POSTER ABSTRACTS

Poster Abstract 1.

EFFECT OF GEOGRAPHICAL VARIATIONS IN THE INTESTINAL MICROBIOTA OF AMERICAN AND EUROPEAN POPULATIONS ON RAID-MONITOR PERFORMANCE

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ABSTRACT

Objectives. Dysbiosis, an unbalanced microbiota composition, has been widely described in Inflammatory Bowel Disease (IBD) patients. This knowledge was used to develop RAID- Monitor, a non-invasive faecal test of bacterial abundance to assess endoscopic activity in IBD. Since this test was developed from a Spanish cohort, we sought to determine its performance in samples from North America patients.

Methods. Two cohorts consisting of 22 IBD patients from the USA (17 Crohn's disease, CD and 5 Ulcerative Colitis, UC) and 16 IBD from Spain (5 CD and 11 UC) were recruited. All patients had active disease (based on symptoms and endoscopy scores). The relative abundance of nine bacterial markers was determined on fecal samples by qPCR.

Results. The abundance of *Faecalibacterium prausnitzii*, *F. prausnitzii* phylogroup II, *Ruminococcus* sp. and *Methanobrevibacter smithii* were significantly lower in American CD patients than in European ones. Despite these differences, RAID-Monitor was able to assess correctly the endoscopic activity of 88.2% of CD patients from Boston.

In UC patients, only *M. smithii* abundance was significantly different, showing an important similarity between both populations for the others bacterial markers analyzed. In this case, RAID-Monitor was able to correctly assign activity on 80.0% of Boston UC patients

Conclusion. American IBD patients showed lower abundance of those bacterial markers considered to be beneficial, such as *Ruminococcus*, *F. prausnitzii* and its phylogroups. Nevertheless, despite the observed differences between populations, RAID-Monitor test was able to correctly classify IBD patients for endoscopic activity regardless of geographic origin.

KEYWORDS

Intestinal Microbiota, Inflammatory Bowel disease, RAID-Monitor, activity assessment

Poster Abstract 2.

MEALS, MICROBIOTA & MENTAL HEALTH OF CHILDREN AND ADOLESCENTS AN OBSERVATIONAL LONGITUDINAL CASE CONTROL STUDY

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ABSTRACT

Recent studies indicate an interaction between diet, intestinal microbiota, gut permeability and mental health in relation to factors such as chronic low-grade inflammation. The aim of this novel observational longitudinal case-control study is to investigate associations between dietary factors, intestinal microbiota, intestinal permeability and mental health among children and adolescents diagnosed with mental health disorders and compare with healthy controls and siblings to identify potential patterns. All children and adolescents referred to the only outpatient psychiatric clinic in Iceland, over a one-year period, will be offered to participate (N=150) (5-15y). Two control groups will be used; same parent siblings close in age (N<150) as well as age and sex-matched children from the same postal area (N=150). A three-day food diary, rating scales for mental health and multiple questionnaires will be completed and biological samples (blood, saliva, urine, faeces, deciduous teeth) will be collected. The scientific value is based on a good quality study design, a longitudinal approach and possibilities for subsequent personalized dietary and lifestyle interventions in subgroups. The originality consists in the new way of approaching mental health conditions/disorders as a group with simultaneous use of categorical and dimensional assessments identifying patterns between food and supplements, intestinal microbiota, intestinal permeability and mental health. This is a novel approach as more population-based multidimensional transdisciplinary studies, have been called for as a basis for lifestyle treatment options for improving mental health and fits very well most of the priorities recently put forward in the Roadmap for Mental Health in Europe Research.

KEYWORDS

Microbiota, intestinal permeability, children & adolescents, mental health

Poster Abstract 3.

INTERPLAY BETWEEN THE GUT MICROBIOTA, PRO-INFLAMMATORY GENOTYPES, AND COLORECTAL ADENOMAS IN HISPANICS

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ABSTRACT

Background. Although colorectal cancer (CRC) is a potentially preventable, it is still one of the leading causes of cancer-related mortality in Puerto Rico and the US. However, CRC prevention strategies, other than routine screening, remain a challenge. Interplay between host genetics, environmental factors, gut microbiota and inflammation are accepted as major contributors to the colorectal carcinogenic process. There is limited information regarding how host genetics may modulate the inflammatory response and affect the gut microbial composition. The aim of this study was to examine the association of between having pro-inflammatory genotypes, the presence of bacterial toxin genes in stool and colorectal adenomas.

Methods. Using a case-control study design, we evaluated 60 individuals with colorectal adenomas (cases) and 60 healthy individuals (controls) recruited through the Puerto Rico Colorectal Cancer Registry. SYBR Green bacterial gene detection assays, and TaqMan Assays were performed according to the manufacturer's recommendations.

Results. A higher prevalence of the IL-1β and IL-10 pro-inflammatory genotype was found in cases compared to controls. Individuals with adenomas had a higher frequency of 3 of the 6 gut bacterial toxin genes compared to controls.

Conclusion. Our preliminary data support an association between the presence of gut bacterial toxin genes in stool and colorectal adenomas. An evaluation of the association between having pro-inflammatory genotypes, the presence of bacterial toxin genes in stool and colorectal adenomas using a larger sample size is warranted. Future research examining the SNPs and gut bacterial toxins could provide information about host genetic susceptibility to develop CRC.

KEYWORDS

Adenocarcinoma, Microbiome, Pro-inflammatory, Toxins and Genetics

Poster Abstract 4.

OPIOID TREATMENT DRIVES A SHIFT OF ENTERIC BACTERIA, *ACTINOBACTERIA* & *VERRUCOMICROBIA, IN VIVO* AND STRENGTHENS THE INTESTINAL BARRIER *IN VITRO*

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ABSTRACT

Clinical use of opioids is associated with severe GI symptoms, potentially linked to alterations in the composition and distribution of the microbiota (dysbiosis) and changes in the intestinal epithelial barrier. After opioid administration mice show a dysregulated immune response, increased intestinal barrier permeability, and bacterial translocation. The effects of opioids on human fecal microbiota and the intestinal barrier are not well understood. Using Deep Gene Sequencing, we characterized the fecal microbiota of individuals on methadone treatment. Our findings show no global differences in the *α* and β diversity between control and methadone treatment. However, we identified two microbial phyla with altered relative abundance in the methadone group: increased *Actinobacteria* and decreased *Verrucomicrobia*, which in the healthy gut are important for intestinal barrier homeostasis and mucus degradation, respectively. To study the direct effects of opioids on the intestinal barrier, we developed an *in vitro* model using human intestinal epithelial cells that establish an intact, semi-permeable monolayer. Measuring Transepithelial Electrical Resistance we observed that μ-Opioid Receptor (OR)- and *κ*-OR-agonist treatment strengthened the intestinal barrier in a dose and time-dependent manner, while δ-OR agonist treatment had no effect. Due to our laboratory's observations that δ-OR agonists regulate human T lymphocyte activation, we used an established epithelial/T cell co-culture model to demonstrate that δ-OR agonist treatment strengthens the intestinal barrier by acting indirectly on T lymphocytes. Together these results indicate that exposure to exogenous opioids modulates the intestinal microbiome and epithelial barrier function in a cooperative manner.

KEYWORDS

Actinobacteria, *Verrucomicrobia*, opioids, epithelial barrier, T lymphocytes

Poster Abstract 5.

ARE NON-NUTRITIVE SWEETENERS OBESOGENIC BY ALTERING FECAL SHORT-CHAIN FATTY ACIDS?

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ABSTRACT

Objectives. The fecal short-chain fatty acids (SCFA) acetate, butyrate and propionate have anti-obesogenic effects. This study explored changes in SCFA related to intake of starch, non-nutritive sweeteners (NNS) and Metformin.

Methods. Patients aged 18-60 years with morbid obesity (BMI > 40 kg/m2 or > 35 kg/m2 with obesity-related complications) were included. The dietary intake was assessed with a food frequency questionnaire. One unit NNS was defined as 100 ml beverage with NNS or 2 tablets/teaspoons for coffee or tea. The total amount of SCFA, acetic, propionic, n-butyric, i-butyric, n-valeric, i-valeric, n-caproic, and i-caproic acids in feces were analyzed and expressed in mmol/kg wet weight.

Results. 14 (16%) men and 75 (84%) women with a mean age of 44.6 years (SD 8.7) and BMI 42 kg/m2 (SD 3.6) were included. The intake of NNS (mean and median) was 7.5 and 3.2 (SD 10; range 0-43) units respectively. The amounts (median and range) of acetate, propionate and butyrate were 16.4 (2.9 – 67.9), 5.2 (1.3 – 25.6), and 5.6 (1.0 – 34.5) mmol/kg wet weight respectively. In a linear regression analysis adjusted for age, gender and use of Metformin, NNS and starch were significantly associated with butyric acid. NNS: B = -0.159; 95%CI = -0.280 to -0.037; p=0.011; partial correlation -0.274. Starch: B=0.030; 95%CI = 0.06 to 0.054; p=0.015; partial correlation 0.264. NNS was also significantly negatively associated with n-valeric acid.

Conclusion. The significant negative association between intake of NNS and fecal butyric acid indicates an obesogenic effect of NNS.

KEYWORDS

Butyrate; Non-nutritive sweeteners; Obesity; Short-chain fatty acids;

Poster Abstract 6.

MICROBIOME-DRIVEN REGULATION OF P-GLYCOPROTEIN EXPRESSION ON THE INTESTINAL EPITHELIUM IN MAINTENANCE OF HOMEOSTASIS

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ABSTRACT

Inflammatory bowel disease (IBD) is characterized by debilitating intestinal inflammation with neutrophil infiltration, as well as perturbation of the healthy gut flora. Our lab has discovered a novel mechanism by which P-glycoprotein (P-gp), expressed on the apical surface of intestinal epithelial cells, suppresses neutrophil infiltration via secretion of endocannabinoids (eCB). P-gp expression is high in healthy mice and humans, while diminished or dysfunctional P-gp is associated with intestinal inflammation and IBD. Our objective is to elucidate the mechanism that regulates P-gp expression, thereby promoting a healthy gut. Because the resident microbiota are known to contribute to tolerance and homeostasis in the healthy intestine, we hypothesize that the normal microbiota actively drives the eCB/P-gp axis to prevent unnecessary inflammation. To test this hypothesis, we observed loss of P-gp with broad- spectrum antibiotic treatment in mice, suggesting a role of the microbiota in maintaining P-gp expression. We next utilized antibiotics to eliminate subsets of the intestinal microbiota. Whole- genome sequencing of feces of these mice revealed genera within the Clostridium class that are correlated with P-gp expression. Additionally, we demonstrated recolonization by this subset of bacteria is sufficient to rescue P-gp expression in microbiome-depleted mice. These bacterial genera participate in production of metabolites, including short-chain fatty acids, which are beneficial to the host. Butyrate in particular is associated with intestinal health, and we have shown butyrate induces P-gp expression and function *in vitro.* We conclude that the commensal microbiota regulates P-gp function, playing a key role in controlling the balance between health and disease.

KEYWORDS

Inflammatory Bowel Disease, Microbiome, P-glycoprotein, Neutrophil, Metabolites

Poster Abstract 7.

THE EFFECT OF DIETARY FIBER INTAKE ON SHORT CHAIN FATTY ACID-PRODUCING BACTERIA DURING CRITICAL ILLNESS: A PROSPECTIVE COHORT STUDY

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ABSTRACT

Objective. Dietary fiber increases short chain fatty acid (SCFA)-producing bacteria yet is often withheld in the intensive care unit (ICU). This study evaluated the safety and effect of fiber in ICU patients with sampling of the gut microbiome at ICU admission and after 72 hours.

Methods. Consecutive adults 18 years or older were eligible if they were newly admitted to the ICU. Rectal swabs were performed at ICU admission and 72 hours later. The primary exposure was fiber intake over 72 hours, classified in tertiles and adjusted for caloric intake. The primary outcome was the relative abundance (RA) of SCFA-producers based on 16S rRNA sequencing and the tolerability of dietary fiber.

Results. In 129 ICU patients, median fiber intake was 13.4 g (IQR 0-35.4g) over 72 hours. The high fiber intake group had less abdominal distension (11% high fiber vs 28% no fiber, $p<0.01$), and no increase in diarrhea (15% high fiber vs 13% no fiber, $p=0.94$) or other adverse events. After 72 hours, the median RA of SCFA producers was 0.40%, 0.50%, and 1.8% respectively for no, low, and high fiber intake ($p=0.05$). After correcting for total caloric intake, the median RA of SCFA producers was 0.41%, 0.32% and 2.35% in the no, low and high corrected fiber categories ($p<0.01$ for trend). These associations remained significant after adjusting for other factors including antibiotics.

Conclusions. During the 72 hours after ICU admission, higher fiber intake was well tolerated and was associated with higher levels of SCFA-producing bacteria.

KEYWORDS

Dietary fiber, critically ill, gut microbiome, SCFA

Poster Abstract 8.

DIFFERENT GUT MICROBIOTA PROFILES IN PROFESSIONAL SOCCER PLAYERS

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ABSTRACT

Introduction. Emerging insights have demonstrated the relevance of the gut microbiota in the maintenance of human health. Physical exercise has been associated with a distinct compositional profile in professional athletes compared to non-athletes characterized by a higher diversity of the gut microbiota and positive effects on health indicators.

Objectives. The aim of this study was to analyze the influence of the sport season on gut microbiota composition of elite soccer players and to identify associations with athlete's health and performance.

Subjects and Methods. Sixteen soccer players were recruited, and faecal samples were obtained at the beginning and at the end of the sport season using OMNIgene GUT kit. DNA was extracted following specifications of the DNeasy PowerSoil kit and PCR amplification of 16S rRNA variable region V3-V4 was carried out following the instructions of the Illumina protocol 16S Metagenomic Sequencing Library Preparation. Data were analyzed applying algorithms such as decision trees, gradient boosting and artificial neural nets (RapidMiner software). Statistical differences were identified with Wilcoxon signed-rank test.

Results. Different gut microbiota clusters were identified among athletes that were related to physical, biochemical and sports performance variables. Moreover, statistically significant differences ($p < 0.05$) were observed at phylum level (Chloroflexi), class level (alpha-, delta- and gammaproteobacteria) and order level (*Desulfuromonadales, Anaerolineales, Dehalococcoidales*).

Conclusion. This study shows different gut microbiota profiles on professional soccer players that vary during the sport season. Furthermore, these gut microbial clusters might be related to specific physical and sports performance variables.

KEYWORDS

soccer players, gut microbiota, performance, health

Poster Abstract 9.

DIET MODULATES *CLOSTRIDIOIDES DIFFICILE* PATHOGENESIS THROUGH HOST AND MICROBE BILE ACID METABOLISM

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ABSTRACT

Objectives. Emerging data shows that low fiber intake is associated with increased colonization of *Clostridioides difficile* in mice. Additionally, saturated fat intake increases excretion of taurine-conjugated primary bile acids, known germination factors for *C. difficile,* but these bile acids can be converted by a healthy microbiota to secondary bile acids that can kill *C. difficile.* We sought to assess the effect of a high-fat/low-fiber Western Diet (WD) on antibiotic-induced microbiota disturbance, *C. difficile* infection (CDI) and primary and secondary bile acid levels.

Methods. We utilized a murine-model of CDI (5 oral antibiotics and clindamycin injection, *C. difficile* VPI-strain). Mice were fed either standard mouse chow or a WD. Gut microbiome analysis was performed by 16S rRNA gene sequencing and bile acid levels in cecal contents was assessed by LC/MS.

Results. WD-fed mice had a 3.21-fold increased risk of death (CI 1.30-7.91; p=0.01) compared to chow-fed mice. WD-fed mice showed increased microbiome disturbance after antibiotic challenge, with a greater increase of facultative anaerobes (Proteobacteria, Lactobacillales) and disappearance of the strictly anaerobic Clostridiales. WD-fed mice demonstrated higher levels of taurine-conjugated bile acids, decreased unconjugated primary bile acids and a near absence of secondary bile acids.

Conclusion. The ecologic and metabolic differences between chow-fed and WD-fed mice suggest that the double-insult of WD and antibiotic treatment leads to a pro-*C. difficile* bile acid composition and drives increased disease severity. These animal data indicate that dietary intervention with a low-fat/high-fiber diet has potential for preventing CDI in high-risk populations.

KEYWORDS

Clostridioides difficile, bile, western diet

Poster Abstract 10.

FECAL SHORT FATTY ACIDS AND KYNURENINE/TRYPTOPHAN IN SERUM AND THE CEREBROSPINAL FLUID IN SUBJECTS WITH DEPRESSION

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ABSTRACT

Objective. The objective was to study fecal Short fatty acids (SCFA) and Kynurenine and Tryptophan in serum and cerebrospinal fluid (CSF); and their relation to cognition in subjects with depression.

Methods. Thirty patients with depression were examined. The SCFA (Acetic, Propionic, Buteric, Isobuteric, Valeric and Isovaleric) were analyzed with gas chromatography. Kynurenine, Tryptophan, and Kynurenine/Tryptophan ratio (KT Ratio) were examined in serum and CSF. The SCFA, Kynurenine, Tryptophan, and KT ratio served as independent variables in linear regression analyses controlled for age. Montgomry Aasberg Depression Rating Scale (MADRS) and Neuropsychological tests served as dependent variables.

Results. Propionic (p=.001) and Isobutyric acid (p=0.049) were inversely associated with scores on MADRS, while Valeric acid (p=0.015) were positively associated with MADRS. Tryptophan and Kynurenine were associated with poor neuropsychological performance. The strongest association was between Kynurenine in CSF, and Grooved Pegboard test (fine motor control) dominant hand (p=.03) and non dominant hand (p=.009).

Also, other tests showed significant associations with poor performance on neuropsychological tests at a lower significance level.

Conclusion. The results indicate that the short fatty acids are related to the affection component in depression (MADRS), while Kynurenine in spinal fluid and the KT ratio in both CSF and serum are related to poor neuropsychological performance.

KEYWORDS

Depression, immunology, Microbiome, Short fatty acids, Kynurenine/Tryptophan.

Poster Abstract 11.

REDUCED ORAL NUTRITION CONTRIBUTES TO GASTROINTESTINAL TOXICITY OF TOTAL BODY IRRADIATION VIA CHANGES TO THE GUT MICROBIOME

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ABSTRACT

Objectives. Reduced oral nutrition (RON) is common after treatment for hematologic malignancies. We aimed to examine interactions between nutrition, intestinal bacteria and barrier function.

Methods. We characterized oral intake, the microbiome, colonic mucus, and intestinal barrier function in mice following total body irradiation (TBI).

Results. Following 9 Gy TBI, C57BL/6 mice had reduced oral intake (50%) and displayed changes in the microbiome with expansion of mucolytic bacteria *Akkermansia muciniphila* and *Bacteroides thetaiotaomicron*. Mice lost 20% of body weight and showed compromise of intestinal barrier function by FITC-dextran absorption.

To ask if RON could drive microbiome changes, we limited food access of unirradiated mice to 2g/day. This produced remarkably similar changes, including expansion of mucolytic bacteria. The colonic mucus layer was thinned, and metabolic activity of colonic bacteria during RON was also perturbed. Bomb calorimetry demonstrated reduced substrates in the cecum and colonic luminal pH showed reduced acidity. IC-MS quantified lower concentrations of acetate, propionate, butyrate, and lactate, and elevated succinate. Bacterial RNA sequencing revealed broad downregulation by several species of phosphoenolpyruvate carboxykinase, which facilitates production of propionate from succinate.

Finally, we evaluated oral administration of a well-absorbed sugar (glucose), and a poorly-absorbed prebiotic sugar. We found that prebiotic supplementation acidified the colonic lumen and prevented thinning of the mucus layer. Following 9 Gy of TBI, prebiotic dosing prevented weight loss, maintained the intestinal barrier function and improved overall survival.

Conclusion. Impaired nutrition and microbiome-mediated loss of colonic mucus appear to be important contributors to intestinal toxicity after total body irradiation.

KEYWORDS

microbiome, mucus, barrier, nutrition, radiation

Poster Abstract 12.

POTENTIAL ROLE OF THE GUT MICROBIOME IN HYPERTENSION RACIAL DISPARITY

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ABSTRACT

Objectives. African Americans (AA) have the highest prevalence of hypertension compared with other races in US; earlier onset and more severe HTN-related adverse outcomes are also observed. A crucial gap in knowledge exists to explain these disparities. We have recently observed significant changes of gut pathology and altered microbiomes in hypertensive animals and human patients. Our objective was to test the hypothesis that a distinct microbiome profile exists in AA HTN that contributes to blood pressure (BP) elevation.

Methods. Fecal samples were collected from 28 AA subjects (16 hypertensive and 12 normotensive) and 35 White American (WA) subjects (20 hypertensive and 15 normotensive). Mean systolic/diastolic BP for AA and WA hypertensive subjects were not significantly different (153/86 vs. 148/81 mmHg, respectively). Gut microbiomes were analyzed using shotgun metagenomics and the USEARCH6.1 algorithm for OTU clustering. Metaphlan, Qiime, Phyloseq and Galaxy web applications were used for further analyses.

Results. Core microbiome and network plot analysis indicated unique metagenome profiles in each cohort. Burkholderiales, Peptostreptococcaceae, Clostridium, and Lactobacillus were enriched in the WA HTN cohort; Coprococcus, and Megasphaera in AA HTN cohort. Functional analysis showed cell motility associated pathways (such as flagella assembly and bacterial chemotaxis) were decreased while antibiotic biosynthesis and resistance were increased in AA HTN.

Conclusion. 1) There are significant functional/taxonomic differences between gut microbiota of AA HTN and WA HTN cohorts. 2) Cell motility and antibiotic resistance may be important bacterial/immune regulatory mechanisms contributing to the increased prevalence and severity of HTN in the AA population.

KEYWORDS

Hypertension, African American, Racial disparity, Metagenomics, Blood Pressure

Poster Abstract 13.

DEVELOPING MICROBIOME RESTORATION BIOMARKERS FOR *CLOSTRIDIUM DIFFICILE* INFECTIONS: CONTINUED EVALUATION OF A PROTOTYPE MICROBIOME HEALTH INDEX™

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ABSTRACT

Objectives. We evaluated a unidimensional Microbiome Health Index(MHI) from two Phase 2 clinical trials of RBX2660, a standardized microbiota-based therapeutic with demonstrated clinical efficacy for preventing recurrent *Clostridium difficile* infections(rCDI), as a potential biomarker of microbiome restoration.

Methods. MHIs were calculated from sequencing data from patient fecal samples and RBX2660 product samples from two trials of RBX2660 to prevent rCDI: a randomized, blinded, placebo-controlled Phase 2B trial(16S sequencing) and an open-label Phase 2 trial(shallow shotgun sequencing). MHI values from the trials were compared and pooled. Receiver operator characteristic(ROC) analysis defined an MHI cut-point for distinguishing rCDI subjects prior to treatment(baseline) from the RBX2660 drug product. Post-treatment MHIs were assessed longitudinally and by outcome.

Results. Baseline and RBX2660 MHI values were not significantly different between the two trials, despite data derivation from different sequencing methods($p>.05$). ROC analysis indicated that the pooled baseline samples could be distinguished from the pooled RBX2660 profile with a maximum likelihood ratio of 121 (AUC=0.99, sensitivity=0.96, specificity=0.99, cutpoint=8.2). Among treatment responders, MHIs were significantly higher 7±4 days after treatment($p<.001$) with 58% of responders having an MHI>8.2. Among patients who failed treatment, only 21% were above the MHI=8.2 cutpoint. More importantly, MHI of successes could be distinguished from failures at 7±4 days post-treatment($p=.003$, Wilcoxon test).

Conclusions. MHI values are consistent across two trials using two different sequencing methods, suggesting generalized utility. MHI can effectively distinguish patients with dysbiosis from healthier patients and can differentiate successes from failures post-treatment. These results generate prospectively evaluable hypotheses for future clinical trials.

KEYWORDS

Clostridium difficile infection; biomarker; fecal microbiota transplantation; microbiota-based therapy; Microbiota Health Index

Poster Abstract 14.

IMPACT OF TWO BREAST-MILK DERIVED POTENTIAL PROBIOTICS ON THE GUT MICROBIOTA OF AN OBESE CHILD

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ABSTRACT

Objectives. The gut microbiota is emerging as a new factor in the development of obesity. This study aimed at evaluating the effects of two potential probiotic strains isolated from human breast milk, Lactobacillus plantarum 73A and Bifidobacteria animalis subsp. lactis INL1 on the microbiota of an obese child using the Simulator of the Human Intestinal Microbial Ecosystem (SHIME®), a dynamic model of the human gut.

Methods. The SHIME was run on the following program: stabilization (2 weeks), L. plantarum 73A (2 weeks, 1010 CFU/ day), washout (1 week) and L. plantarum 73A/B. lactis INL1 (1010 CFU/ day each, for 2 weeks). Analysis of the intestinal microbial composition (16S rRNA gene amplicon sequencing) was performed, short-chain fatty acids (SCFAs) levels were measured by gas chromatograph and ammonium (NH4+) concentration was assessed by an ammonia selective ion electrode.

Results. Both treatments significantly decreased ammonia concentration: from 483 ppm (stabilization) to 434 ppm (L. plantarum 73A, p = 0.0001), and from 530 ppm (washout) to 460 ppm (mix of strains, p = 0.015). No changes in SCFA were observed. Metagenome analysis of intestinal microbiota showed that both strains influenced the increase on phyla Bacteroidetes modifying the microbiota structure (p= 0.04). In addition, some Clostridium species decreased whereas Roseburia intestinalis significantly increased, beneficial specie linked to a healthy gut.

Conclusion. Breast milk-derived L. plantarum 73A and B. animalis subsp. lactis INL1 have a potential to undergo further studies to promote gut health in obese child.

KEYWORDS

bifidobacteria, lactobacilli, SHIME® model, obese microbiota, 16S rRNA sequencing

Poster Abstract 15.

THE CORRELATION BETWEEN VISCERAL FAT, LEPTIN AND MICROBIOME IN JAPANESE PATIENTS WITH OBESITY

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ABSTRACT

Objective. To clarify the correlation between gut microbiome and visceral obesity related to metabolic diseases in Japan.

Methods. Eighteen Japanese patients and two Caucasian patients with obesity lived in Japan were enrolled into the clinical trial by an intragastric balloon therapy. These patients were divided into two groups; visceral and subcutaneous obesity groups. Control group is consisted of 15 normal body weight subjects. Before the bariatric therapy, their visceral and subcutaneous fat were evaluated by CT and their gut microbiomes were evaluated by fecal 16SrRNA metagenomic analysis. The statistical significances between the obesity related factors in microbiome (diversity index, richness, Firmicutes to Bacteroidetes ratio (F/B ratio) and the specific spices) and amount of clinical data (serum leptin level, visceral and subcutaneous fat areas) were analyzed in the obesity groups.

Results.:1) The correlation coefficient between serum leptin levels before breakfast and visceral/ subcutaneous fat ratio was o.70. 2) The F/M ratio of control group was 0.9±0.4 and that of the obesity group was1.29± 0.7 (visceral 1.31±0.5, subcutaneous 0.94±0.3) respectively. There was tendency of increasing F/B ratio in obesity but no significant difference between groups. 3) Bacterial diversity was significantly lesser in visceral obesity groups.

Conclusion. The results show that the gut microbiota possibly differs between visceral and subcutaneous obesity.

KEYWORDS

visceral fat, subcutaneous fat, Firmicutes to Bacteroidetes ratio, Bifidobacterium

Poster Abstract 16.

THE GUT MICROBIOTA COULD COMPENSATE ENZYMATIC ACTIVITY IN PATIENTS WITH PANCREATIC EXOCRINE INSUFFICIENCY

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ABSTRACT

Objectives. Pancreatic exocrine insufficiency (PEI) is an inflammatory condition of the pancreas in which fibrosis development and loss of pancreatic parenchyma lead to an alteration of the endocrine and exocrine function. The possible involvement of certain microbial groups in scenarios where the disease and inflammation have control needs to be elucidated.

Methods. Two cohorts were included in this study: 11 patients with PEI and 6 healthy subjects. Patients with PEI had fecal elastase values <15 µg/g or between 15 and 200 µg/g and values below 29% of C13-triglycerides in the breath test. Patients brought a sample of feces from which 17 bacterial markers were analyzed. Two different indexes were defined according to the different functional groups of microorganisms based on the enzymatic activities of amylase, lipase and protease. In addition, 1 index indicative of eubiosis was also defined.

Results. Significant differences were observed when comparing PEI and healthy subjects when bacterial indexes were combined. The 2 indexes based on enzymatic activity were significantly higher in healthy controls than in PEI patients (p-value=0.044 and p- value=0.032, respectively). In contrast, the eubiosis index was significantly higher in PEI patients than in healthy controls (p-value=0.039).

Conclusion. Patients suffering from PEI have lower (log)-ratios indexes defined according to amylase, proteolytic, and lipase bacterial activities and an increase in the eubiosis. Since no clinical/physiological implications were derived from these enzymatic activity differences, the results suggest a possible involvement of the bacteria present in the digestive tract to compensate the lack of enzymatic activity characteristic of PEI.

KEYWORDS

Pancreatic exocrine insufficiency, enzymatic activity, gut microbiota, bacterial indexes

Poster Abstract 17.

ASSOCIATIONS BETWEEN PLASMA METABOLOMIC SIGNATURES AND GUT MICROBIOTA COMPOSITION IN THE 1,000-INDIVIDUAL *MILIEU INTÉRIEUR* STUDY

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ABSTRACT

Objectives. Products of the host-microbial co-metabolism comprise a vast range of molecules entangled in complex “host-microbial metabolic axes”. Various studies have functionally characterized specific classes of molecules and elucidated individual metabolic pathways. However, studies considering host-microbial metabolic relationships more globally remain scarce. Metabolomics seems to hold promise to comprehensively elucidate such interactions. This work aimed to explore the associations between host plasma metabolomic signatures and gut microbiota composition in healthy French adults of the Milieu Intérieur study.

Methods. For 846 subjects, gut microbiota composition was established through sequencing of the 16S rRNA gene in stool samples, and metabolomic signatures were acquired through proton

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Nuclear Magnetic Resonance analysis of plasma samples. The associations between NMR spectra and α- and β-diversity indexes and relative taxa abundances were tested using multi-adjusted partial Spearman correlations, PERMANOVAs, and MaAsLins respectively. Q-values<0.1 after Benjamini-Hochberg correction were considered statistically significant.

Results. Observed richness was negatively associated with metabolomic signals related to several classes of lipids and positively associated with proteins, amino acids; choline, creatinine, methylamine… Specific associations between metabolomic signals and abundance of taxa were also detected. Notably, strong and consistent associations were observed for creatinine, which was positively associated with 12 genera and 11 species and negatively associated with g_*Faecalibacterium* and more especially with *Faecalibacterium prausnitzii*.

Conclusion. This large-scale population-based study highlights certain metabolites associated with several gut microbial features and provides new insights into the understanding of complex host-gut microbiota metabolic relationships. Detailed exploration of metabolic pathways and implications for host health deserve further investigation.

KEYWORDS
Gut microbiota; metabolomics; NMR; healthy population; *Milieu Intérieur* Consortium.

Poster Abstract 18.

ASSOCIATIONS BETWEEN USUAL DIET AND GUT MICROBIOTA COMPOSITION: RESULTS FROM THE 1,000-INDIVIDUAL *MILIEU INTÉRIEUR* STUDY

Partula V[1,2], Mondot S[3], Torres MJ[4], Kesse-Guyot E[1], Deschasaux M[1], Assmann K[1], Latino-Martel P[1], Buscail C[1,5], Julia C[1,5], Galan P[1], Hercberg S[1,5], Rouilly V[6,7], Thomas S[7,8], Quintana-Murci L[9], Albert ML[10], Duffy D[8], Lantz O[11,12], Touvier M[1], The *Milieu Intérieur* Consortium[13]

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ABSTRACT

Objectives. Diet is widely recognized as one of the main modifiable drivers of gut microbiota variability, and its influence on microbiota composition is an active area of investigation. This work aimed to explore the associations between usual diet and gut microbiota composition in healthy French adults.

Methods. Gut microbiota composition was established through sequencing of the 16S rRNA gene in stool samples from 862 healthy French adults of the Milieu Intérieur study. Usual dietary consumptions were determined through the administration of a food frequency questionnaire. The associations between dietary variables and α- and β-diversity indexes and relative taxa abundances were tested using Spearman correlations, PERMANOVAs, and MaAsLins respectively.

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Results. Foods generally considered as healthy (raw fruits, fish) were associated with increased α-diversity whereas food items for which a limited consumption is generally recommended (fried products, sodas/sugary drinks, fatty sweet products, processed meats, ready-cooked meals, and desserts) were associated with decreased α-diversity. Raw fruits, fried products, ready-cooked meals, and cheese significantly contributed to shifts within microbiota composition (β-diversity) (all p-values < 0.05). Our results also highlighted a number of associations between various food group intakes and abundances of specific phyla, genera, and species. For instance, the consumption of cheese was negatively associated with species *Akkermansia muciniphila*.

Conclusion. This large-scale population-based study supports that the usual consumption of certain food items is associated to several gut microbial features. These results provide new insights into the understanding of complex diet-gut microbiota relationships, and their implications for host health deserve further investigation.

KEYWORDS
Gut microbiota; usual diet; healthy population; epidemiology; *Milieu Intérieur* Consortium.

Poster Abstract 19.

GUT MICROBIOME AND PSYCHOLOGICAL DISTRESS: IS GUT BACTERIA ASSOCIATED WITH MOOD?

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ABSTRACT

Objective. Gut microbiota can impact the central nervous system and are important for healthy neurological functioning. Alterations in the gut microbiome may impact the development of anxiety and depression, thus may provide novel treatment options for psychological illness. The current study aims to further elucidate the relationship between gut microbiome bacteria and stress, anxiety, and depression symptoms.

Methods. Participants include female adults (N=63) ages 18-42 years old. Participants completed self-report measures assessing psychological distress (State-Trait Inventory, Beck Depression Inventory, and the Perceived Stress Scale). Participants provided fecal samples to measure gut bacteria counts (e.g., *Lactobacillus*, *Bifidobacterium*). Samples were mailed in sterile tubes preserved with a stabilization buffer and 16S sequencing was conducted.

Results. Pearson's correlations and Cohen's d effect sizes were calculated comparing gut bacteria counts with self-report measures of psychological distress. Gut diversity showed a small negative effect with PSS scores (d=-0.22). *Lactobacillus* was not correlated with psychological measures. Small to moderate positive effects were found for *Bifidobacterium* for all self-report measures except STAI-State. *Firmicutes* and PSS scores demonstrated the only significant positive relationship (r=0.30, p=0.03) with a moderate effect (d=0.63). *Firmicutes* demonstrated small to moderate effects for all measures.

Conclusions. Although preliminary, small to moderate effects were detected between gut bacteria, depression, and anxiety signaling that potential relationships exist. Additional research is needed to understand the impact of the gut microbiome on emotional functioning. A more thorough understanding of these relationships may influence treatment considerations.

KEYWORDS

gut microbiota, psychological distress, emotional functioning

Poster Abstract 20.

ASSESSING DIETARY INTAKE OF OMEGA-3 FATTY ACIDS: BIOMARKERS VERSUS SELF-REPORT

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ABSTRACT

Objective. While self-report dietary questionnaires like the Diet Health Questionnaire-II (DHQ-II) are economically beneficial and simple to administer, in general self-reported dietary questionnaires are methodologically limited by the potential for under- or misreporting. The current study aimed to examine the reliability of the DHQ-II to assess omega-3 fatty acid (ω-3 FA) consumption as compared to an objective physiological measure, dried blood spot (DBS) samples. The current study addresses a methodological challenge in the literature, comparing self-report dietary assessments to physiological measures.

Methods. Healthy adults (*n*=63) completed the DHQ-II and provided a DBS sample collected via finger prick. The Shapiro-Wilks Test was conducted to test the normality of the data, and was found to be significant ($p<.05$). Thus, the Spearman rank ordered correlation analysis was selected to examine the relationship between ω-3-FA consumption estimated by the DHQ-II and ω-3-FA proportion in the red blood cell (RBC) membranes from the DBS.

Results. DHQ-II estimates were weakly correlated with total ω-3 FA consumption in the RBC membrane. There was, however, a moderate to strong-moderate relationship between specific ω-3 FA's (eicosapentaenoic acid (EPA), $rs = .43$ and docosahexaenoic acid (DHA), $rs = .66$).

Conclusions. This study provides conflicting evidence for the utility of self-report dietary measures as compared to physiological measures in assessing ω-3 FA. Overall, self-report measures are not strongly correlated with objective measures. As future research focuses more on nutrition to ameliorate a variety of negative health outcomes, it is increasingly essential that researchers can accurately measure different aspects of dietary intake.

KEYWORDS

biomarkers, self-report, omega-3 fatty acids, dried blood spot

Poster Abstract 21.

THE ANXIOLYTIC EFFECT OF OMEGA-3 FATTY ACIDS: EXAMINING THE ROLE OF BUTYROGENIC BACTERIA AS A POTENTIAL MECHANISM

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ABSTRACT

Objectives. Omega-3 fatty acids (ω-3 FAs) may have anxiolytic effects, perhaps through butyrogenic gut bacteria. Accordingly, this study investigates whether ω-3 FAs impact levels of butyrogenic bacteria, and subsequently whether levels of butyrogenic bacteria affect anxiety levels.

Methods. Female adults (n=63) ages 18-42 were recruited in an ongoing study (expected enrollment=135). State-Trait Anxiety Inventory (STAI) and dried blood spot samples (red blood cell (RBC) ω -3 data, specifically docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA)) were collected. Fecal samples were analyzed by 16S rRNA gene sequencing for the butyrogenic *Roseburia* species.

Results. Linear regressions tested whether levels of ω-3 FAs predicted levels of fecal *Roseburia inuvilorans (R. inuvilorans*). RBC ω-3 FA predicted *R. inuvilorans*, $F(3,41) = 2.878$, $p = .047$, $R2 = .174$. As RBC-DHA levels increased, *R. inuvilorans* levels decreased ($\beta = -.495$). As RBC-EPA levels increased, *R. inuvilorans* levels also increased ($\beta = .447$). Another linear regression tested whether levels of *Roseburia faecis* predicted trait anxiety. Results moderately supported this relationship $F(1,51) = 3.345$, $p = .073$, $R2 = .062$, and showed that as *Roseburia faecis* increased, trait anxiety also increased ($\beta = .248$).

Conclusion. DHA predicted lower, while EPA predicted higher levels of *R. inuvilorans*. Additionally, *Roseburia faecis* did not significantly predict trait anxiety. This study is limited by small sample size; further analyses can confirm initial results supporting the differential role of specific ω-3 FAs on *R. inuvilorans*, as well as determine the potential significance of the relationship between butyrogenic bacteria and subsequent levels of anxiety.

KEYWORDS

omega-3 fatty acids, butyrate-producing bacteria, butyrate, anxiety

Poster Abstract 22.

CLINICAL GUIDE TO PROBIOTIC PRODUCTS AVAILABLE IN CANADA AND IN US: 2018 EDITION

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ABSTRACT

Objective. This guide is designed to translate scientific evidence available for probiotic products into practical, clinically relevant information, enabling clinicians to easily select the appropriate product, dose, and format for a specific indication.

Methods. Published studies with defined clinical outcomes for probiotic strain(s) were searched, using defined inclusion criteria. Commercially available products containing said strain(s) were identified, and the levels of evidence were used to rate the strength of the recommendation.
This information was compiled into a chart form, assessed by independent expert reviewers. This guide is a clinical decision-making tool to assist health care professionals in providing evidence-based recommendations for their patients. In the case of probiotics, the clinical evidence supports only certain formulations/brand names of the probiotics (including the genus, species, alphanumeric designation or strain, number of live bacteria present, the blend of probiotic strains present, and finally, the non-active ingredients present). Every attempt was made by the authors to include the published clinical data for the available probiotic formulations.

Results. In the clinical guide, the available strains were organized based on probiotic strain(s), doses, and evaluated levels of evidence based on our pre-defined criteria.

Conclusion. There is evidence to support the use of oral and vaginal probiotic products for various aspects of human health, however applications and results are strain-specific. Lack of adverse effects supports the wide use of these products, and further investigation is recommended.

KEYWORDS

Probiotics; translational medicine; clinical; indications

Poster Abstract 23.

ASSESSMENT OF THE MICROBIOTA METABOLOME AND ITS ROLE IN CHRONIC SYSTEMIC DISEASES

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ABSTRACT

Introduction. The microbiome research has reshaped our understanding of human biology and how microbes impact our pathophysiological processes. The role of the microbiome and its symbiotic relationship with the host have shed light on understanding many chronic systemic diseases. Metabolomics is known to provide a snapshot of the phenotype of the holobiont and help investigate its metabolic activities. Here, we discuss the application of newly developed standardized, quantitative targeted assay for multiplexed analysis of host and gut bacteria-derived metabolites by mass spectrometry.

Methods. Human plasma and fecal samples were analyzed using the MxP® Quant 500 targeted metabolomics kit (Biocrates). 10 µL sample volumes were pipetted on a 96 well-plate, preloaded with internal standards. After derivatization and extraction, LC-MS/MS and FIA- MS/MS analyses were performed. Met*IDQ*™ software was used for sample analysis.

Results. Over 500 metabolites (14 small molecule and 12 lipid classes) including metabolites produced and/or biochemically modified by gut microbiota were analyzed. LC-MS analysis provided quantitative results of small molecules covering bile acids, indole derivatives, and amino acids. Acylcarnitines, lipids, and monosaccharides were analyzed by FIA-MS. Mostly, the metabolites quantified in feces overlap with those in plasma. A higher number of lipids, especially phosphatidylcholines and triglycerides, were identified in plasma compared to fecal samples.

Conclusions. The functional microbiome-host interaction is a key aspect to understanding commonalities in chronic systemic diseases. The ability to identify and quantify the metabolites produced or modified by gut microbiota like the ones involved in the choline, and tryptophan metabolism will help better understand these commonalities.

KEYWORDS

Microbiome, Metabolomics, Quantification, Chronic Systemic Diseases