Neonatal probiotic administration has long-lasting effects on gut permeability responses to stress in adult pigs born to sows treated with antibiotics around parturition

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around parturition (d-10 till d+21). Offspring (1 litter) were sacrificed during the suckling period (d14, d28) and after weaning (d42), and ileal tissues were collected. HSF27, HSF60, HSP60, and HSP70 were quantified by quantitative real-time PCR (Q-PCR) as the expression levels were determined by western blotting and tissue levels expressed relative to β-actin. Enzyme activity of intestinal alkaline phosphatase (IAP), an HSP-like protein crucial in the detoxification of pro-inflammatory bacterial components (e.g. LPS) was also investigated in comparison. Results: Ileal tissue levels of HSP27 in offspring were unaffected by antibiotic treatment of mothers. HSP60 tended to be (p<0.07) and HSC70 was (p<0.05) higher in offspring born to ATBQ sows than in CTL (p<0.01) and this difference was significant (p<0.01) at day+21 and day+42 (39%) (treatment by age interaction, p<0.05). Real protein expression of HSF1 in offspring was unaffected by ATBQ treatment of sows or offspring post-natal age. In comparison to HSPs, IAP activity displayed a treatment by time interaction: it was twice lower at day 14 in offspring born to ATBQ sows than in CTL (p<0.01) with no differences at days 28 and 42. A treatment by time interaction in perinatal antibiotic treatment has a differential consequences on protein expression of intestinal heat shock proteins in their offsprings in the swine. This did not involve the modulation of HSP gene transcription factor HSF1, suggesting alternate regulatory mechanisms. Collectively, the data suggest complex, time-dependent interactions between colonizing microorganisms and local microbiota on the modulation of intestinal HSP expression. Changes in offspring intestinal microbiota and long-term effects of perinatal antibiotic treatment on offspring intestinal HSP family are being investigated.

**Tu2019**

**Neonatal Probiotic Administration Has Long-Lasting Effects on Gut Permeability Responses to Stress in Adult Pigs Born to Sows Treated With Antibiotics Around Parturition**

Jean-Paul Lalles, Dominique Bertacchini, Gerard Savary, Hauke Smidt

Background: Periapartum antibiotics are thought to have long-lasting negative consequences on intestinal barrier function, immune system development and long-term health, e.g. allergy. Various kinds of stress (e.g. nutrition, environment) can be deleterious to gut barrier function. We have shown that broad-spectrum antibiotic treatment of mothers alters various facets of gut barrier in their offspring during development and in adulthood. We tested with this model the hypothesis that early administration of a probiotic to offspring can modulate gut barrier function in young adults depending on diet and stressor.

Methods: Sows (n=20) received amoxicillin orally (40mg/kgBW/d) around parturition (d-10 till d+21). Offspring (1/litter) were reared under the sow until weaning (dPND21). They were reared with a similar diet until dPND14. Then, each group was split into two halves. One half in each group remained on the control (low fat, LF 2%) diet while the other halves were fed a high fat (HF, 11%) diet. Piglets were sacrificed at dPND19 and pieces of ileum and colon were collected for anatomical and functional studies. PCR and qPCR-based treatment included control, oxidative stress (monochloramine) and mast cell degranulation stress (48/80). Mucosal para- and trans-cellular permeabilities (PCP, TCP) were measured using FD4 and HRP, respectively. Results: Early PK/βG supplementation had no effect on oxidative ileal and colonic permeability. Ileum from PROB pigs fed LF diet displayed reduced PCP in oxidative (p<0.05) and degranulation (p<0.10) conditions. No differences between PROB and CTL were seen for colonic TCP. Contrasting with this, ileal TCP was much higher (x2 to 3) in PROB pigs with both LF and HF diets (p<0.01) after degranulation stress. An interaction (p<0.05) between early PROB treatment and adult diet was observed for TCP after oxidative stress (decrease with LF, increase with HF). Coloric TCP was increased after both oxidative and degranulation stress in PROB pigs fed LF (but not HF) diet (p<0.05). Conclusion: Our data in the swine model suggest that probiotics provided early to gut barrier-disturbed offspring could protect to mothers treated with broad-spectrum antibiotic around parturition can contribute to long-term modulation of gut barrier function following stress. However, the responses are complex and depend on gut diet, and diet composition and type of stressor in adulthood. Work in progress is to investigate long-term changes in gut microbiota composition induced by early probiotic administration.

**Tu2020**

**Chronic Ingestion of Lactose: Malabsorber Host and Intestinal Microbiota Adaptations**

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Introduction: Physiological and metabolic consequences of chronic lactose ingestion by malabsorbers are poorly described. In order to highlight the suspected microbiota dysbiosis and adaptations, intestinal microbiota and host’s physiology have been very much studied in hypolactasia rats, over a prolonged ingestion of lactose. Wistar male rats ingested a diet containing 25% of lactose (L25 group) or 25% of sucrose (HF group) from birth. Ileal and colonic TCP, SCFA blood concentrations significantly increase at day 1, then stabilise at day 2. At last, MPO activity and mucosa histology undergo a transitional inflammation at days 1 and 2 in the L25 group, especially with an MPO activity higher in proximal colon (p<0.04) and distal colon (p<0.03), a smaller ratio (mucosa area/section area) (p<0.03) and a higher ratio ( goblet cells/colonicocytes) (p<0.04). Conclusions: Prolonged lactose ingestion modifies both composition and activity of the intestinal microbiota, stimulating a turn-over of the lactose colorectal microbiota and a reduction of the mucosa inflammation. These findings underline the role of intestinal host-eutroph and suggest that small but regular amounts of lactose could improve the malabsorber host’s tolerance.

**Tu2021**

**Intestinal Epithelial Cells Apically Secrete Exosomes Taken up by Neighboring Epithelial Cells and Bacteria**

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Background and Aims: Exosomes are small membrane vesicles of endosomal origin secreted from a variety of cell types. Exosomes contain proteins, mRNAs, and microRNAs, and may play roles as mediators of cell-to-cell communication. Herein, we characterized exosomes secreted by intestinal epithelial cells and investigated exosome uptake by epithelial cells and bacteria. Methods: Release of exosomes from Caco2-BBE monolayers grown under basal or inflammatory conditions was evaluated by differential ultracentrifugation after growth of such cells in conditioned apical and basolateral media. Exosome size and morphology were assessed employing light-scattering techniques, atomic force microscopy, and scanning electron microscopy. The exosomal marker CD63 was used to assess the purity of exosome preparations. Fluorescent microscopy was employed to visualize intracellular uptake of secreted Caco2-BBE exosomes (fluorescently labeled by electroporation of FITC-siRNA complexed with PEI) by macrophages RAW264.7, Caco2-BBE monolayers, and bacteria. Results: Caco2-BBE cell monolayers released vesicles 80-150 nm in diameter bearing the exosomal marker CD63 from the apical side and from the basolateral side. The extent of such release was increased when the monolayers were pre-stimulated with LPS (10ng/mL). For 4h). FITC-labeled secreted exosomes from Caco2-BBE monolayers were taken up by such monolayers (70%), macrophages (30%), and bacteria. Conclusion: Caco2-BBE cell monolayers specifically secrete exosomes toward the luminal side of the intestinal cell monolayer. Such apical exosome secretion by intestinal epithelial cells is a regulated process. Secreted exosomes may fuse with neighboring epithelial cells, thus transferring membraneous and cytoplasmic contents from one cell to another, and may also be taken up by bacteria of the colorectal microbiota. Secreted exosomes may play key roles in epithelial cell-cell and epithelial cell/bacterium communication under pathophysiological conditions.

**Tu2022**

**Role of Food and Enterobacteria in the Formation and Prevention of Small Intestinal Lesions Induced by Enteric Coated Aspirin in Cats**

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**BACKGROUND/AIM:** Recently, low-dose aspirin (ASA) has been widely used as the first-choice drug for the prophylaxis and treatment of thrombosis. Enteric-coated (EC) ASA has been used to limit gastric lesions as a side effect, but even low doses of EC ASA often cause mucosal damage in the small intestine in humans. However, there are few studies on the role of food and enterobacteria in the formation and prevention of the intestinal damage. We examined the effect of various foods and antibiotics on the formation of intestinal lesions induced by EC-ASA in cats. METHODS: Adult cats were used (4 to 6 animals per group). Several types of diet containing dietary fiber (DF) at various percentages were given to the animals once daily during the experiment. In the fed group, 1 EC-ASA tablet (containing 100 mg ASA) was administered p.o. once daily after the morning meal for 7 days, whereas in the fasted group, EC-ASA was given in the morning after an overnight fast. The animals were sacrificed 24 h after the final EC-ASA dose and mucosal lesions in the GI tract were examined. RESULTS: 1) EC-ASA tablets did not cause any visible lesions in the stomach. In the fasted condition, EC-ASA given orally once a day for 7 days caused mild ulcers in the duodenum and small intestine; the mean lesion area (MLA) was 0.17±0.07 cm2 and 0.23±0.07 cm2 respectively. When EC-ASA was given after feeding of dry food (Dry) containing 2.8% DF, the duodenal and intestinal lesions were markedly increased, the MLA was 0.9±0.11 cm2 and 1.1±0.31 cm2 (P<0.01 and 0.05 vs. fasted). 2) In the cats ate canned food (Can) containing 0.4% DF, the lesions were markedly decreased; the MLA was 0.01±0.03 cm2 and 0.08±0.05 cm2 (P<0.001 and 0.01 vs. Dry). Results: The addition of insoluble DF (cellulose) 6% to the food appeared to ameliorate the lesions again; the MLA was 0.32±0.20 cm2 and 0.69±0.32 cm2 (P<0.05 vs. Can), respectively. The addition of soluble DF (pectin 6%) to dry food markedly decreased the lesions; the MLA was 0.07±0.07 cm2 and 0.10±0.03 cm2 (P<0.001 and 0.01 vs. Dry). Neomycin (20 mg/kg, p.o.) given 30 min before morning meal (Dry) for 7 days decreased the lesions in the fasted condition, the MLA was 0.13±0.03 cm2 (P<0.05 vs. Can). Conclusions: Adverse effects of EC ASA on the duodenal and intestinal mucosa depend on the feeding conditions (fasted or fed) when EC ASA was administered, i.e., the lesions were markedly increased when EC ASA was given after feeding of dry food. 2) Contents of diet, especially insoluble DF such as cellulose and soluble DF such as pectin, play an important role in the formation and prevention of duodenal and intestinal lesions induced by EC ASA. 3) Gam negative enterobacteria such as E. coli may play some role in the formation and aggravation of intestinal lesions.