Growth and Development Symposium: The mitochondrion—A powerhouse for the cell or a key to animal productivity?

665 Mitochondrial bioenergetics—Bringing the cell to life. Darrell Neufer*, *East Carolina Diabetes and Obesity Institute, East Carolina University, Greenville, NC.*

This presentation will provide an overview of mitochondrial bioenergetics and redox systems biology—how life for cells is generated and maintained. Mitochondria are known as the engines of the cell, converting fuel derived from food into a chemical form of energy (ATP) used to support various cellular processes. A lesser-known but no less important role of the mitochondria is to generate and maintain an "electrical" charge throughout the cellular proteome. The respiratory system is composed of a series of proteins imbedded within the inner mitochondrial membrane that transport electrons by default, using oxygen as the final acceptor to produce water. The engine relies on a type of electrical circuit or redox system that is primed or "pressurized," with energy demand decreasing and energy supply increasing that pressure. Normally the mitochondrial respiratory system operates as a demand based system, meaning that the rate of fuel utilization and oxygen consumption is determined by the rate at which energy is being utilized by cells, even at rest (i.e., idling). In fact, because skeletal muscle represents a high percentage of body mass, this idling of mitochondria represents a significant source of heat generation by animals. However, when energy supply exceeds energy demand, the redox pressure within the system increases, causing electrons to leak from the circuit to oxygen prematurely, leading to the formation superoxide and other reactive oxygen species (ROS) that can react with and damage proteins, lipids and DNA. Fortunately, antioxidant scavenging systems are extremely efficient and convert the majority of superoxide to the non-radical hydrogen peroxide (H_2O_2). H_2O_2 can freely diffuse out of the mitochondria and influence various signaling pathways. Thus, the mitochondrial respiratory system functions as a redox pressure gauge that senses and reflects cellular metabolic balance. When in positive balance, electron leak serves as a release valve, accelerating mitochondrial H_2O_2 emission which has been implicated to play a significant role in numerous diseases related to disorders of metabolism.

Key Words: mitochondria, energy, redox

666 Mitochondrial bioenergetics and aging. Hazel H. Szeto*, *Research Program in Mitochondrial Therapeutics, Department of Pharmacology, Weill Cornell Medical College, New York, NY.*

Mitochondria play a central role in energy generation in the cell, providing ATP to carry out essential biological functions. As energy output declines, the most energetic tissues are preferentially affected, including the skeletal muscles, heart and eyes. Age-related decline in function has been observed in these systems and is associated with a decline in mitochondrial function in both animals and humans. Furthermore, age-related decline in skeletal muscle and cardiac function results in immobility that further promotes loss of skeletal muscle mass (sarcopenia). This talk will summarize the current literature on the effects of age and immobility on mitochondrial function and ATP production in skeletal muscles, heart, and the retina. A novel compound (SS-31) that promotes mitochondrial bioenergetics has been shown to reverse skeletal and cardiac muscle dysfunction, and loss of visual acuity, associated with aging. The mechanism of action of SS-31 and its effects on aging will be presented.

667 Mitochondria function in Rendement Napole pig growth. David E. Gerrard[1], Samer W. El-Kadi[1], and Tracy L. Scheffler*[2], *[1]Virginia Tech, Blacksburg, VA, [2]University of Florida, Gainesville, FL.*

The capacity for lean growth may be related to muscle fiber type characteristics. Previously, much emphasis has been placed on contractile phenotype and myosin heavy chain isoforms, yet metabolic properties (oxidative versus glycolytic) may play a more intimate role. Muscle oxidative capacity, largely determined by mitochondrial content and functional properties, has immense potential to fuel anabolic processes including protein synthesis. Yet, enhanced oxidative capacity is also associated with increased protein degradation and may restrict hypertrophy. Intriguingly, the relationships between metabolic phenotype, energy status, and protein accretion change during the lifetime of the animal. Thus, the influence of oxidative capacity on the potential for muscle growth likely depends on growth stage, along with input from various signaling pathways. These signaling pathways integrate cues related to energetic and nutritional status, hormones and other factors; this interplay coordinates adaptations in fiber metabolism, structure, and size to optimize function. In particular, AMP-activated protein kinase (AMPK) plays a key role in regulating energy producing and energy consuming pathways to maintain cellular energy homeostasis. Activated AMPK affects acute regulation of enzyme activity, as well as long-term adaptation through changes in gene and protein expression. Specifically, activated AMPK limits protein synthesis, while simultaneously promoting mitochondrial biogenesis and oxidative capacity. Pigs with the Rendement Napole (RN) mutation possesses a single nucleotide polymorphism in the γ3 subunit of AMPK, which results in increased AMPK activity. Therefore, the RN pig is a valuable model for investigating the effect of AMPK, energy status, and muscle metabolic phenotype on efficiency of lean gain during different stages of growth. Ultimately, understanding the relationship between muscle oxidative capacity and protein accretion and defining how this relationship evolves from birth to adult, is important for maximizing quantity and efficiency of meat production.

Key Words: mitochondria, AMP-activated protein kinase, skeletal muscle

668 Mitochondrial and cellular metabolism in response to selection for residual feed intake in pigs. S. M. Lonergan*, S. M. Cruzen, J. K. Grubbs, E. Huff Lonergan, J. C. M. Dekkers, and N. K. Gabler, *Iowa State University.*

A primary goal of animal agriculture is to improve the efficiency of meat production by optimizing the growth performance of livestock. Divergent genetic selection of swine for improved residual feed intake (RFI) has resulted in a line of pigs selected for low RFI that reaches the same market weight while consuming 10 to 15% less feed than the high RFI line. Our long-term goal is to define the contribution of mitochondria function to this improved growth efficiency. Investigations using RFI selection have demonstrated that muscle mitochondria from pigs in the low RFI line exhibited less electron leakage from the electron transport chain. This is particularly evident in the mitochondria from the red portion of the semitendinosus (complex I and II) and the white portion of the semitendinosus (complex I, II, and III). Reactive oxygen species production from electron leakage in the mitochondria

was positively correlated with RFI, demonstrating a link between poorer mitochondria function and poorer growth efficiency. A parallel observation was that muscle from more efficient pigs had a greater capacity to decrease protein degradation and conserve muscle mass. Mitochondria from muscle of the more efficient low RFI pigs had a greater abundance of heat shock protein 70, heat shock protein 60, malate dehydrogenase, ERO1 α, and subunit 1 of the cytochrome *bc*1 complex. Mitochondria from muscle of the less efficient high RFI pigs had a greater abundance of pyruvate kinase and glyceraldehyde 3-phosphate dehydrogenase. It is important to note that post-translational modification of proteins plays a central role in mitochondria function. Heat shock protein 70, heat shock protein 60, and ATP synthase are among the mitochondria proteins modified by phosphorylation. The combined evidence demonstrates that muscle growth and maintenance is directly influenced by mitochondria efficiency and cellular protein homeostasis. (Funded in part by the AFRI competitive grant number 2010–65206–20670 from USDA NIFA and by Iowa Pork Producers grant number 10–009).

Key Words: mitochondria, RFI, swine

669 Browning of adipose tissue. Shihuan Kuang*, Pengpeng Bi, and Tizhong Shan, *Department of Animal Sciences, Purdue University, West Lafayette, IN.*

Adipose (fat) tissues mediate systemic energy homeostasis, and play an important role in animal growth, health and reproduction. In addition, adipose tissues contribute to meat marbling and are thus a key determinant of meat quality. Fat cells within adipose tissues can be classified into white, beige and brown adipocytes mainly based on their mitochondria content. White adipocytes contain few mitochondria and are the predominant cell type in various subcutaneous and visceral fat depots. Brown adipocytes contain numerous mitochondria and are mainly found in interscapular brown adipose tissues of many mammals. Beige adipocytes are a newly defined type of adipocytes containing intermediate abundance of mitochondria and are found to coexist with white adipocytes in subcutaneous fat depots. While white adipocytes are primarily involved in energy storage (storing lipids), brown and beige adipocytes are highly specialized in energy expenditure due to their higher mitochondria content and abundant expression of uncoupling protein 1 (UCP1), which detours mitochondrial proton gradient from regular ATP production to instead generate heat to warm up the body. Recent studies indicate that white and beige adipocytes are interconvertible, and the conversion of white to beige adipocytes is called browning. In this talk, I will present our latest results on the molecular regulation of adipose browning and its implication in animal health, production and meat quality.

Key Words: white adipose tissue, brown adipose tissue, beige adipocyte

670 Mitochondrial adaptations to physiological states in bovine adipose tissue. Susanne Häussler*, *University of Bonn, Institute of Animal Science, Physiology & Hygiene Group, Bonn, Germany.*

Mitochondria are key cellular components in energy metabolism. Their number and function varies depending on environmental, physiological or pathological conditions. The amount of mitochondria within a cell can be determined by measuring the mitochondrial DNA (mtDNA) copy number. In white adipose tissue (AT), mitochondria are important because they deliver energy for the differentiation of adipocytes. In addition, mitochondria provide key substrates in support of lipogenesis during adipogenesis. Therefore, the number of mitochondria is lower in mature adipocytes than in differentiating preadipocytes. Besides its role as an energy depot, AT is established as a major endocrine organ. Taking a focus on dairy cows, the extensive changes that AT undergoes during the course of lactation indicate alterations in mitochondrial content in that tissue. Differing needs for energy during lactation may lead to changes of mtDNA content. Being crucial for the lipogenic capacity of adipocytes, the number of mitochondria within bovine AT is thus important for the storage capacity for energy in dairy cows. In our laboratory, we investigated the number of mtDNA copies within AT by multiplex qPCR. Comparing different AT depots in dairy cows, more mtDNA copies were observed in visceral (vc) as compared with subcutaneous (sc) AT, which is in accordance with the higher metabolic activity of vcAT. Furthermore, increased mtDNA copy numbers were detected in scAT after excessive fat accretion in nonlactating, non-pregnant dairy cows. In that study, the number of mtDNA was positively associated with indicators of oxidative stress, thus pointing to an adaptive response to mtDNA damage caused by oxidative stress which resulted from increasing metabolic load. When compared with other tissues being of major importance in energy metabolism and lactation, such as liver and mammary gland, the mtDNA content in AT of high-yielding dairy cows was distinctively lower. Nevertheless, mitochondria are important for the cellular energy supply in AT of dairy cows and thus for the adequate adaptation by AT to the changes of energy balance and oxidative stress throughout lactation, that is important for animal health and efficiency.

Key Words: mitochondria, adipose tissue, cow