ment. β-diversity was summarized using Unifrac and Bray-Curtis distance with significance assessed using nonparametric PERMANOVA method. Differentially abundant taxa were identified using a multivariable linear model with permutation to assess statistical significance, accounting for non-normality of abundance data. To investigate microbiome regulation of luminal PA, stool from a subset of these patients (n=6 stool/PA classification) were used to humanize 4-week old germ-free (GF) mice (ex-GF). Six weeks post humanization, fecal PA and stool frequency was measured and serum was collected after administration of creatinine, 4kDa FITC-Dextran and 70kDa Rhodamine B-Dextran to assess *in vivo* permeability.
**Results:** 12/29 PI-IBS {8 females}, were classified as High PA (>85$^{th}$ percentile of HV, >891 BAEE/mg of protein). Compared to Low PA patient stool, High PA patients had significantly decreased microbial diversity (Bray-Curtis, PERMANOVA p< 0.001). Low PA patients had an increased abundance of genus *Prevotella* and *Firmicutes* and decreased abundance of *Bacteriodes*. Humanization of mice with microbiota from Low PA stool suppressed baseline PA of GF mice while microbiota from High PA patients resulted in unchanged PA from baseline (% of baseline, Low PA 17.2 ± 30.0; High PA 100.4 ± 122.0, p< 0.05). High PA mice had increased PA at six weeks post humanization (BAEE units/mg protein, High PA 1570.9 ± 1834.3, Low PA 240.5.2 ± 374.8; p< 0.05). No difference was observed in stool frequency (pellets/hr, High PA 9.4 ± 3.0; Low PA 9.0 ± 3.6); however High PA mice had looser pellets when scored for fecal consistency (Scored 0=normal to 4=diarrhea, High PA 0.82 ± 0.49; Low PA 0.18 ± 0.33 p< 0.001. Permeability of creatinine increased only in mice humanized with High PA microbiota (mg/dL, High PA 0.81 ± 0.28); Low PA 0.58 ± 0.24; HV 0.51 ± 0.36 p< 0.05), while permeability of 4kDa FITC-Dextran increased in both Low and High PA humanized mice compared to HV humanized mice (mg/dL, High PA, 19.1 ± 14.6; Low PA 23.9 ± 23.9; HV 13.7 ± 30.3 p< 0.05). Creatinine and 4kDa FITC-Dextran permeability positively correlated with terminal PA (Spearman r=0.31 and 0.27 respectively, p< 0.05).
**Conclusion:** High PA PI-IBS patients have significantly decreased fecal microbial diversity. Low PA microbiota suppresses host luminal PA while High PA microbiota did not change host PA. Compared to Low PA microbiota, High PA microbiota causes increased intestinal permeability through the pore pathway. Therefore, microbiota may influence intestinal permeability in PI-IBS through modulation of proteases. *Supported by NIH K23 DK 103911.*
**References:** Edogawa S, Edwinson AL, Peters SA, et al. Serine proteases as luminal mediators of intestinal barrier dysfunction and symptom severity in IBS. Gut 2019:gutjnl-2018-317416.
**Disclosure:** Nothing to disclose

## OP030 CIPROFLOXACIN TREATMENT AFFECTS THE STRUCTURE AND ACTIVITY OF ENTERIC NERVOUS SYSTEM IN MOUSE SMALL INTESTINE

Caputi V.[1,2], Marsilio I.[1], Cerantola S.[1], Renzulli C.[3], Calanni F.[3], Viscomi G.C.[3], De Martin S.[1], Giron M.C.[1]
*[1]University of Padova, Department of Pharmaceutical and Pharmacological Sciences, Padova, Italy, [2]University College Cork, APC Microbiome Ireland, Cork, Ireland, [3]AlfaSigma S.p.a, Corporate R&D Department, Bologna, Italy*

**Contact E-Mail Address:** cecilia.giron@unipd.it
**Introduction:** Commensal gut microbiota ensures the functional and structural integrity of enteric nervous system (ENS) circuitries. Any change of its composition elicited by environmental factors or drugs could disrupt ENS homeostasis and determine the onset of functional bowel disorders. Ciprofloxacin is a synthetic broad-spectrum antimicrobial agent, belonging to the fluoroquinolone family, used for treating respiratory, urinary tract, gastrointestinal and abdominal infections. Ciprofloxacin usage has been associated with many adverse reactions, including neurotoxicity.
**Aims & Methods:** The aim of the present study was to evaluate the effect of ciprofloxacin on ENS integrity and gastrointestinal motility in young mice. Male C57Bl/6 mice (age=9±1 weeks; N=44) were orally gavaged with ciprofloxacin (50 mg/kg, suspended in 1% methylcellulose; CPX group) or vehicle (CNTR group) for 14 days. In CPX and CNTR animals we assessed:
i) gastrointestinal transit 30 minutes after intragastric administration of nonabsorbable-FITC-labeled dextran;
ii) pellet frequency, measured as changes in stool output during a 60-minute collection period;
iii) stool water content;
iv) contractile activity of isolated ileum segments, measured as changes in isometric muscle tension following carbachol (0.001- 100 μM), KCl (60 mM), electric field stimulation (EFS, 1-40 Hz) or inhibition in non-adrenergic, non-cholinergic (NANC) conditions (EFS=10 Hz, 1 μM atropine, 1 μM guanethidine, with or without 0.1 mM L-NAME);
v) distribution of the neuronal HuC/D and glial S100β markers by confocal immunofluorescence in ileal frozen cryosections;
vi) neurochemical coding integrity, evaluated by acetylcholinesterase and NADPH-diaphorase biochemical staining in longitudinal-muscle myenteric plexus preparations (LMMPs).
**Results:** Ciprofloxacin treatment determined a significant reduction in the number/hour output of fecal pellets (-36±8%, N=5/group, P< 0.01) and increased stool water content (+32±9%, N=5/group, P< 0.01). Gastrointestinal transit was delayed in CPX mice compared to CNTR mice (geometric center: 8.3±0.2 vs 7.3±0.2, N=6/group, P< 0.01), respectively). In vitro contractility studies showed a significant downward shift of the concentration-response curve to carbachol in CPX group (Emax=-36±5%, N=5/group, p< 0.01) compared with CNTR group, together with a reduced KCl-induced excitatory responses (-32±8%, N=5/group, p< 0.05). Altered excitatory and inhibitory neurotransmission in CPX mice was shown by decreased EFS-elicited contractions with a significantly reduction of 10 Hz-neuronal cholinergic response (CPX=-67±11%, N=5/group, p< 0.01) and by an impaired NANC-mediated relaxation of ileal segments from CPX mice. In the ENS of CPX mice, increased HuC/D immunoreactivity and NADPH-d-positive cells (+38±2%, N=5/group, P< 0.01) in the ileum of CPX mice together with reactive gliosis, evidenced by S100β immunofluorescence distribution.
**Conclusion:** Ciprofloxacin-induced gut dysbiosis determines complex anomalies in ENS architecture, neurochemical coding and function leading to neuromuscular dysfunction. Such neuroglial plastic changes are highly indicative of the negative effects mediated by ciprofloxacin on the integrity of gut microbiota-ENS axis, possibly contributing to promote functional bowel disorders later in life.
**Disclosure:** FC, CR, GCV are employees of Alfasigma SpA. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

# Hot topics from Latin America

10:30-12:00 / C2

## OP031 A COMPARATIVE ANALYSIS OF DIGITAL CHOLANGIOSCOPY AND PROBE-BASED CONFOCAL LASER ENDOMICROSCOPY FOR THE MALIGNANCY DETECTION IN BILE DUCT LESIONS

Robles-Medranda C., Oleas R., Olmos J., Alcivar-Vasquez J., Puga-Tejada M., Baquerizo-Burgos J., Pitanga-Lukashok H.
*Instituto Ecuatoriano de Enfermedades Digestivas (IECED), Gastroenterology and Endoscopy Division, Guayaquil, Ecuador*

**Contact E-Mail Address:** robertoleas@gmail.com
**Introduction:** The differentiation of malignant from the benign biliary lesion is challenging in clinical practice. Peroral digital cholangioscopy (POCS) predicts malignancy through the visual impression of biliary lesions; whereas, Probe-based confocal laser endomicroscopy (pCLE) via in vivo, real-time tissue examination. Currently, both pCLE and cholangioscopy classification systems are available; however, a comparison between these classification systems remains unknown.
**Aims & Methods:** To compare the Paris classification criteria (pCLE) and the visual impression classification system (POCS) for the detection of malignancy in biliary lesions.
The following is a cross-sectional study. Data from patients referred for cholangioscopy and pCLE due to indeterminate biliary stricture was consecutively recorded and analyzed. The visual impression of biliary lesions during POCS were recorded following the classification system proposed by Robles-Medranda et-al. pCLE was performed using the Cellvizio CholangioFlex probe (Mauna Kea Technologies, Paris, France) during the ERCP procedure, and the pCLE findings for the diagnosis malignancy were recorded according to the Paris classification. pCLE videos were reviewed by one endoscopist, blinded to any clinical or ERCP information, and indicated which descriptive criteria (Paris classification) were observed in the videos displayed. Malignancy detection was defined following histopathology results. A video-set of 20 patients with pCLE were evaluated for interobserver agreement by two endoscopists (J.O and J.A).