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Poster Presentation Abstracts

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Poster Title	A randomized controlled trial to evaluate impact of a novel probiotic and nutraceutical formulation on symptoms of canine atopic dermatitis (CAD) in privately-owned dogs
Abstract	Atopic dermatitis is a chronic inflammatory skin disease affecting >7% of US adults. CAD, closely resembling the human disease and manifesting as erythema, skin lesions, and pruritus, is estimated to affect 10-15% of dogs. The disease has a complex pathogenesis, influenced by immunological factors including the gut microbiome (GM). While many conventional treatments exist, the multiformity of disease pathways results in a heterogeneity of clinical presentation and treatment responses. Complementary therapies with multimodal actions must be explored. A formulation containing six strains of probiotics ($5x10^9$ CFU/g), prebiotics, vitamins, nutrients, and a postbiotic was contrived based on existing literature. To examine the combined efficacy of this formulation, a 10-week double-blind randomized placebo-controlled trial was conducted. Adult household dogs with a compatible history and symptoms consistent with CAD were enrolled. Owners completed a health survey containing clinically validated scales for the assessment of CAD and pruritus severity at baseline and weeks 2, 4, 7, and 10. Additionally, owners collected a stool sample for GM shotgun metagenomic profiling at baseline and week 10. Dogs receiving the formulation had improved skin redness (p=0.004), pruritus severity (p=0.024), and overall CAD severity (p=0.007) at week 2 compared to placebo. Furthermore, compared to baseline a significantly higher proportion of dogs on the nutraceutical blend had normal pruritus severity by week 4 (p=0.024) as compared to week 7 for the placebo. These findings collectively supported faster improvement of CAD symptoms with the formulation. A shift in the GM beta-diversity was observed with the formulation (p=0.025), but not with the placebo. All probiotic species in the formulation had increased abundance at week 10, while Proteobacteria also markedly decreased. Given the prominence of allergic skin diseases the results of this trial are pertinent to both human and canine well-being.

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Poster Title	Mapping of gut microbial species from 16S data across 29,000 individuals from around the world
Abstract	The human gut microbiome has been linked to health and disease. Investigation of the human microbiome has largely employed 16S amplicon sequencing, with limited ability to distinguish microbes at the species level. Herein, we develop Reference-based Exact Mapping of microbial amplicon variants (RExMap) that enables mapping of microbial species from standard 16S sequencing data. RExMap analysis of 16S data captures ~75% of microbial species identified by whole-genome shotgun sequencing, despite hundreds-fold less sequencing depth. RExMap re-analysis of existing 16S data, from 29,349 individuals across sixteen regions around the world, reveals a detailed landscape of gut microbial species across populations and geography. Moreover, RExMap identifies a core set of fifteen gut microbes shared by humans. Core microbes are established soon after birth and closely associate with BMI across multiple independent studies. RExMap and The World Microbiome Database are presented as resources with which to explore the role of the human microbiome.

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Poster Title	Probiotics role in the gut-brain axis: an orally multispecies formulation with beneficial effects on the management of daily stress
Abstract	Stress has been defined as the “Health Epidemic of the 21st Century”. Stressful situation can affect quality of sleep which provokes fatigue, irritability and concentration difficulties. Stress may modify the gut microbiota and the gut-brain communication. According to the in-vitro screening on the modulation of the epigenetic response to stress, stimulation of GABA production and improvement in serotonin secretion, *L. reuteri* PBS072 and *B. breve* BB077 have been selected for clinical investigations. *L. reuteri* PBS072 and *B. breve* BB077 have been clinically tested in a proof-of-concept trial on 30 stressed students (4B CFU/day) evaluating the ability in improving stress-related parameters (cognitive functions and psychophysiological markers) for 28 days. Subsequently, a crossover clinical trial to evaluate probiotics influence on mood and sleep during pandemic has been carried-out. A total of 33 volunteers were randomly assigned into two groups and treated for 30 days with an inverted administration of probiotic and placebo interspersed with a 4-week wash-out period. The efficacy on stress response were assessed using: The Pittsburgh Sleep Quality Index (PSQI) and the Profile of Mood State (POMS) questionnaires (ISRCTN15033071). Last, a RDBC trial was carried out on 200 post-partum women to observe a positive effect on post-partum blues evaluated through the Edinburgh Postnatal Depression Scale (EPDS) and Breastfeeding Self-Efficacy Scale Short-Form (BSES-SF) for 90 days (ISRCTN99047904). Results observed in the open study showed a significant improvement ($p<0.05$) of cognitive functions and psychophysiological markers. Crossover results showed that both questionnaires reported a significant lower score after 30 days compared to placebo, which reflected a worsening of mood and sleep quality. RDBC trial evidenced that probiotics are able to significant improve ($p<0.001$) mothers’ mood in the first trimester as well as breastfeeding confidence and crying episode reduction. According to our results, *L. reuteri* PBS072 and *B. breve* BB077 are potential candidates in improving stress resilience in acute and chronic conditions.

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Poster Title	Impact of ridinilazole and vancomycin on the human gut microbiome and bile acid metabolism and their recovery at 30-day post-treatment
Abstract	**Introduction:** *Clostridioides difficile* infection (CDI) is primarily cause by alterations to the gut microbiome. Ridinilazole is a targeted antibiotic developed to cure CDI while sparing the microbiome. In a phase 2 study, ridinilazole reduced recurrence by ~60% vs vancomycin at 30 days post-treatment. We compare the effects of ridinilazole and vancomycin on patients' microbiota diversity, bile acid (BA) metabolic potential and production of protective BAs. **Methods:** In this study, CDI patients received 10 days of oral ridinilazole or vancomycin. Microbial DNA from stool samples collected at baseline (BSL), end of treatment (EOT), and 30 days post-EOT (D40) from 62 patients were analyzed by shotgun sequencing to assess microbiome diversity (richness) and presence of *bsh* and *bai* genes. Results are reported as median values. Wilcoxon signed-rank tests assessed changes from BSL. **Results:** Microbiome richness was similar at ridinilazole EOT and BSL (-2%, *P*=0.34) and significantly higher than BSL at D40 (+50%, *P*=0.001). In contrast, richness was significantly lower at VAN EOT compared to BSL (-61%, *P*=0.0001) and similar to BSL at D40 (0%, *P*=0.70). The gut microbiota produces protective secondary BAs that inhibit *C. difficile* growth through two transformations that successively require the *bsh* and *bai* gene products. At ridinilazole EOT, changes in relative abundance of *bsh* and *bai* genes were not significantly different to BSL, +1.1-fold (*P*=0.54) and 1-fold (*P*=0.28), respectively, compared to -11-fold (*P*=0.0064) and -58-fold (*P*=0.0017) decrease with vancomycin. This was coincident with preservation of protective BA levels at ridinilazole EOT and a ~10-fold decrease following vancomycin therapy. At D40, *bsh* and *bai* gene abundance was similar to BSL in both treatment groups. However, in ridinilazole-treated patients *bai* genes trended to higher abundance than BSL (+1.2-fold, *P*=0.056). This was coincident with higher levels of protective BAs at D40 compared to BSL in the ridinilazole group while these BAs were similar to patients with active CDI in the vancomycin group. **Conclusions:** Ridinilazole was superior to vancomycin in preserving the gut microbiome diversity, allowing faster recovery of species richness and protective secondary bile acid production. This provides a rationale for the reduced CDI recurrence rate observed in the phase 2 study.

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Poster Title	Altered gut microbiota associated with consumption of novel resistant starch blend derived from potato, banana and apple
Abstract	While dietary fiber has a recommended daily intake, resistant starch does not have a defined, universally recognized intake. The specific fiber type of resistant starch type 2 (RS2) does not break down in the small intestine due to its native granular structure and has demonstrated benefits similar to those known to occur from dietary fiber in general. RS2 has been evaluated at multiple doses, and different types, for benefits varying from improving gut motility and fecal bulk to improving glycemic control and increasing satiety. RS2 includes native resistant starch from high amylose maize, raw potatoes or green bananas. While some starches have been associated with an impact on increasing specific types of bacterial species associated with health, others have not. A randomized clinical trial evaluated doses ramping from 10 to 30 g/day over 6 weeks of a novel resistant starch blend (RSB) or 10 g/day for 6 weeks of a potato starch. This study sought to explore the gastrointestinal impact of different doses of a blend of resistant starches from green banana flour and raw potato starch as well as apple fibers. The exploratory microbiome findings are presented, showing an association of the resistant starch blend consumption with 16S rRNA gene sequences classified as taxa associated with human health: *Faecalibacterium* and *Akkermansia*.

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Poster Title	Identifying predictors of response in longitudinal multiomic study designs
Abstract	Gut microbiome imbalances are linked to diseases including HIV, autism, and obesity. The gut microbiome is commonly described by the relative abundance of bacterial species, as assessed using next-generation sequencing of the 16S rRNA gene region in DNA extracted from fecal material. Because the gut microbiome can be modified via diet or other environmental influences, there is hope for disease treatment. Longitudinal microbiome (and multiomic) studies (LMS) are increasingly common with promise for understanding how microbiome changes relate to factors they may influence such as metabolites or immune factors, and symptoms of disease. However, LMS involve analytical challenges when trying to integrate different data types. Furthermore, LMS can be observational (i.e., measurements made over time, related to natural fluctuations in symptoms) or involve interventions, such as diet modifications. In an observational study of autistic individuals, we identified relationships between intraindividual changes in microbial communities over time and changes in behavior using linear mixed effects models using all pairwise comparisons. In an interventional study, we have been exploring agrarian diet effects on inflammatory and metabolic phenotype changes compared to baseline values in HIV+ individuals using mixed-effects Random Forests. Hence, changes in features can be calculated for each subject over time, and these differences are dependent on reference values important in different LMS. Thus, different delta datasets are created which also include categorical changes. We are developing a workflow for exploratory analysis in LMS using machine learning methods to address challenges such as feature reduction, compositionality, and diverse data (clinical, omic, numeric, categoric, etc.). Next, mixed-effects Random Forest regression identifies important predictor variables that explain changes in a response variable using raw data and delta datasets. Finally, post-hoc testing is performed. Preliminary results on simulated and real data identified novel important features. Overall, this analytical workflow will reduce barriers to hypothesis generation.

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Poster Title	Omega-3 fatty acids and fiber modulate the gut-brain axis in dogs
Abstract	The study evaluated the effect of omega-3 fatty acids and a fiber blend (citrus pulp, carrot, and spinach, with or without tomato pomace) on metabolites that influence the gut-brain axis. Forty dogs were fed food with lower omega-3 fatty acid and no fiber blend (washout) for 1 month. Twenty dogs were given food containing higher omega-3 fatty acids and the fiber blend without tomato pomace (Control) for 30 days, while the other twenty dogs were fed a similar food with added tomato pomace (Test). After 30 days on the washout food, the groups were switched to the control or the test food for 30 days. Blood and fecal samples were collected at the end of each 30 day period. Several metabolites previously associated with anxiety-like behaviors were altered after dogs consumed the control and the test food. Dogs had lower plasma and feces concentrations of glutamine, glutamate and lactate after consuming the control and the test foods. Dogs had lower levels of 4-ethylphenyl sulfate (4EPS), citrate, dimethylarginines (ADMA + SDMA), choline and higher levels of docosahexaenoic acid (DHA), 1-methylnicotinamide and 2-aminobutyrate in plasma. Plasma phenol sulfate, hippurate, gamma-glutamylglutamate, and kynurenine were lower on test compared to the washout food. The test food led to more significant reductions in plasma 4EPS compared to control food. Plasma 4EPS correlated negatively with plasma 1-methylnicotinamide, DHA, gamma-glutamylglutamate and hippurate; and positively with plasma indolelactate, kynurenine, N-acetylkynurenine and phenolsulfate. Plasma 4EPS correlated negatively with fecal azelate, choline, dimethylarginine, DHA, kynurenine and N-acetylkynurenine. Plasma 4EPS correlated positively with fecal microbial abundance of Class Gammaproteobacteria unclassified, *chitosanitabida, Eubacterium biforme, Anaerovibrio, Flexispira* and Pseudomonadaceae unclassified; it correlated negatively with *Odoribacter, Blautia, Parabacteroides, Anaerovorax,* Coxiellaceae, *Campylobacter,* Enterobacteriaceae unclassified, *Brenneria,* Actinomycetaceae, *parainfluenzae* and *Sanguibacter*. These results indicate that anxiety-related metabolites can be reduced by nutrition that impacts the gut microbiome composition and function

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Poster Title	Potential biomarkers of infertility associated with microbiome disbalances
Abstract	**Objective:** The aim of this study was to investigate the possible relationship between vaginal/rectal dysbiosis and miRNA expression with infertility. We also investigated if a customized diet, a nutraceutical and probiotic supplementation on pregnancy and live birth rates. **Method:** Observational, prospective study. A total of 287 infertile patients were recruited. Twenty fertile women were recruited as the control group. Swab samples were collected from the vagina and rectum of the patients. Microbial composition by NGS and miRNA expression by real time PCR of vaginal and rectal samples were measured. The study was approved by the CEIH Ethics Review Committee, Buenos Aires- Argentina (#CEI 1590). **Results & Conclusions:** Infertile patients showed an increased *Firmicutes/Bacteroidetes* ratio at rectal level and a vaginal dysbiosis (an increased *Lactobacillus brevis*/*Lactobacillus iners* ratio). In the same rectal swab samples, we found that miR-21-5p, which is associated with tight junction disruption and yeast overgrowth, is upregulated and that miR-155-5p, which is associated with inflammation, is overexpressed in the unexplained infertile group (*$p < 0.05$). These deregulated miRNAs were also upregulated in the vaginal samples from the same patients. Considering all these parameters and the peripheral blood markers, patients were treated using a nutraceutical combination of biomedical diets, probiotics, and micronutrition, and the pregnancy and the live born rates went from 26% to 75% and from 0% to 60%, respectively. A nutraceutical supplementation according to our novel microbiome miRNA diagnostic platform improved the reproductive health of unexplained infertile patients.

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Poster Title	A Cellulose-Hydrogel Matrix that Sequesters Sugars to Promote Metabolic Health
Abstract	Biolumen is a proprietary fiber composed of ingredients normally found in food: a series of nano-cellulose sponges impregnated with a blend of hydrogels which expand in an acidic environment. It is the microgeometry of the components that allows for sequestration of sugars and simple starches in the duodenum that renders them unavailable for absorption, thus protecting the liver. However, they offload in the jejunum and ileum, thus feeding the gut. In vitro studies of swelling, absorption, and retention in acidic condition demonstrate the ability for these sponges to swell to 20-30 times their weight, and affinity of the hydrogels for sequestration of glucose, fructose, sucrose, and simple starches. Retention during passage through the upper GIT was initially tested for a mixture of glucose, fructose, sucrose, and starch-derived molecules in a separate batch by ProDigest (Ghent, Belgium). The results of analysis in their Simulated Human Intestinal Microbial Ecosystem (SHIME) show that our product was able to successfully retain a proportion of these materials during passage through the stomach. The absorbed sugar concentration was significantly lower as compared to the blank control. Hence, all non-absorbed sugars were expected to be transferred to the colonic environment, potentially allowing stimulation of gut microbial activity. Moreover, acetate, propionate, and butyrate production significantly increased, while production of bSCFA decreased.