

# Cell Biology Symposium: Molecular Basis for Feed Efficiency

**472 Unique roles for agouti proteins and melanocortin signaling in lower vertebrates.** C. Zhang<sup>1,2</sup>, P. M. Forlano<sup>3</sup>, and R. D. Cone\*<sup>1</sup>, <sup>1</sup>*Department of Molecular Physiology and Biophysics, Vanderbilt University School of Medicine, Nashville, TN*, <sup>2</sup>*Department of Cell and Developmental Biology, Oregon Health Science University, Portland*, <sup>3</sup>*Department of Biology and The Aquatic Research and Environmental Assessment Center, Brooklyn College of The City University of New York, Brooklyn*.

The agouti proteins and the central melanocortin circuits have been identified in all vertebrate species studied, from the most primitive fish to humans. These circuits regulate energy storage in adipose depots and somatic growth from fish to humans as well. However, deletion of the MC4R has only modest effects on somatic growth and reproduction in mammals, but large effects on larval teleosts, suggesting a fundamental difference in the neuroendocrine function of central melanocortin signaling in lower vertebrates. We have shown in a teleost that the hypothalamic proopiomelanocortin and AgRP neurons are hypophysiotropic, projecting to the pituitary to coordinately regulate multiple pituitary hormones. Indeed, AgRP-mediated suppression of MC4R appears essential for early larval growth. This identifies the mechanism by which the central melanocortin system coordinately regulates growth and reproduction in teleosts, and suggests it is an important anatomical substrate for evolutionary adaptation. Plasticity in growth and reproductive behavior is found in many vertebrate species, but is common in male teleost fish. Typically, “bourgeois” males are considerably larger and defend breeding territories while “parasitic” variants are small and use opportunistic breeding strategies. The P locus mediates this phenotypic variation in *Xiphophorus* and encodes variant alleles of the melanocortin-4 receptor (MC4R), also explained mechanistically by our findings. These data also suggest potential commercial applications in lower vertebrates for the regulation of growth, and potentially feed efficiency as well, since inhibition of MC4R significantly stimulates early growth.

**473 The physiological basis defining feed efficiency differences in pigs selected on residual feed intake.** N. K. Gabler,\* J. K. Grubbs, A. Harris, S. M. Cruzen, E. Huff-Lonerger, J. F. Patience, J. C. M. Dekkers, and S. M. Lonergan, *Iowa State University, Ames*.

In recent years, much attention has been given to feed efficiency in livestock production due to the rising costs of feed and other inputs. However, compared with growth and development, our understanding of the molecular biology and physiology regulating feed efficiency (FE) in swine is relatively limited. Residual feed intake (RFI) is a unique way to measure FE computed as the difference between the amount of feed a pig actually consumes and what it is expected to consume, based on its rate of growth and backfat. Therefore, selecting pigs for lower RFI results in animals that require less feed for a given rate of growth. The main biological factors that contribute to differences in RFI may include physical activity, feed intake patterns and behavior, stress, nutrient digestibility and efficiency of utilization, composition of gain and metabolism. In other words, both the maintenance and growth components of nutrient and energy utilization may be involved. In particular, the contributions of protein turnover, mitochondrial leakage and ion pump activity (i.e., Na<sup>+</sup>, K<sup>+</sup>-ATPase) may provide the primary basis for divergence FE. Results from our lines of pigs that have been selected for high versus low RFI show that changes in body composition may help explain some of the variation observed in RFI divergence. Our data also suggests that a significant part of RFI variation may also be

related to the level of protein turnover and degradation rates. These differences could be linked to mitochondrial function and oxidative stress in muscle and liver tissues. Furthermore, increased ion pump activity may contribute to reduced FE in pigs selected for high RFI, as maintaining high ion pump activity and membrane potentials are energetically expensive processes in metabolism. Altogether, this paper will discuss the molecular and physiological explanations for the observed phenotype in response for selection based on RFI. This project was supported by USDA-AFRI Competitive Grant #2010-65206-20670 and the Iowa Pork Producers Association.

**Key Words:** pig, feed efficiency, residual feed intake

**474 Genetics of feed efficiency in dairy and beef cattle.** D. P. Berry\*<sup>1</sup> and J. J. Crowley<sup>2</sup>, <sup>1</sup>*Teagasc, Moorepark Dairy Production Research Center, Fermoy, Co. Cork, Ireland*, <sup>2</sup>*Department of Agricultural, Food and Nutritional Science, University of Alberta, Edmonton, AB, Canada*.

Increasing food production for the growing human population off a decreasing land-base will require greater efficiency of production. Feed efficiency in cattle can contribute to this, and breeding, which is cumulative and permanent, is one likely vehicle to achieving efficiency gains within animal. A meta-analysis of up to 25 studies in growing cattle clearly showed that genetic variation in feed efficiency exists with a pooled heritability for residual feed intake and feed conversion efficiency of  $0.34 \pm 0.01$  (range of 0.14 to 0.62) and  $0.25 \pm 0.01$  (range of 0.06 to 0.46), respectively. However, what is not clear from the literature is what is the best breeding strategy to ensure food security, long-term—a conflict exists between focusing on improving feed efficiency per day or efficiency of an entire sector. Also, the studies to-date that highlight the importance of feed efficiency in breeding programs seem to ignore selection index theory that most of the variation in feed intake can actually be accounted for by other performance traits. Selection index calculations on a genetic covariance matrix between feed intake, live-weight and average daily gain generated from a meta-analysis of up to 12 studies showed that 84% of the genetic variation in feed intake could be explained by these traits. Therefore the marginal benefit of collecting feed intake data appears to be low. There is now sufficient information available to develop a roadmap on how best to direct research to ensure long-term food security for a growing human population.

**Key Words:** cattle, genetic, efficiency

**475 Feed efficiency: Mitochondrial function to global gene expression.** W. G. Bottje\* and B.-W. Kong, *Department of Poultry Science, Center of Excellence for Poultry Science, University of Arkansas, Fayetteville*.

There is evidence that links mitochondrial function and biochemistry with the phenotypic expression of feed efficiency (FE, gain:feed). Consistent findings observed in low FE in several tissues were evidence of increased protein oxidation or oxidative stress that probably resulted from increased mitochondrial reactive oxygen species (ROS) generation. As ROS are well known to act as second messengers, gene expression in the low FE phenotype could be hypothesized to be due to inherent gene expression that is modulated by increased mitochondrial ROS production. Studies have been conducted to assess global gene expression in breast muscle associated with the phenotypic expression

of FE. In these studies, RNA samples were obtained from broilers that exhibited either high FE ( $0.65 \pm 0.01$ ) or low FE ( $0.46 \pm 0.01$ ) ( $n = 6$  per group). Global RNA expression was investigated using a 44K chicken oligo microarray that was validated by comparison to values obtained by qRT-PCR for 33 different genes. A 1.3 fold cutoff value for expression resulted in over 750 genes that were differentially expressed in muscle between the high and low FE phenotypes. An online software program (Ingenuity Pathway Analysis) was used to group genes by function, gene networks and into established biochemical (canonical) pathways to facilitate data interpretation. The results indicate that animals exhibiting a high FE phenotype had increased expression of genes associated with anabolic activities and signal transduction-cascade mechanisms that

would appear to favor cell growth, development and differentiation. AMP kinase (AMPK) that senses coordinates energy production to meet cell energy needs was also upregulated in the high FE phenotype. In contrast, animals exhibiting a low FE phenotype exhibited upregulation of many genes associated with actin-myosin filaments that would be involved in cytoskeletal architecture and/or muscle development. Several stress-related or stress responsive genes (e.g., heat shock proteins, superoxide dismutase) were also upregulated that might be attributed to higher ROS production. Although these studies are limited mRNA expression in muscle, the results provide additional information to help in understanding the cellular basis of feed efficiency.

**Key Words:** feed efficiency, bioenergetics, gene expression