tract is not known. In this study, we tested the hypothesis that sucrose may increase the expression of cryptdin-5 and cryptdin-7. Methods: To test this hypothesis, we compared cryptdin-5 and cryptdin-7 expression in the small intestine (proximal, mid and distal 1/3), colon and liver by real-time PCR. Twenty-four rats were randomized into 1 of 3 treatments consisting of 24h access to regular rat chow (Control), uncooked red kidney bean-supplemented chow (25%) (RKB) or uncooked red kidney bean-supplemented chow (25%) + sucrose in the drinking water (Sucrose) followed by tissue collection. Data generated by real-time PCR are represented by 2-ΔΔCt values where Ct represents PCR cycle thresholds (Methods 2001;25:402-408). Lower 2-ΔΔCt values represent greater gene expression. Data are mean + SD. Results: 1. In the small intestine, compared with Controls (proximal: 6.72 + 2.4, mid: 2.5 + 1.2, distal: 2.6 + 1.3), cryptdin-5 expression was increased in the Sucrose group across the entire length of the organ (proximal: 3.7 + 0.8, mid: 1.2 + 0.6, distal: 0.7 + 0.5)($p<0.05$); 2. In the liver, compared to Controls (12.6 + 2.0), cryptdin-5 expression was increased in Sucrose (10.8 + 0.9)($p<0.05$); 3. Cryptdin-5 expression was also greater in Sucrose than RKB ($p<0.05$); 4. Similarly, cryptdin-7 expression in the small intestine was greater in Sucrose when compared with Controls ($p<0.05$) but there was only a trend for this effect in the liver (p= 0.7); 5. In addition, cryptdin-7 expression was greater in Sucrose than RKB in the liver ($p<0.05$) but not in the small intestine; 6. There was no effect of sucrose in the colon for either cryptdin-5 or cryptdin-7 expression. Conclusion: Sucrose increased expression of antimicrobial cryptdin-5 and cryptdin-7 in the small intestine and liver. Dr. Lin's research is supported by NIH, VA Research and the Department of Defense.

Su1783

Role of Endogenous GLP-2 in the Intestinal Adaptation to a Chronic High Fat Diet

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BACKGROUND AND AIM: Glucagon-like peptide-2 (GLP-2) is a nutrient-dependent peptide hormone with multiple effects on the intestine, including expansion of the mucosal surface area through stimulation of crypt cell proliferation and enhancement of nutrient digestion and absorption. Effects of GLP-2 occur via the GLP-2 receptor (GLP-2R), a G-protein-coupled receptor, mainly present in the gastrointestinal tract. We sought to determine if GLP-2 is involved in the regulation of the gut morphological changes following chronic high fat (HF) diet METHODS: C57BL6/J mice, fed a high fat diet for six weeks, and the age-matched control animals were injected once a day intraperitoneally (i.p.) with 100 µl of GLP-2 (3-33), a GLP-2 receptor antagonist (30 or 60 ng) or PBS (vehicle control) for four weeks. Plasma GLP-2 concentrations, by ELISA, small intestinal GLP-2R expression levels by real-time RT-PCR and western blot analysis, and intestinal morphometric parameters were determined. Immunohistochemistry for the proliferative and apoptotic markers, respectively Ki67 and caspase-3 was performed. RESULTS: Compare with age-matched control animals, HF fed mice exhibited increase of crypt-villus height, cell number per villus and Ki-67 positive cell number of the crypt region. None difference was seen in the number of goblet cells per villus and in the thickness of the external muscular layer. The chronic exposure to HF diet also caused a significant increase in GLP-2 plasma levels and in GLP-2R intestinal expression. Treatment with GLP-2 (3-33) did not significantly modify the crypt-villus height in control animals. On the contrary, in HF fed mice administration of GLP-2 (3-33) significantly reduced the crypt-villus height, the number of cells per villus as well as the number of Ki-67 positive cells, and it increased the percent of caspase-3 positive cells in the small intestine. CONCLUSIONS: This study suggests that GLP-2 may play a role in the murine intestinal adaptation to HF diet, leading to enhancing energy intake. Prolonged HF diet could induce dysregulation of GLP-2/GLP-2R system. Supported by MIUR, Italy

Su1784

Enteral Deprivation Leads to a Loss of Intestinal Epithelial Barrier Function

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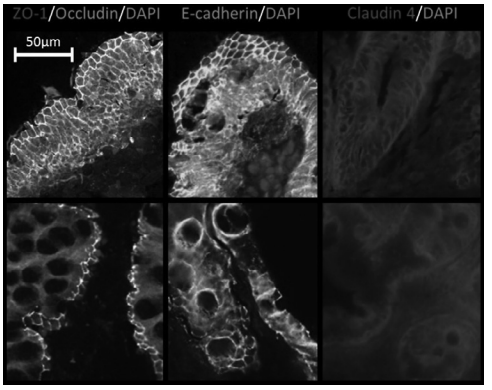
Objective: Total parenteral nutrition (TPN) increases risk of infections versus enteral feeding. As a major source of these infections is the gastrointestinal tract, we hypothesized that underfed mucosa has decreased epithelial barrier function (EBF), and tested this in a series of human resection specimens.. Methods: Small bowel, excluding Crohn's disease, was obtained from pediatric patients (aged 2 days to 19 years) undergoing intestinal resection. EBF was assessed in Ussing chambers for trans-epithelial resistance(TER) and passage of FITC-Dextran(4kD). Immunofluorescence staining was used to evaluate intensity and distribution of tight junctional (TJ) and adherence junctional (AJ) proteins. Abundance of junctional proteins was also measured with Western Immunoblot. Statistical significance for TER used Student T-test. Results: Interestingly, initial examination of specimen(N=22) failed to correlate lack of feeding and TER($p=0.09$). However, in fed samples, TER increased with patient age ($p<0.01$). Therefore results were then stratified by patient's age. Fully fed bowel had significantly higher TER versus unfed bowel in teenagers($p<0.05$). This trend was also observed in infants($p=0.053$). These changes in TER correlated with permeation of FITC-Dextran($p=0.03$). We next correlated these findings with Western immunoblot. There was an increase in protein abundance in unfed patients. To localize these protein, we next looked at immunofluorescence staining. Dramatic declines in staining of ZO-1, occludin, E-cadherin and Claudin-1 were observed in unfed segments. Conclusion: EBF declined in unfed segments of human bowel. This finding may explain increased infectious complications seen in patients not receiving enteral feeds.



Su1785

Differences in the Degree of Cerulein Induced Chronic Pancreatitis in C57BL/6 Mouse Substrains Lead to New Insights in Identification of Potential Risk Factors in the Development of Chronic Pancreatitis

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A frequently used experimental model of chronic pancreatitis (CP) recapitulating human disease is repeated injection of cerulein to mice. C57BL/6 is the most commonly used inbred strain for biomedical research, but widespread demand led to the creation of several substrains with subtly different phenotypes. In this study we found that two common substrains of C57BL/6, C57BL/6J and C56BL/6NHsd , exhibit different degrees of CP with C57BL/6J being more susceptible to repetitive cerulein-induced CP as assessed by pancreatic atrophy, pancreatic morphological changes and fibrosis. We hypothesized that the deficiency of nicotinamide nucleotide transhydrogenase (NNT) protein in C57BL/6J was responsible for the more severe C57BL/6J phenotype but the parameters of CP in NNT expressing transgenic mice created on C57BL/6J background were undistinguished from the wild type C57BL/6J. The highly similar genetic backgrounds but different CP phenotypes of these two substrains presents a unique opportunity to discover genes important in pathogenesis of CP. To exploit this opportunity, we conducted whole mouse genome Affymetrix microarray analysis of pancreatic gene expression of C57BL/6J and C57BL/6NHsd before and after the induction of CP. Differentially regulated gene expression between the two substrains that might be candidates in CP progression included Mmp7, Pcolce2, Itih4 and Vnt. Additionally, we identified several genes associated with the development in CP in both substrains including RIKEN 1810009J06 (trypsinogen5), Ccl8 and Ccl6.

Su1786

Increased Peripheral $Cd19^{+}CD24^{Hi}Cd38^{Hi}$ Regulatory B Cells May Be Involved in the Pathophysiology of Type 1 Autoimmune Pancreatitis

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Background: Autoimmune pancreatitis (AIP) is a newly recognized pancreatic disorder. In 2011, International Consensus Diagnostic Criteria for AIP (ICDC) was published. In this ICDC, AIP was classified into type 1 and type 2. Patients with type 1 AIP have several immunologic and histologic abnormalities specific to the disease, including increased levels of serum immunoglobulin G4 (IgG4) and storiform fibrosis with infiltration of lymphocytes and IgG4-positive plasmacytes in the involved organs. We previously reported that increased numbers of inducible costimulatory molecule (ICOS) (+) regulatory T cells (Tregs) might influence IgG4 production via interleukin-10 (IL-10) in type 1 AIP. In addition to Tregs, it has been reported that regulatory B cells (Bregs) may also produce IL-10, and be involved in the development of various autoimmune diseases such as systemic lupus erythematosus (SLE), immune thrombocytopenia (ITP), and sarcoidosis. However, Bregs has not been investigated in type 1 AIP. On the other hand, depletion of B cells by rituximab (RTX) is effective for treatment of IgG4-related systemic disease such as type 1 AIP. However, in addition to B cell function deleted by RTX, it is unclear whether Bregs are involved in the development of type 1 AIP or not. To clarify the role of Bregs in the pathophysiology of type 1 AIP, we analyzed circulating Bregs in type 1 AIP. Methods: We recruited 21 patients with type 1 AIP on the basis of ICDC for this study. All patients were untreated with corticosteroids. For comparison, we also recruited 14 patients with chronic pancreatitis (CP), 18 patients with pancreatic cancer, and 25 healthy subjects as controls. We analyzed Bregs as $CD19^{+}CD24^{hi}CD38^{hi}$ and $IL10^{+}$ B cells from peripheral blood by flow cytometry. Results: In peripheral blood, $CD19^{+}CD24^{hi}CD38^{hi}$ Bregs were significantly increased in type 1 AIP patients (6.44% ± 3.19%) compared with CP (4.58% ± 2.16%, $P < 0.05$), pancreatic cancer (3.79% ± 1.97%, $P < 0.01$), and healthy control (4.84% ± 2.20%, $P < 0.05$). $IL10^{+}$ B cells were not significantly different from type 1 AIP and healthy control. In untreated type 1 AIP patients, the number of $CD19^{+}CD24^{hi}CD38^{hi}$ Bregs and IgG4 were not correlated ($R = 0.334$, P 0.14). Conclusions: Our data suggested that $CD19^{+}CD24^{hi}CD38^{hi}$ Bregs may be involved in the pathophysiology of type 1 AIP via another mechanism rather than IL-10 production.