 in satellite cell activation and muscle regeneration.

### **Collaborative Grants**

Collaborative NIFA-AFRI Grant between Ohio State University with the Michigan State Station (Gale Strasburg) Strasburg, G., Velleman, S.G. Reed, K., NIFA AFRI, "Influence of Thermal Challenge on Turkey Muscle Development and Meat Quality," \$975,000, 3/2014-2/2017.

USDA 2014-67015-21627. Collaborative NIFA-AFRI Grant between the Iowa and Virginia stations. JT Selsby, L Baumgard, S Lonergan, JW Ross, and R Rhoads. The effect of heat stresses on porcine skeletal muscle. \$499,881, 1/2014-12/2017.

### **Grants**

1. Wise Burroughs Fund. **Selsby** (PI). Au'14-Sp'15. Mechanisms and persistence of heat-stress-mediated factors that contribute to growth attenuation in swine: Graduate student support. \$38,235.
2. USDA/AFRI. **S. A. Reed** Co-PD (PD: S.A. Zinn, Co-PD: K.E. Govoni). 01/01/2014-12/31/2015. Effects of intrauterine growth retardation (IUGR) on fetal development in

- sheep. \$150,000.
3. NIH Eunice Kennedy Shriver National Institute of Child Health and Human Development 1R01 HD070487. **T. G. Anthony** (PI). 07/25/11 – 04/30/16. Molecular Mechanisms of Adverse Metabolic Events by Asparaginase. \$250,000 per year direct.
  4. National Institute of Food and Agriculture, U.S. Department of Agriculture competitive grant: award number 2012-67015-19447. **W. R. Dayton**. 5/1/1012-4/30/2017. Novel role of the Epidermal Growth Factor Receptor in both Insulin-like Growth Factor-1 and Estradiol-stimulated bovine muscle growth. \$500,000.
  5. Zoetis: **W. R. Dayton**. 1/1/2015-12/31/2015 \$14,000.
  6. Arkansas Biosciences Institute: **Baum JI** (PI) and Borsheim E. (2015-2018) Nutrition intervention to improve energy metabolism, energy intake, and metabolic response in overweight and obese school-aged children. \$150,000.
  7. Arkansas Biosciences Institute: Proctor A (PI), Anthony NB, **Baum JI**, Lay JO, Shinn SE. Conjugated Linoleic Acid (CLA) Rich Traditional Egg Breakfast Foods to Combat Obesity Related Diseases in Arkansas. \$150,000 (Baum - \$50,000)
  8. University of Arkansas Honors College Research Grant Award. Inman T and **Baum JI** (PI). (2015-2016) Defining the role of leucine in skeletal muscle energy metabolism for prevention of type 2 diabetes. \$3,500.
  9. University of Arkansas Honors College Research Grant Award. Kubas G and **Baum JI** (PI). (2015-2016). Nutrient modulation of the mammalian target of rapamycin (mTOR) to improve muscle function during aging. \$3,500.
  10. University of Illinois Research Board. **A. Dilger** (PI). June 2014-December 2015. Creation and characterization of a novel mutation to increase postnatal expression of IGF2 in mice. \$20,000.
  11. University of Illinois Division of Nutritional Sciences Vision 20/20. **M. DeLisio** (PI), N. Burd, N. Khan and **A. Dilger** (co-PIs). October 2014-October 2016. The effects of overweight/obesity and acute dietary protein ingestion on muscle stem cell function. \$22,500.
  12. GBH Labs, LLC. **J. M. Gonzalez**. 05/01/15-04/30/15. Effect of a plasma product on fetal and neonatal myoblast activity. \$46,869.
  13. Gates Foundation. petite and Mozdziak. 02/01/2012-03/31/2015. Reducing Disease In Livestock. \$100,000.00.
  14. Agriculture Foundation. Mozdziak. 07/01/2014-06/30/2017. 'Embryonic manipulations aimed at increasing muscle growth and meat yield'. \$65,000.00

## **Publications**

1. Johnson JS, Abuajamieh M, Sanz Fernandez MV, Seibert JT, Stoakes SK, Keating AF, Ross JW, **Selsby JT**, Rhoads RP, and Baumgard LH. The impact of in utero heat stress and nutrient restriction on progeny body composition. *Journal of Thermal Biology*. In Press.

2. Quindry JC, Ballmann CG, Epstein EE, and **Selsby JT**. Plethysmography measurements of respiratory function in conscious unrestrained mice. *The Journal of Physiological Sciences*. In Press.
3. Hollinger K and **Selsby JT**. PGC-1 $\alpha$  gene transfer improves muscle function in dystrophic muscle following prolonged disease progression. *Experimental Physiology*. 100:1145-1158, 2015.  
Designated an Editor's Choice; Art chosen for cover
4. **Selsby JT**, Ross JW, Nonneman D, and Hollinger K. Porcine models of muscular dystrophy. *International Laboratory Animals Research Journal*. 56:116-126, 2015.
5. **Reed S.A.**, E.K. LaVigne, A.K. Jones, D.F. Patterson, A.L. Schauer. The aging horse: effects of inflammation on equine satellite cells. *J Anim Sci*. 2015. Feb; 93:862-870. doi:10.2527/jas.2014-8448
6. LaVigne, E.K., A.K. Jones, A. Sanchez Londoño, A.S. Schauer, D.F. Patterson, J.A. Nadeau, and **S.A. Reed**. Muscle growth in young horses: effects of age, cytokines, and growth factors. *J Anim Sci*, in press.
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### **Book Chapters**

1. Anderson, P. T., **B. J. Johnson**, and M. Dikeman. 2014. Growth of meat animals: Metabolic modifiers. In: Carrick Devine and Michael Dikeman, editors-in-chief. *Encyclopedia of Meat Sciences 2e*, Vol. 2, Oxford: Elsevier, 2014. pp. 62-69.
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3. **Mozdziak**. 2014. Meat Species-Poultry In: Carrick Devine and Michael Dikeman, editors-in-chief. *Encyclopedia of Meat Sciences 2e*, Vol. 2, Oxford: Elsevier.

### **Abstracts**

1. Beyers RJ, Ballmann C, **Selsby JT**, Salibi N, Quindry JC, and Denney TS. Whole-heart T2-mapping at 7T quantifies dystrophic myocardial pathology in mdx/utrn<sup>+/-</sup> mice. *International Society for Magnetic Resonance in Medicine*, Toronto, Ontario, Canada, May 30-31, 2015.
2. Abuajamieh M, Laughlin EJ, Lei SM, Stoakes SK, Mayorga EJ, Seibert JT, Nolan EA, Sanz Fernandez MV, Ross JW, **Selsby JT**, Rhoads RP, and Baumgard LB. The effects of recovery time from heat stress on circulating bioenergetics variables and biomarkers of leaky gut. *FASEB*, Boston, MA March 215.
3. **Selsby JT**, Ballmann CG, and Quindry JQ. Long-term dietary quercetin enrichment improves muscle function in dystrophic skeletal muscle. *FASEB*, Boston, MA March, 2015.
4. **Selsby JT** and Sterle JA. Student perception of achievement influences student evaluation of teaching. *FASEB*, Boston, MA, March 2015.
5. Ballmann CB, Beyer R, Denney T, **Selsby JT** and Quindry JC. Effect of chronic dietary quercetin enrichment on cardiac function in dystrophic mice. *FASEB*, Boston, MA, March 2015.

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9. LaVigne, E.K., A. Sanchez Londoño, **S. A. Reed**. Interleukin-6, tumor necrosis factor- $\alpha$ , insulin-like growth factor-1 and fibroblast growth factor-2 alter proliferation and differentiation of equine satellite cells. J Anim Sci. 2015. 93(E-Suppl 2):336
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14. Pillai, S. M., J. S. Raja, M. L. Hoffman, A. K. Jones, K. K. McFadden, **S. A. Reed**, S. A. Zinn and K. E. Govoni. Effects of under- and over-feeding during gestation on organ development of offspring at days 45 and 90 of gestation. J Anim Sci. 2015. 93(E-Suppl 2):293
15. **Thornton, K. J.**, E. Kamanga-Sollo, M. E. White, **W. R. Dayton**. 2015. Role of epidermal growth factor receptor and erbB2 in trenbolone acetate mediated increases in bovine satellite cell proliferation and protein synthesis and decreases in protein degradation. J. Anim. Sci. 93,Suppl. s3:696.
16. Lu, Y., J.S. Bradley, S.R. McCoski, **J.M. Gonzalez**, A.J. Geiger, R.M. Akers, A.D. Ealy and **S.E. Johnson**. 2015. Caloric restriction reduces protein accretion in skeletal muscle by attenuating IGF-I signaling in young calves. ADSA/ASAS Joint Annual Meeting, July 12-16, Orlando, FL.
17. Lu, Y., J.S. Bradley, S.R. McCoski, A.J. Geiger, R.M. Akers, A.D. Ealy and **S.E. Johnson**. 2015. Muscle fiber hypertrophy is associated with increased expression of key transcriptional and epigenome regulatory genes. ADSA/ASAS Joint Annual Meeting, July 12-16, Orlando, FL.
18. Bradley, J.S., M.E. MacGhee, S.R. McCoski, A.M. Reeg, A.D. Ealy and **S.E. Johnson**. 2015. Plane of nutrition affects muscle fiber hypertrophy and satellite cell activity in neonatal bull calves. ADSA/ASAS Joint Annual Meeting, July 12-16, Orlando, FL.

19. Baggerman, J.O., J.E. Hergenreder, and **B.J. Johnson**. Activity of skeletal muscle satellite cells and shift of skeletal muscle fiber types over time in finishing cattle. 2015, Reciprocal Meats Conference. 2<sup>nd</sup> place in M. S. Poster Competition.
20. **Baum JI**, Shouse SA, Lassiter K, Bottje WG, Dridi S. (2015) Leucine and omega-3 fatty acids regulate cell bioenergetics via mTOR. *FASEB Journal* 29:742.16. *Poster Presentation*
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27. Stockwell-Goering MG, Benavides E, **Keisler DH**, Daniel J. 2015. Impact of visual, auditory, and olfactory cues on circulating concentrations of ghrelin in wethers. Abstract #119 Southern Section ASAS Abstract Book p 48-49.
28. Noel, J. A., T. J. Barstow, R. M. Broxterman, G. D. McCoy, K. J. Phelps and **J. M. Gonzalez**. 2015. Effect of ractopamine-HCl on muscle fiber types and finishing barrow exhaustion. 68<sup>th</sup> Recip. Meat Conf. Proc., Lincoln, NE.

### Theses:

1. "Muscle hypertrophy induced by myostatin inhibition is suppressed by rapamycin administration" Donghyuck Choi, Master degree, July 2015 – **Yong Kim (advisor)**
2. Elizabeth Benavides, PhD Dissertation 2015. Development of a novel immunoassay for simultaneous quantification of endocrine parameters. – **Duane Keisler (advisor)**
3. Rachel Gerrard Felton, M.S. Thesis, 2015 "Identification of California Condor (*Gymnogyps Californianus*) Estrogen Receptors 1 and 2 and their Activation by Suspected Endocrine Disrupting Contaminants" - **Duane Keisler (advisor)**

### **Other publications and presentations:**

1. **Selsby JT.** Quercetin as a novel therapeutic approach for Duchenne muscular dystrophy. Duchenne Alliance International Meeting, March 6<sup>th</sup>, 2015.
2. **Selsby JT, Ballmann CG, and Quindry JQ.** Long-term dietary quercetin enrichment improves muscle function in dystrophic skeletal muscle. FASEB, Boston, MA March, 2015.
3. **Ballmann CB, Beyer R, Denney T, Selsby JT and Quindry JC.** Effect of long term quercetin supplementation on dystrophic cardiac pathology in mdx/utrn<sup>+/-</sup> mice. FASEB, Boston, MA, March 2015.
4. **Selsby JT.** Heat stress mediated changes in skeletal muscle. Heat Stress Symposium, ISU, Ames, IA 4/17/15.
5. **Baum JI and Rodibaugh R (2014) Breakfast and Its Effect on Weight.** FSFCS87. University of Arkansas Division of Agriculture Research & Extension. <http://www.uaex.edu/publications/PDF/FSFCS87.pdf>
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8. **Baum JI Nutrition Unscrambled Blog, December 2014 - Physiological Impacts of Protein and Effects on Weight Management (Dallas Johnson, Undergraduate Student)** <http://www.nutritionunscrambled.org/2014/12/physiological-impacts-of-protein-and-effects-on-weight-management/>
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11. **J. M. Gonzalez.** Effect of Zilpaterol-HCl and Postmortem Aging on Muscle Structure and Cooked Meat Tenderness. 2015. The 101st Annual Kansas State University Cattlemen's Day, Manhattan, KS.
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