

# Growth and Development Symposium: Intestinal Development and Growth

**309 Strategies to alter intestinal development, health and function of poultry to improve growth performance.** T. J. Applegate\*, *Purdue University, W Lafayette, IN.*

The gastrointestinal tract (GIT) in chickens, turkeys and ducks is a dynamic organ system. During early posthatch growth, there is a tremendous energetic allocation to GIT growth. While most research has focused on ontogenic changes to nutrient transporter and/or enzyme production, the structural aspects of intestinal maturation often is not studied in tandem, which may be more limiting to growth. Similarly, researchers often use simple morphometric measures of intestinal structure (villus height, crypt depth, goblet cell numbers). However, these crude measures may not be as reflective of enterocyte proliferation, migration, apoptosis, and necrosis. Remarkably, the turnover of the bird's intestine ranges from less than 2 to over 5 d, but our knowledge of what factors affect cell cycle and functionality are largely lacking in poultry. Recent work has noted that appearance of indigestibility by the young bird is due in part to changes in the pH of the proventriculus and endogenous secretion differences. For example, 60 to 80% of the apparent digestibility differences in amino acid utilization during the first week and later in life are due to differences in basal endogenous amino acid losses. Recent research has also focused on the maintenance needs of the intestine, particularly as it relates to preserving its barrier functionality with or without sub-therapeutic antibiotics. The GIT barrier is far from being static and responds to many challenges through changes to: a) peristalsis, b) enterocyte turnover, c) mucin production, adaptation of commensal microflora, d) innate immune responsiveness (including inflammation and acute phase response), and/or e) alterations to secretions. The extent and duration of each of these responses encompasses the nutrient and growth cost for maintenance of this barrier function. While most antibiotic replacement strategies are not capable of similar physiological and microbiological responses, some probiotic bacteria and plant extracts are able to modify mucin production, preserve intestinal tight junctions and enterocyte cell cycle, as well as alter inflammatory responses within the intestine.

**Key Words:** intestine, poultry

**310 Nutritional support of intestinal health: Insights from a piglet model.** J. Odle\*, S. K. Jacobi, A. J. Moeser, and A. T. Blikslager, *North Carolina State University, Raleigh.*

Early postnatal morbidity and mortality of mammalian neonates represent significant challenges to the agricultural and medical sciences. While many stressors impinge on the newborn, gastrointestinal maladies predominate. This is not surprising given the quiescent state of the intestine in utero and the rapid ontogeny that ensues following birth. Furthermore, the intestinal mucosa, initially sterile, must be protected from viral and bacterial pathogens that are ubiquitous in the postnatal environment. Because the intestine is a "supply organ," overall vitality of the neonate hinges on its proper function. Our studies have employed rotaviral-gastroenteritis and ischemic-injury models to examine the effects of various nutrients on intestinal restitution and recovery. We have been unable to measure beneficial effects of enteral glutamine or alanyl-glutamine. However, supplemental arginine increased intestinal protein synthesis via mTOR signaling, increased crypt depth, and improved transepithelial resistance (TER). Supplemental plasma-protein also effectively abrogated gastroenteritis following rotaviral challenge. Most recently we investigated prophylactic intervention with dietary long-chain polyunsaturated fatty acids using an ischemic-injury

model. Arachidonic acid (ARA) reduced initial villus denudation and accelerated acute restitution, measured as increased TER. Restitution effects of ARA were attenuated by indomethacin, suggesting possible prostaglandin mediation. Our collective findings suggest positive (but modest) effects of selected nutrients on intestinal repair. Further research is needed to understand better the complex interplay between nutrients, growth factors, immunological, and bacterial determinants which impact intestinal health and ultimately neonatal vitality.

**Key Words:** rotavirus, arachidonic acid, arginine

**311 Integral role of the gut in growth signal transduction between the environment and host.** D. G. Burrin\*, *USDA Children's Nutrition Research Center, Department of Pediatrics, Baylor College of Medicine, Houston, TX.*

The gut epithelium serves as a vital biological interface between the environmental microbiota, luminal dietary factors and the mammalian host. The function of the gut barrier is especially critical during early neonatal development and weaning when the diet changes markedly and the immune system is immature in rapidly growing animals. In addition to functioning as a physical barrier, the gut epithelium contains specialized cells and receptors that serve to recognize specific molecules derived from the diet and microbes. The enteroendocrine cell comprises a small proportion (<5%) of gut epithelial cells, but their effects are magnified via release of several hormones that positively impact animal growth and development. The endocrine L-cell is capable of sensing multiple luminal molecules, including glucose and bile acids that trigger the secretion of gut hormones, such as glucagon-like peptide 1 and 2. These 2 hormones have an important stimulatory effect on insulin secretion, insulin sensitivity, glucose absorption and gut epithelial growth. Recent studies also have show that bile acids taken up by enterocytes can activate the nuclear receptor, farnesoid X receptor (FXR), stimulating the release of fibroblast growth factor 19 (FGF19). FGF19 functions as a hormone that alters hepatic lipid metabolism and bile acid homeostasis. In addition to nutritionally significant molecules, the gut epithelium also senses the presence of the microbiota through toll-like receptors (TLR) that transmit signals to the underlying cells within the immune and neuroendocrine systems. The activation of TLR by bacterial products can result in negative feedback on key elements of growth, such as appetite, gut motility, and anabolic hormone signaling. The presentation will discuss the essential role of the gut in novel aspects of these growth signal transduction pathways in the developing animal.

**Key Words:** glucagon-like peptides, bile acids, toll-like receptors

**312 Nutrient transporters in support of ruminant growth and development: novel and updated findings.** J. C. Matthews\*, *University of Kentucky, Lexington.*

This literature review summarizes recent findings in cattle (primarily) about urea, SCFA, thyroid hormones, amino acid, and calcium transporters. In ruminants, the relationship between diet and urea cycling is complex. Expression of urea transporter-B (UT-B; SLC14A1) is upregulated throughout the rumen in response to high vs low concentrate diets, but apparently not increased levels of rumen ammonia. In growing lambs, the relative tissue content of UT-B in gastrointestinal tract epithelia, liver, kidney, and parotid salivary glands, was not affected by varying dietary CP. Monocarboxylate transporters (MCT) 1 (SLC16A1) and 4 (SLC16A3) are expressed throughout the ruminant gastrointestinal

tract and are likely responsible for the absorption of SCFA across these tissues, especially the rumen. However, a recent finding suggests that at least rumen tissue content of MCT4 mRNA and fractional rate of SCFA absorption appear insensitive to increased rumen fluid SCFA concentrations in cattle fed high vs low concentrate diets. Regarding the fate of absorbed ruminal SCFA during lactation, the cellular localization of MCT1 and 4 in the mammary gland of lactating Holsteins has been identified, along with a thyroid hormone transporter (MCT8, SLC16A2), and the aromatic amino acid transporter TAT1 (SLC16A10). In Belgian Blue cattle, association mapping has identified a mutation in the neuronal glycine transporter GLYT2 (SLC6A5) that leads to a decrease in pre-synaptic accumulation of glycine and is likely the cause of congenital muscular dystonia 1. Similarly, a mutation in Ca<sup>2+</sup>ATPase (ATP2A1) results in decreased cytosolic Ca<sup>2+</sup>, thus impaired fast-twitch muscle function. In summary, several recent and important findings have been made in delineating existing relationships between nutrient transporter expression and specific physiological states of cattle. When combined with results of additional functional capacity studies, these findings will lead to a greater understanding of ideal physiological conditions required to support optimal nutrient use by cattle.

**Key Words:** biological transport, nutrient-gene interaction, SLC

**313 Out of the black box and back to the future: New frontiers and challenges for rumen microbiology to advance animal growth and development.** M. Morrison<sup>\*1,2</sup>, <sup>1</sup>*CSIRO, St. Lucia, Queensland, Australia*, <sup>2</sup>*The Ohio State University, Columbus*.

Ruminant microbiology has been studied for more than a century, initially via microscopic examinations of rumen fluid providing morphological and compositional descriptions of the microbiota. Cultivation techniques for obligate anaerobes were developed in the mid-20th Century, and the principal way of studying rumen microbiology shifted, to culture and isolate as many species as possible then study select physiological processes. In the late '80s and '90s, with the development of tools such as PCR, and the application of reverse transcriptase and DNA polymerases, the field of rumen microbial ecology was transformed to a largely cultivation-independent field of inquiry, using 16S rRNA and/or the gene encoding that molecule as a semantide. During this period, recombinant DNA technologies also made an impact on the field of rumen microbiology, principally via a level of reductionism that provided deeper knowledge about fewer rumen microbial interac-

tions and processes. In the first decade of the 21st Century, microbial biology has advanced from the sequencing of individual genomes, to comprehensive assessments of microbial diversity and the genetic potential resident within entire microbial communities. This has been driven largely by the appreciation that culturable microbes represent only a small percentage of the microbial world and advances in high throughput sequencing technologies. As such, there has been a renewed interest in the interrogation of rumen and other gut microbiomes via (meta)genomic approaches. So, are these efforts resulting in more of the same, or something "new" in relation to our understanding of the microbial biology underpinning rumen function, nutrient availability, and animal growth and development; and from which, new opportunities might emerge? This presentation will examine some of the latest observations and findings arising from the study of individual rumen bacteria, as well as rumen microbiomes. The field of rumen microbiology still has something to offer the animal industries, as well as other sectors of science and industry.

**Key Words:** rumen microbiology, growth and development, microbial genomics

**314 The human intestinal microbiome—Applications to animal agriculture.** D. N. Frank<sup>\*</sup>, *University of Colorado, Boulder*.

Advances in DNA sequence-based technologies now permit genetic analysis of complex microbial populations without the need for prior cultivation. My talk will summarize the molecular methods of culture-independent microbiology ("metagenomics") as exemplified by their application to studies of the human gastrointestinal tract in both health and disease. Such culture-independent metagenomic surveys reveal unprecedented microbial biodiversity in the human intestine. Large-scale shifts in gut commensal populations ("dysbiosis"), rather than occurrence of particular microorganisms, are associated with several gastroenterological conditions, including antibiotic-associated diarrhea, Crohn's disease, ulcerative colitis, and obesity. These findings demonstrate the importance of commensal microorganisms in maintaining GI health and suggest that redress of disease-associated imbalances may ameliorate human pathogenic conditions. Metagenomic techniques are readily applicable to animal agricultural science and are likely to provide important new microbiological perspective, as they have in human biomedicine.

**Key Words:** microbiome