シンポジウム | 全診療科

2026年11月21日(土) 10:25 ~ 11:40 | 第5会場（1F 会議室102）

シンポジウム７　Gut Microbiota and Colorectal Diseases: A Future Unlocked by the Microbiome

Moderator: Hiroto Miwa (Kawanishi City Medical Center, Japan), Tomohisa Takagi (Molecular Gastroenterology and Hepatology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Japan)

[SY7-1] Right-sided Predominance of Primary Sclerosing Cholangitis–Associated Colitis: Insights from Gut Microbiota

*Haruka Okada[1], Shinya Sugimoto[1], Nobuhiro Nakamoto[1], Ryosuke Kasuga[1], Hiroki Kiyohara[1], Hiroki Kiyohara[1], Yohei Mikami[1], Takanori Kanai[1] (1. Division of Gastroenterology and Hepatology, Department of Internal Medicine, Keio University School of Medicine, Japan)

[SY7-2] Gut Microbiota Profiles in Reactive and Metastatic Lymphadenopathy in Colorectal Cancer

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[SY7-3] Microbiome Determinants of Sustained Remission after Antibiotic-Preconditioned FMT in Ulcerative Colitis: A Prospective Multicenter Study with One-Year Follow-up

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[SY7-4] Gut Microbiota Analysis for Predicting Clinical Relapse in Patients with Quiescent Ulcerative Colitis: Multivariate Analysis Using MaAsLin2 and Development of a Predictive Score

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[SY7-5] Correlation between changes in intestinal microbiota and defecatory function before and after radical resection of right-sided colon cancer.

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[SY7-6] Analysis of Inflammasome-Related Gene Variants in Colchicine-Responsive, MEFV Mutation-Negative Patients with Inflammatory Bowel Disease Unclassified

*Kohei Wagatsuma[1], Masashi Idogawa[1,2], Motohiro Esaki[3], Taku Kobayashi[4], Fumihito Hirai[5], Katsuhiro Arai[6], Reiko Kunisaki[7], Shinichiro Shinzaki[8], Tadakazu Hisamatsu[9], Hiroshi Nakase[1] (1. Division of Gastroenterology and Hepatology, Department of Internal Medicine, Sapporo Medical University School of Medicine, Japan, 2. Division of Medical Genome Sciences, Department of Genomic and Preventive Medicine, Sapporo Medical University School of Medicine, 3. Division of Gastroenterology, Department of

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[SY7-7] Efficacy of Colchicine in Mild-to-Moderate Ulcerative Colitis and Identification of Treatment Response–Associated Molecular Profiles

*Hiroki Kurumi[1,2], Kohei Wagatsuma[1], Yuta Shimomori[1], Kotaro Akita[1], Yoshihiro Yokoyama[1], Tomoe Kazama[1], Hiroshi Nasuno[3], Atsushi Yawata[4], Hajime Isomoto[2], Hiroshi Nakase[1] (1. Division of Gastroenterology and Hepatology, Department of Internal Medicine, Sapporo Medical University School of Medicine, Japan, 2. Division of Gastroenterology and Nephrology, Faculty of Medicine, Tottori University, Japan, 3. Department of Gastroenterology, Kushiro City General Hospital, 4. Department of Gastroenterology and Hepatology, Hakodate Goryoukaku Hospital)

[SY7　Special Remarks] Special Remarks

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[SY7-1] Right-sided Predominance of Primary Sclerosing Cholangitis–Associated Colitis: Insights from Gut Microbiota

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[Objective] Primary sclerosing cholangitis (PSC) is frequently associated with inflammatory bowel disease, and gut microbiota involvement has been suggested. We previously reported that *Klebsiella pneumoniae* (Kp) is frequently detected in PSC feces and is associated with disease activity and prognosis. PSC-associated colitis (PSC-colitis) is characterized by right-sided predominance, rectal sparing (RS), and backwash ileitis (BI); however, their frequencies vary among studies. This study aimed to investigate the significance of right-sided colitis by systematic evaluation of endoscopic images and by using a mouse model.
[Methods] We retrospectively analyzed PSC patients at our institution between January 2012 and July 2025. All colonoscopic images were reviewed, and PSC-colitis cases with evaluable active phase were included. For comparison, Ulcerative colitis (UC) without PSC (n = 3,419) were used to generate a 1:1 matched control group. In mice, PSC-derived Kp strains were orally administered, and their gut localization and bacterial translocation were quantitatively assessed.
[Results] Among 212 PSC patients, 170 (80.2%) had concomitant colitis. The majority (98.2%) exhibited a UC-like phenotype. In PSC with UC-like colitis and evaluable active phase endoscopy (n = 126), disease distribution was predominantly extensive (97.6%), with minimal left-sided (2.4%) and no proctitis, whereas UC-only patients showed extensive (66.7%), left-sided (20.6%), and proctitis (12.7%) ($P < 0.001$). RS and BI were significantly more frequent in PSC-colitis (92.1% vs. 11.1% and 24.1% vs. 3.2%, respectively; both $P < 0.001$). In mice, PSC-derived Kp preferentially accumulated in the ileocecal region and translocated to mesenteric lymph nodes draining this region.
[Conclusion] PSC-colitis is characterized by right-sided predominance, frequent RS and BI, and a phenotype distinct from UC. Preferential localization of PSC-derived Kp to the ileocecal region suggests a role for regional microbiota in the right-sided colon, consistent with gut–liver axis involvement.

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[SY7-2] Gut Microbiota Profiles in Reactive and Metastatic Lymphadenopathy in Colorectal Cancer

*Toru Miyake[1,2], Masatsugu Kojima[1], Soichiro Tani[1], Keiji Muramoto[1], Nobuhito Nitta[1], Reiko Otake[1], Haruki Mori[1], Hiromitsu Maehira[1], Sachiko Kaida[1], Tomoharu Shimizu[2] (1. Department of Gastrointestinal and General Surgery, Shiga University of Medical Science, Japan, 2. Medical Safety Section, Shiga University of Medical Science Hospital, Japan)

Purpose: In advanced colorectal cancer, pre-operative lymphadenopathy may represent either metastasis or reactive changes. This study aimed to compare the gut microbiota between patients with reactive and metastatic lymphadenopathy and explore its association with non-metastatic lymph node swelling.
Methods: This study was a retrospective observational analysis of fecal and tumour tissue samples from colorectal cancer patients, utilizing 16S rRNA gene sequencing, conducted at Shiga University of Medical Science Hospital between 2018 and 2021. A comparison was made of the bacterial profiles in patients with reactive and metastatic lymphadenopathy. Sixty-three patients with a pre-operative diagnosis of lymphadenopathy who underwent resection were included. DNA was extracted from both fecal samples collected pre-operatively and surgically resected tumour tissues.
Results: Median age was 70 years, with 49% male. Among 63 patients with preoperative lymphadenopathy, 34 (54%) had pathological metastasis and 29 (46%) were diagnosed with reactive lymphadenopathy. Fecal samples had higher alpha diversity than tumour samples. Proteobacteria were enriched in metastatic tumours, while Firmicutes predominated in non-metastatic cases. Metabolic pathways related to oxygen-dependent metabolism were active in metastatic cases, whereas anaerobic glycolysis and lipopolysaccharide synthesis pathways were more active in non-metastatic cases.
Conclusion: Distinct microbiota compositions were identified between reactive and metastatic lymphadenopathy in colorectal cancer patients, suggesting that bacterial-induced inflammation may be involved in reactive lymphadenopathy.

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Ulcerative colitis (UC) is a chronic inflammatory bowel disease characterized by relapsing and remitting inflammation of the colonic mucosa. Although its pathogenesis remains incompletely understood, UC is thought to arise from complex interactions among genetic susceptibility, immune dysregulation, and environmental factors. Accumulating evidence indicates that intestinal dysbiosis is a hallmark of UC, with patients showing reduced microbial diversity and disruption of the normal microbial community structure compared with healthy individuals.

To address this, we developed antibiotic-preconditioned fecal microbiota transplantation (A-FMT), combining a 2-week course of amoxicillin, fosfomycin, and metronidazole (AFM) with anaerobically prepared FMT. A-FMT was administered as repeated FMT consisting of one colonoscopic infusion followed by two enemas. This strategy was designed to reduce colonization resistance, preserve oxygen-sensitive donor microbes, and enhance donor microbial engraftment.
To evaluate efficacy and safety, we performed a prospective multicenter study of A-FMT. Clinical remission at week 8, short-term safety, donor microbial convergence, and exploratory microbiome signatures associated with remission were assessed. Seventeen of 37 treated patients (45.9%) achieved clinical remission at week 8, exceeding the rate reported in a historical placebo cohort from a Japanese budesonide foam trial (20.5%).

Despite remission at week 8, maintenance of long-term remission remains an unmet medical need, as some patients experience subsequent clinical deterioration. Therefore, as a follow-up to the above study, we conducted an additional longitudinal investigation focusing on microbiome determinants of sustained versus non-sustained remission.

Here we present longitudinal findings from this extension study, in which stool samples were collected and shotgun metagenomic analyses were performed for up to one year after FMT to characterize microbiome differences between patients with sustained and non-sustained long-term remission.

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[SY7-4] Gut Microbiota Analysis for Predicting Clinical Relapse in Patients with Quiescent Ulcerative Colitis: Multivariate Analysis Using MaAsLin2 and Development of a Predictive Score

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Background: Predicting relapse in quiescent ulcerative colitis (qUC) remains challenging. The utility of gut microbiota as a relapse predictor has not been fully evaluated.
Methods: A total of 59 qUC patients attending Kyoto Prefectural University of Medicine between November 2016 and September 2017 were prospectively enrolled and followed for up to 3.5 years. Clinical remission was defined as a Lichtiger index score of 4 or less. Fecal microbiota was analyzed by 16S rRNA sequencing. After centered log-ratio (CLR) transformation, MaAsLin2 identified relapse-associated genera. A Ridge regression-based predictive score was validated by leave-one-out cross-validation (LOO-CV). Cox regression and Youden index-based cutoff analysis were performed.
Results: Of 59 patients, 19 (32.2%) relapsed. MaAsLin2 identified five genera associated with relapse (all $p<0.05$): *Prevotella* ($p=0.008$), *Faecalibacterium* ($p=0.023$), *Odoribacter* ($p=0.033$), *Christensenellaceae* ($p=0.035$), and *Mogibacteriaceae* ($p=0.042$). Of these, four remained significant in multivariate analysis: *Prevotella*, *Faecalibacterium*, *Odoribacter*, and *Christensenellaceae*. A 4-genera Ridge regression score achieved LOO-CV AUC=0.804, demonstrating good discriminative ability for predicting relapse. At the optimal cutoff, sensitivity=84.2%, specificity=72.5%, and negative predictive value (NPV)=90.6%. Cox regression showed HR=51.0 (95%CI 7.1–368.0, $p<0.0001$). Kaplan-Meier analysis showed significantly different relapse-free rates between risk groups (log-rank $p<0.0001$).
Conclusions: A 4-genera fecal microbiota score using Ridge regression achieved LOO-CV AUC=0.804, enabling risk stratification and potentially guiding personalized treatment in qUC remission.

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[SY7-5] Correlation between changes in intestinal microbiota and defecatory function before and after radical resection of right-sided colon cancer.

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Postoperative bowel dysfunction after colorectal cancer surgery impairs quality of life; however, its longitudinal course and association with gut microbiota dynamics after right-sided colon cancer surgery remain unclear. This single-center retrospective observational study included 60 patients with pathological stage I–III right-sided colon cancer who underwent curative ileocecal resection or right hemicolectomy between November 2023 and November 2024. Bowel function was assessed preoperatively and at 1, 6, and 12 months postoperatively using the Bristol Stool Form Scale, Constipation Scoring System, and Wexner score. Gut microbiota composition was evaluated using full-length 16S rRNA sequencing of fecal samples collected preoperatively and at 1 and 6 months postoperatively. Bowel function parameters showing significant postoperative changes were identified, and patients were stratified according to the presence or absence of symptom worsening to assess the effects of sampling time, symptom-based phenotype group, and their interaction on microbial diversity.

At 1 month postoperatively, stool softening, incomplete evacuation, and liquid stool incontinence were observed in 42, 21, and 5 patients, respectively. These symptoms improved by 6 months and generally returned to preoperative levels by 12 months. Microbiota analysis revealed decreased α-diversity and marked early shifts in β-diversity, followed by gradual reconstruction with substantial interindividual variability. In phenotype-stratified analyses, microbial diversity changes were consistently associated with sampling time, whereas symptom-based group effects and time × group interactions were not significant. Overall, bowel dysfunction after right-sided colon cancer surgery was common but largely transient, and postoperative microbiota alterations appeared to reflect generalized, time-dependent ecological reconstruction rather than direct microbial correlates of individual bowel symptoms.

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Background: We previously reported that 60.1% of patients with inflammatory bowel disease unclassified (IBDU) carried Mediterranean fever (*MEFV*) gene mutations, and that colchicine was effective in 84.6% of these patients. We also demonstrated that their intestinal microbiota composition differed from that of healthy controls (HCs) and patients with inflammatory bowel disease. However, some *MEFV* mutation-negative patients also responded to colchicine, suggesting the existence of a subgroup of enterocolitis associated with variants in inflammasome-related genes other than *MEFV*.

Methods: Whole-genome sequencing was performed in 31 colchicine-responsive, *MEFV* mutation-negative patients with IBDU [variant(-) group] to identify variants in inflammasome-related genes. Clinical characteristics and intestinal microbiota profiles were compared with those of 190 *MEFV* mutation-positive patients with IBDU [variant(+) group].

Results: Variants were identified in *CARD8* (80.6%), *ATG16L1* (61.3%), *NLRP6* (54.8%), *NLRP1* (38.7%), *NLRP3* (25.8%), *IRGM* (19.4%), *ATG16L2* (16.1%), *NEK7* (12.9%), *NLRC4* (9.7%), *NAIP* (9.7%), *AIM2* (6.5%), and *NOD2* (3.2%). Multiple variants were detected in 93.5% of the patients. Rare variants with a frequency of <1% or unknown frequency in the Japanese population were identified in *NLRP3*, *NLRC4*, *NOD2*, and *AIM2*. Compared with the variant(+) group, the variant(-) group had higher frequencies of asthma (25.8% vs. 7.4%), drug allergy (29.0% vs. 4.7%), and oral aphthae (25.8% vs. 8.4%), but a lower frequency of hematochezia (35.5% vs. 56.3%). CRP (7.4 vs. 0.8 mg/dL) and serum amyloid A levels (161.7 vs. 16.5 μg/mL) were markedly elevated in the variant(-) group. In the intestinal microbiota analysis, *Enterococcus*, which was increased in the variant(+) group compared with HCs, was not increased in the variant(-) group, whereas *Subdoligranulum*, which was decreased in the variant(+) group, was further decreased in the variant(-) group.

Conclusions: These findings suggest the presence of a subgroup of IBDU associated with inflammasome-related gene variants.

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Background

Inflammasome activation is a central driver of innate immune signaling and can amplify intestinal inflammation by releasing IL-1β. Our previous studies suggest that aberrant inflammasome activation contributes to the pathophysiology of ulcerative colitis (UC) in a subset of patients. This study aimed to evaluate the efficacy of colchicine, an inflammasome inhibitor, in patients with mild-to-moderate UC and to identify molecular profiles associated with treatment response using omics analyses.

Methods

Fifteen patients with mild-to-moderate UC (treatment-naïve or 5-ASA–refractory/intolerant) received colchicine 0.5 mg/day, escalated to 1.0 mg at day 14 if non-responding; non-responders at day 28 discontinued, while responders continued through day 84. The primary endpoint was clinical response at day 14. Secondary endpoints included clinical and endoscopic remission at day 84 and safety (CTCAE v5.0). Omics analyses comprised genomic (blood), transcriptomic (colonic mucosa), and gut microbiome analyses (fecal).

Results

Clinical response at day 14 was achieved in 53.3% (8/15), clinical remission at day 84 in 33.3% (5/15), and endoscopic remission in 13.3% (2/15). Adverse events were mild: one patient experienced grade 1 diarrhea, and one grade 1 liver dysfunction. Responders (R) carried MEFV variants in 87.5% (7/8), significantly higher than non-responders (NR) (28.6%, 2/7; p=0.041). Transcriptomic analysis showed enrichment of adaptive immune–related pathways in NR, with significantly elevated KLRG1 expression (p<0.001). Gut microbiome analysis revealed no difference in α-diversity between R and NR, whereas β-diversity differed significantly (PERMANOVA, p=0.049). In R, potentially inflammasome-activating bacteria such as Enterobacter were significantly enriched, whereas NR showed increases in anti-inflammatory taxa (e.g., Bifidobacterium longum), suggesting a compensatory expansion.

Conclusion

Colchicine may benefit a subset of patients with UC who show linked inflammasome signatures across genetics, microbiota, and mucosa.

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