aim to identify the faecal fungal secretome in patients with CRC-stricken gut.

Methods Faecal samples from 26 clinically-diagnosed patients with CRC and 20 non-CRC control individuals were collected, homogenized and filtered followed by protein extraction and profiling by quantitative label-free proteomics using Nano-Liquid Chromatography TripleTOF Mass Spectrometry. The mass spectra datasets were searched using MaxQuant against the fungi's Uniprot Fasta databases. Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) version 22. Fungal taxa associated with clinical parameters were identified using multivariate association with linear models.

Results We identified 570 fungal proteins secreted into the human gut. A distinct alteration in the diversity and composition of the fungal microbiota was observed in the CRC, with tremendous reductions of the overall fungal proteins, the diversity and composition of fungal microbiota as compared to the control ($p<0.05$). Interestingly, the proportion of candida was increased in the CRC, indicating a modified gut microenvironment that favours the fungi. However, the discriminative distributions of the fungi secretome proteins in both CRC and non-CRC were observed with great individual variation.

Conclusions The distinct alteration of fungal proteins observed in CRC may suggest a possible CRC-specific gut microenvironment for fungi. This knowledge may be exploited for new therapeutic approaches for gut-related issues.

Basic Hepatology

IDDF2019-ABS-0174 TARGETING MONOCYTE-INTRINSIC ENHANCER REPROGRAMMING IMPROVES IMMUNOTHERAPY EFFICACY IN HEPATOCELLULAR CARCINOMA

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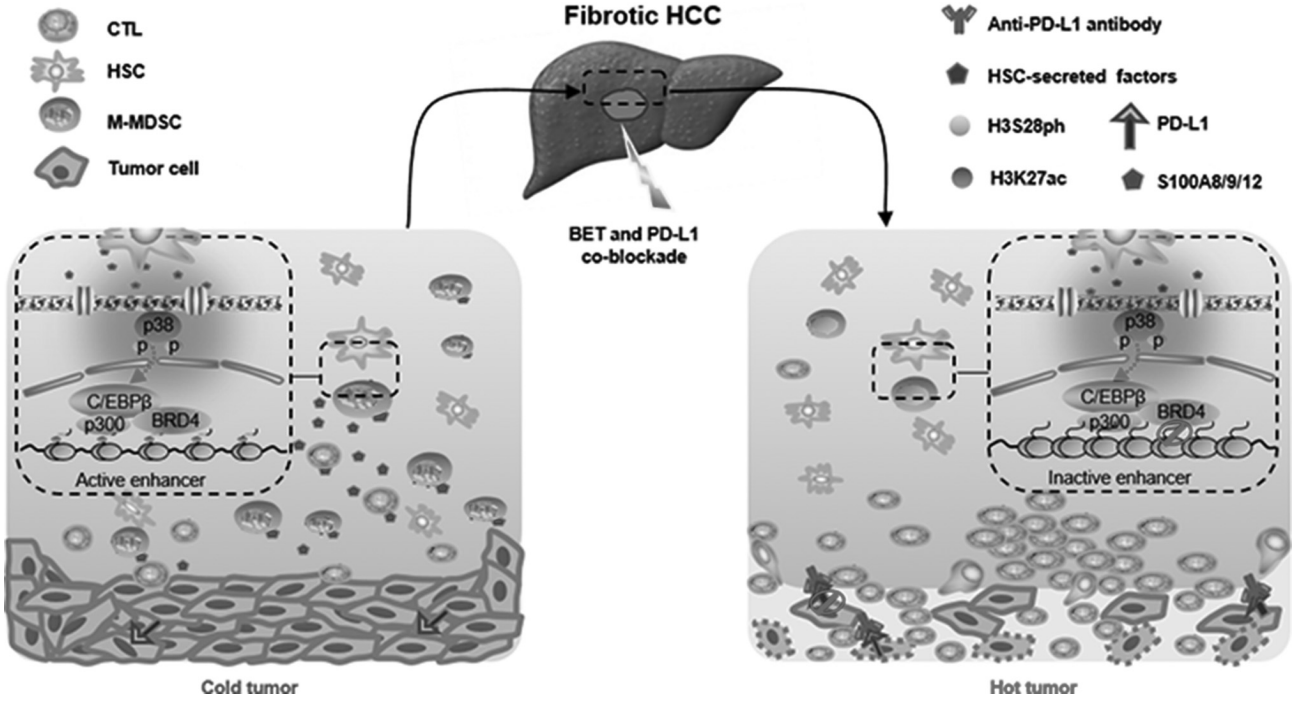
Background Hepatocellular carcinoma (HCC), mostly developed in fibrotic/cirrhotic liver, exhibits relatively low responsiveness to immune-checkpoint blockade (ICB) therapy. As



Abstract IDDF2019-ABS-0174 Figure 1 BET and PD-L1 co-blockade synergistically enhanced TILs and eradicated HCC

myeloid-derived suppressor cell (MDSC) is pivotal for immunosuppression, we investigated its role and regulation in the fibrotic microenvironment with an aim of developing mechanism-based combination immunotherapy.

Methods Functional significance of MDSCs was evaluated by flow cytometry using two orthotopic HCC models in fibrotic liver setting via carbon tetrachloride or high-fat high-carbohydrate diet, and verified by clinical specimens. Mechanistic studies were conducted in the human hepatic stellate cell (HSC)-peripheral blood mononuclear cell culture systems and fibrotic-HCC patient-derived MDSCs. The efficacy of single or combined therapy with anti-programmed death-1-ligand-1 (anti-PD-L1) and a clinically-trialed BET bromodomain inhibitor i-BET762 was determined.

Results Accumulation of monocytic MDSCs (M-MDSCs), but not polymorphonuclear MDSCs, in fibrotic livers significantly correlated with reduced tumor-infiltrating lymphocytes (TILs) and increased tumorigenicity in both mouse models. In human HCCs, the tumor-surrounding fibrotic livers were markedly enriched with M-MDSC, with its surrogate marker CD33 significantly associated with aggressive tumor phenotypes and poor survival rates. Mechanistically, activated HSCs induced monocyte-intrinsic p38 MAPK signaling to trigger enhancer reprogramming for M-MDSC development and immunosuppression. Treatment with p38 MAPK inhibitor abrogated HSC-M-MDSC crosstalk to prevent HCC growth. Concomitant with patient-derived M-MDSC suppression by i-BET762, combined treatment with anti-PD-L1 synergistically enhanced TILs, resulting in tumor eradication and prolonged survival in the fibrotic-HCC mouse model.

Conclusions Our results signify how non-tumor intrinsic properties in the desmoplastic microenvironment can be exploited to reinstate immunosurveillance, providing readily translatable combination strategies to empower HCC immunotherapy (figure 1).

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IDDF2019-ABS-0299 GUT MICROBIOME DIVERSITY AND SPECIFIC MICROBIAL GENERA CORRELATE WITH THE SEVERITY OF NON-ALCOHOLIC LIVER DISEASE IN INDONESIA

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Background The prevalence of nonalcoholic fatty liver disease (NAFLD) is increasing. In Indonesia **Hasan, I et al. (2002)** reported the prevalence of 30.6%. This study evaluated the first time the profile of gut microbiota and correlation with severity of NAFLD in Indonesia.

Methods We included 37 subjects age 18–60 years. The characteristic data of the patients and the food recalls were recorded. Abdominal ultrasound, liver transient elastography with controlled attenuation parameter (CAP) were performed. Next generation 16S rRNA metagenomic sequencing was conducted using stool samples. The Spearman correlation test was used to examine the correlation between specific microbial taxa with the severity of NAFLD based on fibrosis and steatosis degree.

Results The subjects included 62.2% (n=23) females and 37.8% males (n=14), mean age 50 ± 7.93 years old. They were divided based on fibrosis and steatosis degree into non-significant and significant fibrosis using cut off 7 KPa, mild and moderate-severe steatosis based on cut off 270 dB/m. From all subjects, we got 73% vs 27% non-significant and significant fibrosis, 51.4% vs 48.6% mild and moderate-severe steatosis. At the phylum level, the proportion of *Bacteriodetes* did not change in fibrosis or steatosis group. The proportion of *Proteobacteria* and *Firmicutes* was different in fibrosis and steatosis groups. *Actinobacteria unknown bifidobacteriales bifidobacteriaceae bifidobacterium Bifidobacterium adolescentis* correlate positively with non significant fibrosis (r = 0.532; p=0.004). *Firmicutes clostridia clostridiales lachnospiraceae unknown fusicatenibacter saccharivorans* and *Firmicutes clostridia clostridales ruminococcaceae unknown [clostridium] leptum* correlate negatively with significant fibrosis (r = -0.695; p=0.026 vs r = -0.732; p=0.016). In the group of steatosis, we got *Bacteroidetes bacteroidia bacteroidales rikenellaceae alistipes alistipes onderdonkii* and *Firmicutes clostridia clostridales oscillospiracea oscillospiraceao scilibacter ruminantum* correlate negatively with moderate-severe steatosis (r = -0.478; p=0.045 vs r = -0.518; p=0.028); *Bacteroidetes bacteroidia bacteroidales rikenellaceae alistipes alistipes putredinis* correlate positively with mild steatosis (r = 0.503; p=0.028).

Conclusions The abundance of microbiota in NAFLD are not significantly different based on the group of fibrosis and steatosis, especially in phylum level. But at the lower level, some specific microbiota may correlate with the degree of fibrosis and steatosis.

Clinical Gastroenterology

IDDF2019-ABS-0042 PROSPECTIVE STUDY OF RISK SCORE STRATEGIES IN THE PREDICTION OF ADVANCED COLORECTAL NEOPLASIA AT COLONOSCOPY

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10.1136/gutjnl-2019-IDDFabstracts.6

Background Current referral pathways in Australia for colorectal cancer (CRC) screening do not differentiate well between low and high-risk populations, and therefore may not be efficiently utilising resources. Whilst multiple CRC risk scoring systems currently exist and are utilised to stratify patients into low and high risk groups for priority of