Glucagon-like peptide-2 (GLP-2) is an ileum-derived trophic hormone that may be the limiting factor for neonates with SBS. We aimed to study the effect of GLP-2 administration in a novel preclinical model of nSBS with distal resection.

METHODS: Neonatal piglets were block randomized to receive either sham control or a 75% distal intestinal resection with jejunocolic anastomosis, and either saline control or GLP-2 treatment (11 nmol/kg/day). Piglets were pair-fed for 7 days then underwent terminal laparotomy. Structural adaptation was assessed by the change in intestinal length, intestinal weight, and histopathology. Functional adaptation was assessed via Üssing techniques. Quantitative reverse transcription polymerase chain reaction was performed to assess the gene expression of the GLP-2 receptor (GLP-2r) and the insulin-like growth factor-1 (IGF-1) system. Data were analyzed by 2-way ANOVA.

RESULTS: There was no difference in the change in intestinal length. Therapy with GLP-2 augmented remnant bowel weight per length and mucosal weight more than saline control ($p<0.01$), and GLP-2 treatment increased jejunum villus height more than saline control ($p<0.001$). The permeability of both mannitol and polyethylene glycol were decreased with GLP-2 therapy ($p<0.05$). Treatment with GLP-2 decreased IGF-1 expression in the resection group ($p<0.03$) and did not affect IGF-1r or GLP-2r expression.

CONCLUSIONS: Exogenous GLP-2 administration in a translational model of nSBS results in structural and functional adaptation. There is a beneficial increase in absorptive surface area and also a decrease in intestinal permeability. Our findings have implications for neonates with SBS, who most commonly lack ileum and distal intestine.

Intestinal Alkaline Phosphatase Deficiency Leads to Dysbiosis and Bacterial Translocation in the Newborn Intestine

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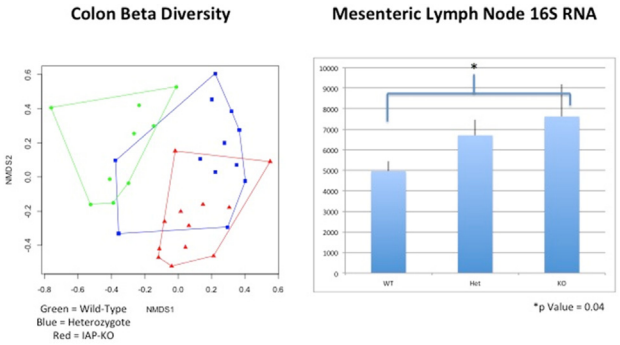
INTRODUCTION: Intestinal alkaline phosphatase (IAP) has been shown to help maintain intestinal homeostasis. Decreased expression of IAP has been linked with pediatric intestinal diseases associated with bacterial overgrowth and subsequent inflammation. We hypothesized that the absence of IAP leads to dysbiosis, with increased inflammation and permeability of the newborn intestine.

METHODS: Sprague-Dawley heterozygote, IAP cross-matched rats were bred. Pups were dam fed ad lib and euthanized at weaning. The microbiotas of terminal ileum (TI) and colon were determined by quantitative reverse transcription polymerase chain reaction (RT-PCR) of subphylum-specific bacterial 16S rRNA, and RT-PCR was performed on TI for inflammatory cytokines. Intestinal permeability was quantified by FITC-dextran permeability and bacterial translocation by quantitative RT-PCR for bacterial 16S rRNA in mesenteric lymph nodes. Statistical analysis was done by chi-square analysis.

RESULTS: All 3 genotypes had similar concentrations of bacteria in the TI and colon. However, IAP-knockout (KO) rats had significantly decreased diversity of bacterial species in their colonic stool compared with heterozygous and wild-type (WT) rats. IAP-KO pups had a 3.9-fold increased iNOS mRNA expression compared with WT (IAP-KO, 3.92 ± 1.36; WT, 1.0 ± 0.27; $p=0.03$). IAP-KO also had a trend toward increased permeability (IAP-KO, 0.297 mg/mL ± 0.2; WT, 0.189 mg/mL ± 0.15 $p=0.07$) and significantly increased bacterial translocation to mesenteric lymph nodes occurred in IAP-KO (IAP-KO, 7,625 relative fluorescent units [RFU]/g ± 3,469; WT, 4,957 RFU/g ± 1,552; $p=0.04$) (Fig).



CONCLUSIONS: Deficiency of IAP in the newborn intestine is associated with dysbiosis and increased inflammation, permeability, and bacterial translocation. Supplemental IAP may be a novel treatment strategy to prevent dysbiosis and bacterial translocation.

Intratumoral Implantation of Vincristine-Loaded Sustained-Release Silk Sponge Is Effective in Tumor Control in an Orthotopic Neuroblastoma Murine Model

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INTRODUCTION: Current treatment of advanced neuroblastoma, the most common pediatric solid extracranial tumor, involves intensive systemic chemotherapy. We hypothesized that intratumoral implantation of a sustained-release chemoagent using silk sponge can control tumor growth.

METHODS: Human neuroblastoma KELLY cells were cultured with different concentrations of vincristine or doxorubicin to determine half maximal inhibitory concentration (IC50). In vitro release profiles of silk sponges loaded with optimal doses were determined. Orthotopic neuroblastoma tumors were established in

immunocompromised mice and assigned the following interventions after the tumor was >300 mm^3 on ultrasound measurement: intra-tumoral implantation of sponges containing (1) vincristine 25 μg (Vin25S); (2) 50μg (Vin50S); (3) doxorubicin 200 μg (Dox200S); (4) 400 μg (Dox400S); or (5) drug-free sponge (CONT), with 8 mice per group. An equivalent dosage of the most effective drug was administered intravenously after sham surgery. Tumor growth was analyzed using ANOVA and logistic regression. Tumor sections were stained with hematoxylin and eosin, TUNEL assay, and Ki67.

RESULTS: The half maximal inhibitory concentration of vincristine was 5.7±2 ng/mL, and for doxorubicin, was 20 ng/mL. Eighteen μg of Vin50S and 25 μg of Dox400S were released immediately in vitro; 18 μg and 100 μg, respectively, were released over the next 20 days. The number of days for tumors to reach >1,000 mm^3 (NODTR1000) after intervention was similar between CONT (10.62±3.3 days), Dox200S (7.43±2.9 days), and Dox400S (9.25±3.8 days) (p=0.16-0.57). The NODTR1000 was longer for animals treated with Vin25S (22.5±13.8 days) (p=0.017) and Vin50S (30.45±15.5 days) (p=0.002) compared with CONT. The NODTR1000 was similar between CONT and intravenous vincristine 25 μg (Vin25IV) treatment alone (9±3 vs 10.62 days) (p=0.35), but vincristine 50 μg (Vin50IV) was superior to CONT (13.25±1 vs 10.62 days) (p=0.037). Vin25S was more effective than Vin25IV (p=0.028); Vin50S was superior to Vin50IV (p=0.014). Histology of Vin50S-treated tumor showed necrosis adjacent to the sponge, with viable and apoptotic cells beyond necrosis.

Agent	Days until tumor >1,000 mm	Compared with control foam, p value
Control foam	10.62 ± 3.3	Reference
Dox200S	7.43 ± 2.9	0.156
Dox400S	9.25 ± 3.84	0.545
Vin251V	9 ± 3	0.349
Vin25S	22.5 ± 13.8	0.017
Vin501V	13.25 ± 1	0.037
Vin50S	29.5 ± 15.5	0.002

CONCLUSIONS: Intratumoral implantation of vincristine-loaded, sustained-release silk sponge was effective in tumor control and superior to equivalent intravenous administration.

Lactobacillus rhamnosus Is Protective Against Experimental Necrotizing Enterocolitis in the Setting of *Cronobacter sakazakii* Infection

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INTRODUCTION: Necrotizing enterocolitis (NEC) is a gastrointestinal emergency of neonates, with a mortality of 15% to 30%. Clinical administration of prophylactic *Lactobacillus rhamnosus* (LR) may decrease NEC; however, underlying mechanism(s) are unknown. *Cronobacter sakazakii* (CS) is implicated in human NEC. Tight junctions (TJ) are protein complexes conferring epithelial barrier integrity. We hypothesized that LR is protective against experimental NEC when CS is present.

METHODS: Caco-2 cells were pretreated with LR with and without CS. Timed transepithelial resistance (TER) was measured. Transmembrane flux of fluoroscein isothiocyanate (fitc)-dextran was used to assess permeability. In vivo effects of LR were analyzed using the CS rat pup model of NEC. Pups were subjected to hypoxia and CS-formula feeding with and without LR. Controls were fed clean formula. Fitc-dextran permeability was measured. Intestinal injury scoring and TJ protein analysis (Western, immunofluorescence) were performed. Results were analyzed with *t*-test and ANOVA.

RESULTS: *Lactobacillus rhamnosus* increased TER compared with controls and CS; however, the greatest increase (93%) was seen in Caco-2 cells receiving LR plus CS ($p<0.046$). The LR- and CS-treated monolayers were less permeable to fitc-dextran (p=0.01). Rats in the CS group demonstrated significantly higher intestinal injury scores than either the LR or LR plus CS groups (p=0.011, p=0.0002, p=0.21, respectively). Fitc-dextran permeability was increased in pups that received LR or CS alone; no difference was demonstrated for LR plus CS pups compared with controls (p=0.03, p=0.058, p=0.79, respectively). Immunofluorescence revealed increased internalization of the TJ ZO-1 in the CS group, compared with LR plus CS pups.

CONCLUSIONS: Our data suggest that LR is protective against experimental NEC in the setting of a CS infection, and that probiotics alone may cause an increase in permeability.

Matrix Metalloproteinase-8 as a Biomarker of Complicated Appendicitis

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INTRODUCTION: The conventional paradigm that appendicitis requires an appendectomy is being challenged by selective conservative management. This prospective cohort study aimed to determine if matrix metalloproteinase-8 (MMP-8), other MMPs, and tissue inhibitors of metalloproteinase (TIMPs) are candidate biomarkers for estimating the probability of complicated appendicitis.

METHODS: Pediatric patients presenting to the emergency department with suspected appendicitis were enrolled. The primary outcomes variable was complicated appendicitis, defined by an abscessed, perforated, or gangrenous appendix. Matrix metalloproteinase and TIMP serum protein concentrations were measured. Receiver operating characteristic curves were constructed to determine the ability of each candidate biomarker to estimate the