66 Transporters in the absorption and utilization of Zn and Cu. G. M. Hill* and J. E. Link, *Michigan State University*, *East Lansing*.

Before the discovery and elucidation of transporters, mammals were thought to co-transport Cu or Zn as an anionic complex such as binding with an amino acid as a chelate or a receptor such as transferrin. In 1995, the first mammalian transporter gene, ZnT1, was identified. However, it is now thought that two protein families are involved in Zn transport. The ZnT family reduces intracellular Zn by aiding in efflux from the cell or promoting the influx into intracellular vesicles. As noted by Cousins et al., (2006) the mechanism of ZnT transport against a Zn concentration gradient is unknown. However, only the ZnT1 transporter appears to be located at the plasma membrane. It has been shown to respond in tissues in a variety of manners to Zn reduction and supplementation. Our laboratory (Martinez et al., 2004) have found ZnT1 and metallothionein to work in concert during pharmacological Zn supplementation. The second protein family, Zip proteins, provide Zn transport from extracellular fluid or intracellular vesicles into the cytoplasm and has not been identified in a livestock species. Like Zn, no good indicator of status has been identified for Cu. However, the recent identification of Cu transporters and chaperones give researchers the opportunity to understand the regulation of Cu-trafficking where the proteins are modified by post-translational mechanisms. Two Cu transporters, Ctr1 and Ctr3, mediate high affinity Cu uptake. Murr1, a small cytoplasmic protein, has been identified in human hepatic tissue, but its role in Cu metabolism is unknown. The discovery of Cu chaperones that are involved in facilitating Cu absorption into proteins may provide an excellent status indicator. It has been shown that the protein of the Cu chaperone for Cu/Zn superoxide dismutase (CCS) is increased in tissue of Cu deficient rats induced when moderately high Zn diets were fed. We have recently found CCS in the young pig. It is essential that these new molecular findings be utilized to evaluate bioavailability and nutritional needs of Cu and Zn in livestock.

Key Words: Cu, Zn, Transport Proteins

67 Absorption and metabolism of iron and manganese. J. W. Spears* and S. L. Hansen, *North Carolina State University*, *Raleigh*.

This presentation will discuss our current understanding of iron (Fe) and manganese (Mn) metabolism. Iron metabolism and its biochemical functions are closely linked to the ability of Fe to undergo oxidation and reduction. Prior to absorption, ferric Fe (Fe^{+3}) must first be reduced to ferrous Fe (Fe^{+2}) by dietary reducing agents or reductases that reside on the duodenal apical membrane. Divalent Fe is then transported into enterocytes by divalent metal transporter 1 (DMT1). Absorbed Fe is exported from the enterocyte by ferroportin 1 (FPN) and immediately oxidized via hephaestin, a copper-dependent ferroxidase. Iron is then transported in the blood in the Fe^{+3} form bound to transferrin. Transferrin receptors on tissues allow for the uptake of transferrin-bound Fe by cells. Whole body Fe homeostasis is controlled at the level of intestinal absorption, due to limited ability to excrete absorbed Fe. Cellular Fe concentrations are controlled by Fe regulatory proteins in the cytosol that bind to iron responsive elements located on the mRNA of proteins involved in Fe absorption (DMT1, FPN), uptake (transferrin receptor), and storage (ferritin). The same DMT1 protein that transports Fe^{+2} into the intestine also transports Mn^{+2}. Based on limited research with pigs less than 1% of dietary Mn is absorbed. Absorbed Mn is transported to the liver bound to albumin and α-2-macroglobulins. Biliary excretion of Mn from the liver plays an important role in Mn homeostasis. Manganese leaving the liver is transported bound to transferrin; however, the number of transferrin binding sites occupied by Mn is very low relative to Fe. In summary, the last decade has provided incredible amounts of information about absorption and metabolism of Fe, but several steps involved in absorption and metabolism of Mn remain to be elucidated.

Key Words: Iron, Manganese, Metabolism

68 Active phosphate absorption: What do we know and is it important? J. S. Radcliffe*, *Purdue University*, *West Lafayette, IN*.

Phosphorus has probably been the most researched mineral over the last decade. However, research has focused primarily on enhancement of P digestibility, with very little emphasis on the mechanisms of absorption. When abundant in the diet, P, in the form of phosphate is absorbed passively via a paracellular route. However, as phosphate concentrations in digesta decrease, phosphate can be absorbed through an active, sodium dependent route. Historically, diets have been over-formulated with P, and therefore the passive absorption route dominates. However, as the concentration of P in swine diets have been lowered to reduce excretion, active absorption may be more important. Furthermore, most experiments evaluating phytase contain a negative control treatment, where dietary P concentrations are often 0.1-0.2 %-units below the requirement, which will result in an increased active transport of phosphate. To optimize dietary P utilization it is necessary to better understand active phosphate absorption, and how this transport system is regulated. Active phosphate absorption occurs through the sodium phosphate co-transporter, NaPi2b. Data from rodents, and more recently from swine, have demonstrated that as the concentration of P in the diet is decreased, active phosphate absorption is increased. This increase is the result of an increased translocation of Napi2b from a subapical pool to the brush border membrane. Gene expression data is mixed, with the majority of experiments reporting no change in NaPi2b mRNA. The response to decreasing dietary P concentrations has been observed in as little as 3 d in pigs. Active phosphate absorption has been reported to be responsive to serum vitamin D concentrations in rodents, but not to dietary vitamin D concentrations in rodents or swine. Ultimately a better understanding of active phosphate absorption will result in improved diet formulation that will enhance P absorption and retention.

Key Words: Phosphate, Absorption, Phosphorus

69 Intestinal calcium absorption: Mechanisms learned from transgenic and knockout mice. J. C. Fleet*, *Purdue University*, *West Lafayette, IN*.

Although the role of calcium (Ca) in bone health has been well appreciated for nearly a century, in the last decade the use of transgenic and knockout mice has revealed many things about the mechanisms by which this essential nutrient enters the body. Ca crosses the intestinal barrier

using both a paracellular/diffusional pathway that responds solely to the luminal content of Ca and by a transcellular pathway that is active and saturable. While passive diffusion occurs throughout the intestine and accounts for 65-75% of the Ca that enters the body, the active, saturable component is thought to be limited to the proximal small intestine. The hormonally active form of vitamin D (1,25 dihydroxyvitamin D or 1,25 D) is the primary regulator of intestinal Ca absorption. Deletion of the vitamin D receptor (VDR) in mice reveals that the loss of intestinal Ca absorption is the primary defect responsible for disruption of Ca metabolism in these mice. Transgenic recovery of VDR into either the proximal small intestine or throughout the intestine suggest that there vitamin D-regulated Ca absorption is also present in the lower bowel. Recently the facilitated diffusion of transcellular Ca absorption has been challenged by knockout mouse studies. Deletion of the apical membrane transporter gene (TRPV6) or of the gene for the putative Ca ferry protein calbindin D9k, have a minimal impact of basal or vitamin D regulated intestinal Ca absorption. New work will be necessary to fully understand the mechanism of transcellular, intestinal Ca absorption.

Key Words: Calcium, Vitamin D, Absorption