The symposium titled “Gut chemosensing: integrating nutrition, gut function, and metabolism in pigs” preceded the 12th International Symposium on Digestive Physiology of Pigs that was held in Keystone, CO, from May 29 to June 1, 2012. The objectives of the preconference symposium were to provide a comprehensive overview of the state of the art and thereby foster discussion and research aiming to elucidate the role that chemical (i.e., nutrient) sensing by the gastrointestinal (GI) tract plays on regulating gut integrity and body metabolism. The ability of the GI tract to sense ingested nutrients and other chemicals has been suspected since Bayliss and Starling (1902) first demonstrated that luminal protons stimulate pancreatic secretions through a neurally independent mechanism. Almost 100 yr later, the discovery of the expression of taste signaling elements in cells interspersed in the gastric and intestinal mucosa supported the hypothesis that GI chemosensing is a cell-mediated phenomenon (Höfer et al., 1996). In recent years, scientific efforts have increased remarkably to gain a closer understanding of the GI chemosensory system and its involvement in the normal and pathological functioning of the gut and body metabolism. As a result, a number of nutrient-activated guanosine-protein coupled receptors (GPCR) have been de-orphanized and shown to be expressed in different segments of the GI tract. Subsequent functional studies revealed that these putative chemosensors are localized in hormone-secreting enteroendocrine cells that function along with visceral afferent neurons as the interface between the GI lumen and local or distant targets. In this fashion, enteroendocrine cells appear to operate as chemosensory transducers that respond to ingested nutrients and other chemicals by releasing regulatory peptides to initiate humoral and vagal signaling cascades that convey information to the brain and neighbor cells regarding the luminal milieu. As a consequence, a wide array of physiological responses, ranging from stimulation of gastric, intestinal, and pancreatic secretions to inhibition or stimulation of appetite and feed intake, are triggered. For these reasons, the relationship between GI chemosensing, gut integrity, and body metabolism in pigs emerges as an interesting subject of functional importance.

The symposium program consisted of invited speakers from outside, related disciplines that brought a unique view to the context of the presented science including implications for swine species. As the first speaker of the symposium, A. P. Liou (Massachusetts General Hospital, Charlestown, MA) provided an overview of the complex biology of enteroendocrine cells, focusing on the ability of different cell subtypes to directly sense lipids, proteins, and carbohydrates through GPCR-mediated mechanisms that are linked to the release of GI hormones (Liou, 2013). Reviewed studies evidenced that the scarcity and scattered distribution of endocrine cells in the GI mucosa and the coexistence of direct (i.e., via endocrine, cell-surface GPCR) and indirect (i.e., via nonendocrine, neighbor enterocytes) chemosensing pathways are limiting our capacity to clarify the mechanistic functioning of enteroendocrine cells. For these reasons, experimental approaches to address the contribution of enteroendocrine cells to GI chemosensation were proposed and briefly discussed.

At the present time, most of the scientific evidence on nutrient sensing has been garnered for glucose and glutamate (Glu). The second speaker of the symposium, K. Torii (Institute of Innovation,
Ajinomoto Co., Inc., Kanagawa, Japan), discussed Glu sensing in the oral cavity and GI tract, signal integration by the brain, and the resulting changes in efferent nerve activity that control physiological and metabolic responses to ingested Glu (Bannai and Torii, 2013). A number of metabotropic Glu receptors, a calcium-sensing receptor, and the umami taste receptor were identified as the GPCR that jointly mediate detection of Glu and other amino acids in the mouth (i.e., taste sensation) and possibly in many other compartments of GI tract (i.e., visceral sensation). In spite of this, distinct signaling pathways and patterns of brain activation are induced by gastric and intestinal sensations elicited by Glu. Although less surprising, similar differences appear to exist among macronutrients, including glucose and lipids. In addition to discussing the impact of oral and postoral amino acid detection on protein digestion, the speaker presented the notion that visceral nutrient sensing contributes to create preference for the flavor associated with the same nutrients, a paradigm called conditioned flavor preference.

The third speaker, D. Burrin (USDA Children’s Nutrition Research Center, Baylor College of Medicine, Houston, TX) reviewed the emerging role that bile acids play as nutrient signaling molecules, highlighting their regulatory effects on bile acid homeostasis, energy metabolism, and gut integrity (Burrin et al., 2013). In particular, details were provided regarding bile acid-sensing receptors (i.e., farnesoid X receptor and membrane-type receptor for bile acids or TGR5) and associated signaling pathways controlling the secretion of GI hormones, namely fibroblast growth factor (FGF) 19 and glucagon-like peptides (GLP)-1 and -2, which are the likely mediators of the evolving metabolic and physiological actions of bile acids. Among other functions, these hormones are implicated in the regulation of feed intake (i.e., FGF19 and GLP-1), GI motility (i.e., GLP-1 and GLP-2), and intestinal mucosal growth and functioning (i.e., GLP-2). For this reason, the speaker identified GI chemosensing as an area of future investigation to guide the development of therapies against weaning-induced enteric dysfunction in pigs.

The fourth presentation of the symposium, given by J. D. Kaunitz (West Los Angeles Veteran Administration Medical Center, Brentwood Biomedical Research, Center for Ulcer Research and Education, and University of California, Los Angeles, David Geffen School of Medicine, Los Angeles, CA), focused on the relationship between GI nutrient sensing and the physiological mechanisms implicated in the maintenance of the intestinal barrier function (Kaji et al., 2013). The epithelium of the upper small intestine is protected against sudden changes in acidity of the luminal contents by defense mechanisms that comprise premucosal (i.e., secretion of mucus and bicarbonate), mucosal (i.e., buffering of intracellular pH), and submucosal (i.e., regulation of blood flow) factors. Ingested nutrients are potent regulators of these protective factors. For instance, Glu and nucleotides were shown to improve the barrier function of the duodenal mucosa by inducing the secretion of GLP-2 via activation of the intestinal umami taste receptor. This effect was amplified by bile acids (i.e., through TGR5 activation) or inhibitors of the serine protease dipeptidyl peptidase IV, the enzyme that degrades GLP-2, among other gut peptides. In view of these notions, the speaker suggested that targeting GI nutrient sensing may illuminate opportunities for improving the barrier function of the gut.

The fifth speaker, O. J. Mace (Heptares Therapeutics, Welwyn Garden City, U.K.), provided a review of the emerging molecular pathways by which GI chemosensing is implicated in the regulation of nutrient transporters and absorption (Mace and Marshall, 2013). The speaker developed the compelling concept that mucosal chemosensation confers the gut with the capacity to discriminate luminal nutrients and regulate absorption based on nutrient availability and energy demands of the intestines and body. More specifically, evidence reviewed indicates that nutrient-sensing GPCR, such as the sweet and umami taste receptors, modulate the expression or activity of nutrient transporters at the brush border membrane, either directly through activation of downstream effectors (i.e., phospholipase C and protein kinase C) or indirectly through the release of gut hormones from enteroenodocrine cells (GLP-1 and -2). Consequently, the speaker predicted that research aiming to modulate nutrient sensors may uncover venues for influencing nutrient absorption and energy homeostasis in pigs and other farm animals.

The sixth speaker, R. E. Steinert (University of Adelaide, Adelaide, Australia), discussed the impact of luminal nutrients on the secretion of GI hormones that are involved in the control of appetite and food intake (Steinert et al., 2013). Special attention was given to the nutritional factors that induce the secretion of ghrelin, cholecystokinin (CCK), GLP-1, and peptide tyrosine tyrosine (PYY) and the mechanisms that mediate their orexigenic (i.e., ghrelin) or anorexigenic actions (i.e., CCK, GLP-1, and PYY). Although targeting the secretion of gut peptides may offer opportunities for managing feed intake, the speaker concluded that more research concerning GI hormones in livestock is required before such an expectation can be realized.

As the last speaker of the symposium, J. E. Pettigrew (University of Illinois, Urbana, IL) was charged with integrating developments on GI chemosensing to identify research needs and potential practical interventions for improving pig productivity, health, and/or efficiency.
The authors proposed 5 areas in which further investigation targeting GI chemosensors may prove beneficial for the swine industry. These areas are 1) promotion of intestinal growth at weaning, which could lead to improved GI integrity and health, 2) enhancement of the barrier function of the intestinal mucosa, which could result in reduced mucosal inflammation and improved animal health, 3) stimulation of appetite and feed intake, which could greatly benefit piglet performance at weaning, 4) amplification of insulin secretion and sensitivity, which may be especially useful in lactating sows to improve subsequent reproduction, and 5) manipulation of enteric fermentation to link gut microbiota with feed intake and reproductive function through production of short-chain fatty acids.

Over the last few years, it has become clear that in addition to digesting and absorbing nutrients, the GI tract operates as a sensory organ that, through gut–gut and gut–brain signaling pathways, mediates the orchestration of physiological and metabolic responses required to maintain homeostasis. The preconference symposium “Gut chemosensing: Integrating nutrition, gut function, and metabolism in pigs” provided a comprehensive overview of the GI chemosensory system, the implicated cellular and molecular signaling cascades within the gut and among the gut, the brain, and other organs, and the implications for the physiology and metabolism of animals and humans. In addition, the symposium served to stimulate further research and discussion as to whether targeting GI chemosensation can guide the development of practical strategies for improving the productivity and efficiency of the swine industry.

**LITERATURE CITED**