NONRUMINANT NUTRITION: FUNCTIONAL AMINO ACIDS: NEW PARADIGM SHIFTS IN UNDERSTANDING ANIMAL PROTEIN NUTRITION

0458 Amino acid signaling for embryonic and fetal development. G. Wu*, F. Bazer, R. Burghardt, G. Johnson, M. C. Satterfield, and X. Wang, *Texas A&M University, College Station*.

Embryonic death losses in mammals are estimated to range from 20 to 50%, depending on species, with two-thirds of the losses occurring during the peri-implantation period of pregnancy. Additionally, intrauterine growth restriction (IUGR) is primarily responsible for the high rates (up to 15%) of neonatal mortality in livestock species. Among litter-bearing species, swine exhibit the most severe naturally-occurring embryonic loss and IUGR. Nutrient availability, limited uterine capacity, and placental insufficiency are major factors contributing to suboptimal reproduction in mammals. Emerging evidence also shows that concentrations of several AA (arginine, glutamine, and leucine) in the uterine lumen increase markedly during early pregnancy, and are particularly abundant in fetal allantoic fluid during early and mid-gestation. Besides serving as building blocks for proteins, these AA play signaling roles to regulate intracellular protein turnover, water and ion transport, apoptosis, immune responses, and antioxidative reactions in the conceptus (embryo or fetus and extraembryonic membranes). Specifically, arginine is the precursor for synthesis of nitric oxide and polyamines (putrescine, spermidine, and spermine) that are essential to DNA synthesis and cell proliferation. Interestingly, these synthetic pathways are regulated by physiological concentrations of glutamine and leucine to coordinate the cellular actions of arginine. In addition, glutamine and leucine increase expression and activity of glutamine:fructose-6-phosphate transaminase to stimulate formation of glucosamine-6-phosphate from glutamine and fructose-6-phosphate and, therefore, for active synthesis of amino sugars and glycoproteins by trophectoderm cells. Furthermore, arginine, glutamine, and leucine activate (1) the mechanistic target of rapamycin (MTOR) cell signaling through phosphorylation of the MTOR protein and its downstream target proteins (S6K1 and 4E-BP1), and (2) osteopontin-induced cell signaling (a major mechanism for regulation of cell adhesion and implantation) through binding αvβ3 and α5β1 integrin heterodimers and the subsequent phosphorylation of MAPK3/MAPK1 (Erk1/2) and MAPK14 (p38). The beneficial outcome is to promote conceptus growth and development. Arginine and osteopontin appear to activate sequentially PI3K, Akt1, and MTOR to amplify cell signal transduction and exert their physiological effects. Translating the basic research into feeding practices, that is, supplementing 0.4 or 0.8% arginine to a typical corn- and soybean meal-based diet (containing 0.7% arginine) for gilts between d 14 and 25 of gestation, increases embryonic survival and conceptus development. As profitability of the swine industry critically depends on reproductive efficiency of sows, our findings have important implications for increasing pork production to provide high-quality animal protein for human consumption.

Key Words: pig, nutrition and biochemistry

0459 Leucine: A potent nutrient signal for protein synthesis in neonates. T. A. Davis*[1], M. L. Fiorotto, A. Suryawan, and D. Columbus, *USDA/ARS-Children's Nutrition Research Center, Baylor College of Medicine, Houston, TX.*

Neonates are highly efficient at utilizing their dietary AA for skeletal muscle growth. In the neonatal pig, the sharp increase in muscle protein synthesis after eating is triggered by the rise in AA and insulin. Amino acids and insulin induce protein synthesis by activating independent signaling pathways that converge at mechanistic target of rapamycin complex 1 (mTORC1), leading to the activation of key regulators of translation. Leucine is the most effective single AA in triggering translation initiation factor activation. Although most information on leucine's action on mTORC1-dependent translation initiation has been generated from studies performed in cell culture, studies in the neonatal pig have identified components of the AA signaling pathway that regulate protein synthesis in vivo. Acute parenteral leucine administration at physiological levels increases muscle protein synthesis in neonatal pigs and this effect is due to the activation of mTORC1 and its downstream targets, including eukaryotic initiation factor 4E-binding protein 1 and ribosomal protein S6 kinase-1. Although acute administration of the other branched-chain AA, isoleucine and valine, are ineffective, the leucine metabolites, α-ketoisocaproic acid and β-hydroxy-β-methylbutyrate, stimulate muscle protein synthesis by activating mTORC1-dependent translation. The stimulation of protein synthesis by parenteral leucine can be sustained for prolonged periods, but is dependent on maintenance of the supply of other AA to support protein synthesis. Pulsatile administration of leucine during continuous orogastric feeding of a milk replacer enhances muscle protein synthesis by stimulating translation initiation. Enteral leucine supplementation of a low protein meal stimulates protein synthesis similar to a high protein meal, but this effect is diminished but not blocked with more prolonged supplementation. Further studies are needed to establish whether the anabolic effects of leucine can be sustained chronically to promote lean growth. *Supported by NIH AR444474, NIH HD072891, USDA NIFA 2013–67015–20438, and USDA/ARS 6250–51000–055.*

Key Words: amino acids, growth, swine, muscle, nutrition

0460 Tryptophan: Functions beyond protein synthesis. S. W. Kim* and Y. Shen, *North Carolina State University, Raleigh.*

Tryptophan is a limiting essential AA for the growth of pigs. In addition to its important role to support growth, Trp also has unique physiological functions when it is metabolized to other compounds such as serotonin, melatonin, and niacin in the body. Serotonin is a cerebral neurotransmitter, playing a major role in regulating physiological processes such as appetite, stress adaptation, activity, and aggressive behavior. Tryptophan crosses blood-brain barrier, and thus increasing Trp intake is shown to elevate serotonin synthesis in the brain of pigs. However, large neutral amino acids (LNAA) compete for a same type of transporter to cross the blood-brain barrier, and thus dietary ratio of LNAA to Trp can affect Trp availability for serotonin synthesis in the brain. In a typical production environment, pigs can be under social stress conditions as they go through regrouping when they are weaned and when they are moved from nursery to finisher pens. Pigs confront with new mates when they are regrouped in a same pen, causing social mixing stress such as fighting and other aggressive behaviors. Pigs with social stress are shown to undergo increased systemic oxidative stress which is negatively related to animal productivity. In our research, increasing Trp intake up to 10.8 g/d elevated serotonin concentration in hypothalamus, reduced salivary cortisol, and enhanced growth of pigs under social mixing stress. Reducing dietary LNAA content from 4.5 to 3.8% provided similar benefits of increased Trp intake when Trp to LNAA ratio was maintained at 0.157. This allowed reducing supplemental levels of Trp from 0.8 to 0.6%. In summary, in a typical pig production, pigs can be under social mixing stress, and increasing tryptophan intake seems to help to reduce stress and thus improve performance of pigs.

Key Words: pigs, serotonin, social stress, tryptophan

0461 New insights into sulfur amino acid function in gut health and disease. D. G. Burrin*, *USDA-ARS Children's Nutrition Research Center, Houston, TX.*

The gastrointestinal tract (GIT) is a metabolically significant site of sulfur amino acids (SAA) metabolism in the body. Aside from their role in protein synthesis, methionine and cysteine are involved in many biological functions and diseases. Methionine (MET) is an indispensable AA and is transmethylated to homocysteine via S-adenosylmethionine (SAM), the principal biological methyl donor in mammalian cells and a precursor for polyamine synthesis. We have examined the role of SAA metabolism in GIT health and disease. Our studies in young pigs showed that the whole-body methionine transmethylation and remethylation rates were higher during duodenal [^{13}C]-MET than intravenous [$^{2}H_3$]-MET infusion. Thus, transmethylation and transsulfuration in the GIT represented 27 and 23% of whole-body fluxes, respectively. Additional studies show how disruption of methionine cycle activity and dietary supplementation with methionine metabolites affects the susceptibility to colitis in mice. We found that mice fed vitamin B_{12} and B_6 deficient diets are protected against colitis, with reduced inflammation and tissue injury. We also found that B-vitamin deficiency suppressed inflammatory gene expression in association with altered MET cycle activity and indices of methylation status. We also showed that supplementation with the MET cycle metabolite, methylthioadenosine (MTA), prevented inflammation during colitis in mice. These results suggest that MTA also is protective against experimental colitis and reduced tissue injury and expression of multiple inflammatory genes. The presentation will discuss the evidence of SAA metabolism in GIT and consequences of MET cycle activity in health and disease.

Key Words: methionine, cysteine, gut

0462 Glutamate and glutamine: Nonessential or essential amino acid. M. Watford*, *Rutgers, New Brunswick, NJ.*

Rose defined an essential amino acid (EAA) as one that the body cannot make in sufficient amounts to maintain growth or N balance. Despite Rose's finding that glutamate added to diets of traditionally EAA improved the maximal rate of growth, glutamate and glutamine are not usually considered as essential. In part, this is due to the almost total metabolism of dietary glutamate and glutamine in the intestine, and the very high concentration, and turnover, of these 2 AA in the body. In human medicine, however, glutamine has been recognized as a conditionally EAA during hypercatabolic states, and while such conditions are not a concern in the domestic animal industry, the question arises, "is glutamine conditionally essential at other times"? We observed that plasma and skeletal muscle glutamine concentrations fall throughout lactation in both horses, pigs, and mice, and that this was accompanied by a loss of skeletal muscle. We proposed that this was due to the high demand for glutamine (and glutamate) both for milk production and as a fuel for the enlarged maternal intestine. Furthermore, the provision of supplemental glutamine to both suckling and weaned piglets has demonstrated improvements in growth and health, most probably related to improved intestinal status and immune function. The daily supplementation of suckling piglets is not feasible on an industrial scale, and we established that supplementing lactating sows with either glutamine, or a mixture of glutamine and glutamate, increased the glutamine and glutamate content of the milk and also prevented some of the loss of lean body mass in the sow. Furthermore, sows receiving the supplement had higher concentrations of lipids in both colostrum and mature milk, and similar increases were seen in milk somatic cell count. Thus, we propose that glutamate and glutamine should be considered essential both during lactation for the health of both the mother and the neonate.

Key Words: glutamine, glutamate, lactation