Growth and Development: IGF and IGF Binding Proteins

286 Insulin-like growth factor-I, a link between nutrient intake and growth. D. Clemmons*, *University of North Carolina*, *Chapel Hill*.

Insulin-like growth factor-I (IGF-I) is a small poly peptide hormone that is synthesized in multiple tissues. IGF synthesis is controlled principally by nutrient intake and by pituitary GH secretion. In periods of adequate intake, GH is the predominant stimulant of IGF-I synthesis however in periods of caloric or protein restriction organisms become refractory to GH and the effect of nutritional deficiency predominates. This change in IGF-I synthesis functions to regulate protein metabolism in tissues. IGF-I is a predominant stimulant of both skeletal muscle, growth and differentiation and it inhibits apoptosis. In multiple tissues IGF functions to maintain tissue hypertrophy in response to either exercise induced stress or changes in nutrient intake. In adult organisms IGF-I stimulates hyperplasia only in cell types that are susceptible to stimulation but it stimulates hypertrophy in almost all cell types. IGF-I stimulated growth is a mixture of the two processes. Under normal conditions certain cell types such as vascular smooth muscle respond to IGF-I with increases in cell size and protein content however during some periods of stress these cell types such as smooth muscle cells, endothelial cells, osteoblasts, chondrocytes are capable of partially dedifferentiating and responding to IGF-I with a hyperplastic response. In contrast skeletal muscle always responds with a hypertrophic response except for myoblasts that proliferate in response to IGF-I. IGF-I is a potent antiapoptotic factor for both skeletal muscle and neural tissue. The IGF-I synthesis and blood concentrations decline in all aging organisms but the significance of this decline for changes in tissue mass and protein synthesis that occur with aging has not been definitively determined. IGF-I is an important systemic growth factor that is responsible for the growth of multiple tissues. In adult organisms this growth occurs as a result of hypertrophy although certain specialized cell types can undergo a hypoplastic response. IGF-I protein balance, and tissue responsiveness, will continue to be an important goal of future studies.

Key Words: Muscle hypertrophy, Somatic growth, Protein metabolism

287 Effects of short day photoperiod on mammary growth of dry cows: Altered prolactin and IGF signaling. G. E. Dahl*[1], E. H. Wall[2], and T. B. McFadden[2], [1]*University of Illinois*, *Urbana*, [2]*University of Vermont*, *Burlington*.

Manipulation of photoperiod has dramatic physiological and production effects on mature dairy cows. During lactation, exposure to long day photoperiod (LDPP) increases milk yield and circulating IGF-I and prolactin (PRL). In contrast, dry cows housed under a short day photoperiod (SDPP) produce more milk in the subsequent lactation than cows exposed to LDPP or natural photoperiod. Relative to LDPP, exposure to SDPP depresses PRL secretion but expression of PRL-receptor (PRL-R) mRNA increases in mammary and hepatic tissue and in lymphocytes. Under SDPP, PRL signaling emerges as a possible mechanism to drive more extensive mammary cell differentiation and growth relative to LDPP. Using sequential mammary biopsies, we determined temporal changes in mammary cell proliferation and in expression of genes of the IGF and PRL signaling pathways during the dry period and transition into lactation. For both SDPP and LDPP, cell proliferation rate increased significantly as the dry period advanced, then decreased significantly in early lactation. However, timing of the proliferative response differed between treatments, increasing earlier in SDPP cows than in LDPP cows during the dry period. Overall, expression of IGF-II was significantly greater, whereas that of IGFBP-5 was lower, in SDPP versus LDPP cows. IGFBP-5 mRNA increased significantly during lactation in both groups. Expression of IGF-I did not differ over time or between treatments however, the lower IGFBP-5 expression in SDPP cows coupled with increased IGF-II expression may enhance mammary cell growth and survival. Key among the potential modulators of PRL signaling is the suppressors of cytokine signaling (SOCS) family, the best characterized of which are SOCS-1, -2, -3, and cytokine-inducible SH2-containing protein (CIS). Mammary expression of SOCS-1, -2, -3, and CIS were low during the dry period, but increased in lactation. During the dry period, SOCS expression of cows on SDPP was generally reduced, which may enhance PRL induced proliferation and subsequent milk production.

Key Words: Dry cow, Mammary growth, Prolactin signaling

Nonruminant Nutrition: New Frontiers in Amino Acid Research in Nonruminant Nutrition

288 Branched chain amino acid metabolism and nutrition in monogastric animals. S. M. Hutson*[1], P. She[2], T. M. Reid[1], M. Janket[1], S. K. Bronson[2], A. Sweatt[1], and C. J. Lynch[2], [1]*Wake Forest University School of Medicine*, *Winston-Salem, NC*, [2]*Penn State College of Medicine*, *Hershey*.

Studies in our laboratory have shown that several features of indispensable branched chain amino acid (BCAA) metabolism in animals sets them apart from other indispensable amino acids. The initial 2 steps of BCAA catabolism are common to all 3 BCAAs; reversible transamination followed by irreversible oxidative decarboxylation of the branched chain α-keto acid transamination products. Due to the shared steps, dietary intake of individual BCAAs impacts the catabolism of all three. Rather than being restricted to liver, BCAA catabolic enzymes are distributed widely in body tissues. With the exception of the nervous system, all reactions occur in the mitochondria. The tissue specific expression and intracellular compartmentalization of the branched chain aminotransferase isozymes (BCATm and BCATc) impact intra- and inter-organ exchange of BCAA metabolites, nitrogen cycling, and net nitrogen transfer. Transamination of the BCAAs makes them important nitrogen donors for synthesis of alanine and glutamine, as well as giving them a key role in the transfer of nitrogen between skeletal muscle and liver. In brain, BCAAs are important in neurotransmitter glutamate synthesis, and the localization of the BCAT isozymes separately in neurons and glia promotes intercellular shuttling of nitrogen. Dysregulation of the BCAA catabolic pathways that leads to excess BCAAs and their metabolites has been shown to result in severe neural dysfunction. Finally, leucine serves as a nutrient signal that regulates protein synthesis and cell growth pathways affected by mTOR and insulin secretion. Indeed the BCATm knockout mouse (blocked body BCAA catabolism) exhibits increased energy