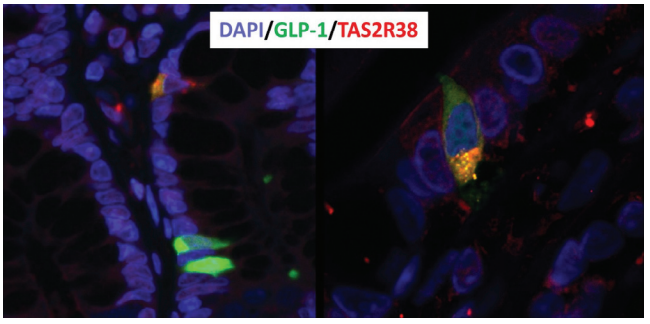
that this receptor along with other known receptors, found on the enteroendocrine L-cells, are potential therapeutic targets for treating type 2 diabetes, for example, through drugs that can induce the release of GLP-1 by activating these receptors to mimic the high postprandial GLP-1 levels observed in bariatric surgery patients, which is thought to be responsible for the essentially immediate diabetes remission for majority of patients. A major advantage of targeting these lumen facing receptors is that potential drug molecules do not need to enter the systemic circulation for a therapeutic benefit, potentially minimizing their side effects.



Immunohistochemical staining of human ileum tissue with TAS2R38 and GLP-1 antibodies.

Sa1834

Long Noncoding RNA PTENP1 Competes With miR-29b to Regulate JAM-A Expression and Intestinal Epithelial Barrier Function

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Gut epithelial barrier protects the subepithelial tissue against a wide array of noxious substances in the lumen, and its integrity and normal function depend on specialized structures composing different intercellular junctions including tight junctions (TJs). The constituent complexes of TJs undergo continuous remodeling and turnover, but the exact mechanism underlying this process remains to be fully investigated. MicroRNAs (miRNAs) and long noncoding RNAs (lncRNAs) regulate expression of different genes and are involved in many aspects of cellular functions. Unlike miRNAs that function as potent post-transcriptional repressors for target mRNAs, the exact biological functions of lncRNAs and their mechanisms remain largely unknown, especially in maintenance of the gut epithelial integrity and barrier function. In this study, we determined the role of the lncRNA PTENP1 in the regulation of TJ expression and further examined its interaction with miRNA-29b (miR-29b). **Methods:** Studies were conducted in Caco-2 cells, and expression of PTENP1 and miR-29b were determined by real-time quantitative (q) PCR and fluorescent *in situ* hybridization (FISH) assays. Loss-of- and gain-of-functions of PTENP1 and miR-29b were completed by transfection with the specific PTENP1 siRNA (siPTENP1) or anti-miR-29b oligonucleotides (anti-miR-29b) and by ectopic overexpression of the *PTENP1* gene or miR-29b precursor (pre-miR-29b). The barrier function was examined by transepithelial electrical resistance (TEER) and paracellular trace flux assay using fluorescent dextran. **Results:** PTENP1 was distributed in both the nucleus and cytoplasm but miR-29b was predominantly located at the cytoplasm as measured by FISH assays. PTENP1 silencing by transfection with siPTENP1 decreased the expression levels of JAM-A (by ~85%), although it failed to alter expression of TJs ZO-1 and ZO-2. Decreased levels of JAM-A by PTENP1 silencing compromised the barrier function as indicated by a decrease in TEER values and an increase in the levels of paracellular flux of dextran. In contrast, ectopic PTENP1overexpression induced JAM-A expression and enhanced the epithelial barrier function. On the other hand, ectopically expressed miR-29b by transfection with pre-miR-29 decreased JAM-A protein levels and disrupted epithelial barrier dysfunction. miR-29b directly bound to the JAM-A mRNA and repressed its translation without effect on total JAM-A mRNA levels. Interestingly, PTENP1could function as sponge antagomirs of miR-29b, since it associated with miR-29b as measured by biotinylated miR-29b pull-down assays. **Conclusion:** These results indicate that 1) PTENP1 is a novel enhancer of JAM-A expression; 2) miR-29b inhibits JAM-A translation; and 3) interaction between PTENP1 and miR-29b plays an important role in the regulation of JAM-A expression and epithelial barrier function.

Sa1835

Effect of Dietary Lipid, Fiber Type, and Particle Size on the Gastrointestinal Endocrine Function and Nutrient Utilization in Growing Pigs

Milena Saqui-Salces, Zhaohui Luo, Brian J. Kerr, Pedro E. Urriola, Gerald C. Shurson

Dietary lipid and fiber play an important role on gastrointestinal (GI) endocrine function. In addition to diet composition (DC), particle size (PS) has been suggested to be an important factor affecting nutrient digestibility and GI function. To determine the role of insoluble (corn dried distillers grains with solubles) or soluble dietary fiber (soybean hulls) sources on GI endocrine function, we fed growing pigs diets of different composition that were fine (374 µm) or coarsely (631 µm) ground. Animal protocols were approved by the Iowa State University Institutional Animal Care and Use Committee. Diets were formulated to meet metabolizable energy (ME) and standardized ileal digestible amino acid requirements of pigs. Diets were: 1) CSB: corn and soybean meal control + 0.3% soybean oil diet (7.2% neutral detergent fiber (NDF); 4.6% ether extract (EE), 16.4% crude protein (CP)) 2) DDGS: CSB + 35% dried distillers grains with solubles (13.7% NDF, 6.2% EE, 17.3% CP) 3) SBH: CSB + 21% soybean hulls + 3.3% soybean oil (20% NDF, 6.8% EE, 16.4% CP) Pigs were individually housed and fed the diets for 49 days (n = 8 per dietary treatment). Total feces and urine were collected from day 21 to day 24 and pooled within individual pig for determination of dry matter, NDF, EE and protein digestibility. Blood samples were obtained on the last day of the experiment after overnight fasting. Plasma was analyzed for gastrin (Gas), insulin (Ins), gastric inhibitory polypeptide (GIP), glucacon-like peptide 1 (GLP-1), and total bile acids (TBA). Data were analyzed using SAS and GraphPad Prism. There were no differences on food intake or body weight gain among dietary treatments. NDF and EE intake correlated negatively with protein digestibility ($P < 0.001$, $r = -0.628$ and $P = 0.004$, $r = -0.408$, respectively). There were no effects of DC or PS on plasma concentration of GLP-1 and GIP. In accordance with the reported association of Gas secretion with dietary protein, we found the highest Gas levels in plasma of pigs fed the coarse DDGS diet, which had the highest protein content. Feeding fine and coarse CSB diets resulted in similar Ins levels, while PS had a differential effect on DDGS and SBH diets: Ins was higher in fine than coarse DDGS ($P = 0.002$) and lower in fine than coarse SBH ($P = 0.009$). Although GIP and GLP-1 levels were strongly correlated ($P \leq 0.001$, $r = 0.74$), GIP correlated with ME and digestible energy, but no correlations were found for GLP-1. TBA were higher in pigs fed DDGS than SBH ($P = 0.02$), with no effect of PS. TBA correlated with gross energy intake ($P = 0.04$, $r = 0.299$), EE digestibility ($P = 0.006$, $r = -0.390$), and net protein utilization ($P = 0.01$, $r = -0.365$). **Conclusion:** Dietary fiber and lipid in non-purified swine diets influence protein utilization and plasma TBA. Insulin secretion was affected by diet composition and particle size.

Sa1836

Impact of High-Fiber Diets of Different Fermentability on Intestinal Cell Differentiation

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High-fiber diets are prescribed as life style strategies to patients to reduce the incidence or severity of gastrointestinal (GI) inflammatory diseases. Long-term feeding of high fiber diets increases villus height, goblet cell number, epithelial cell proliferation, and cell turnover rate. Studies of the effect of fiber on the intestinal epithelium have used purified fiber sources that may not model the effect of complex, common diets. The effect of fiber on cell lineages other than goblet cells has not been reported. We hypothesized that high fiber diets modulate the intestinal epithelilal differentiation signaling favoring the development of secretory cells at the expense of absorptive cells. We analyzed the changes in proliferation, Notch and Wnt signaling induced by diets including fiber sources with different fermentability. Procedures were approved by the University of Minnesota Institutional Animal Care and Use Committee. Wheat straw (WS), corn dried distillers grains with solubles (DDGS), and soybean hulls (SBH) were evaluated as fiber sources that were added (23%, 55% and 30% respectively) to a basal corn-soybean meal diet to obtain similar (16.7 ± 0.1%) neutral detergent fiber content. *In vitro* dry matter fermentabilities of the fiber sources were 22.4%, 71.8% and 84.6% respectively. Twelve pigs per diet treatment were fed the equivalent amount of 2.5% of body weight in two equal meals for 13 days. Ileum samples were collected for histology and gene expression analysis after euthanasia. Goblet cell number and mucin 2 expression were higher in pigs fed WS and DDGS diets compared with those fed the SBH diet. The expression of the enterocyte marker fatty-acid binding protein (Fabp) was lower in pigs fed DDGS compared with WS and SBH. We found no differences in lyzosyme and chromogranin A gene expression. Notch-related genes showed similar expression of Atoh1 when DDGS and WS diets were fed, but were significantly lower for pigs fed SBH compared with other diets. Hes1 was higher when the SBH diet was fed compared with WS and DDGS diets. Feeding DDGS resulted in the lowest expression of Hes1 (trend, $P=0.06$) and Fabp ($P \leq 0.05$), suggesting a decrease in enterocyte population. The expression of delta ligand 4 was lower ($P \leq 0.05$) in pigs fed the DDGS diet compared with those fed WS and SBH diets. We did not observe differences in the expression of the progenitor cell markers Lgr5, Olfm4 or Bmi1. Proliferation evaluated by Ki-67 staining was higher in pigs fed DDGS compared with those fed WS and SBH diets ($P \leq 0.05$), but no different among WS and SBH. Wnt3a expression was 2-fold higher in samples from pigs fed DDGS compared with those from WS, and 10-fold higher compared with SBH. These observations support our hypothesis that high fiber diets modulate the intestinal stem cell niche in ways that are dependent of the fiber biochemical characteristics.

Sa1878

Metabolic Syndrome and the Risk of Barrett's Esophagus in White Males

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Background & Aims: Few studies have examined the association between metabolic syndrome and the risk of Barrett's esophagus (BE). Whether metabolic syndrome confers a risk greater than the sum of its components is unknown. We investigated associations between metabolic syndrome, the individual components of metabolic syndrome, and BE risk in White males. **Methods:** We conducted a case-control study among eligible symptomatic patients scheduled for elective esophagogastroduodenoscopy and a sample of patients eligible for screening colonoscopy recruited at primary care clinics. Metabolic syndrome was defined as the presence of at least three of: high waist-to-hip (WHR) ratio, hypertriglyceridemia, low high-density lipoprotein (HDL) cholesterol, hypertension, or diabetes. We used multivariate logistic regression to calculate adjusted odds ratios (OR) and 95% confidence intervals (95%CI). **Results:** There were 244 BE cases, 209 colonoscopy controls and 615 endoscopy controls. Comparing BE cases with the combined control group, metabolic syndrome was statistically significantly associated with BE risk (OR=1.59, 95%CI 1.05-2.40) and there was a dose effect with increasing number of metabolic syndrome components (P trend < 0.001); when all 5 components were present, the OR was 2.61 (95%CI 1.14-5.99). We found that among the metabolic syndrome components, high WHR, hypertension and hypertriglyceridemia were associated with increased risk of BE, whereas lowered HDL cholesterol was associated with lower risk of BE. When we compared cases with the control groups separately, metabolic syndrome was associated with BE for comparisons with endoscopy controls (OR= 1.67, 95%CI 1.10-2.55) but not colonoscopy controls (OR=0.87, 95%CI 0.49-1.54). Associations with the individual components of metabolic syndrome also depended on the comparison group. **Conclusions:** Metabolic syndrome may be associated with BE in persons undergoing endoscopy. However, not all components of metabolic syndrome contribute to risk equally or in the same direction.