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).

Acknowledgement This project is supported by the University Grants Committee through the Collaborative Research Fund (C4045-18W) and the Theme-based Research Scheme (T11-706/18-N), the Health and Medical Research Fund (16170451), the Terry Fox Foundation, the Focused Innovations Scheme-Scheme B (1907309) from the Chinese University of Hong Kong and the Li Ka Shing Foundation (Canada). Man Liu is supported by China Postdoctoral Science Foundation.

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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10.1136/gutjnl-2019-IDDFabstracts.5

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 *Bacteroidetes* 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 clostridiales 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 clostridiales oscillospiraceae oscillospiraceo 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

colorectal screening, there remains a need to identify which system has the greatest diagnostic accuracy. Therefore, we prospectively compared three existing CRC risk score systems in their ability to predict advanced colorectal neoplasia in Australian population; the Asia-Pacific Colorectal Screening (APCS) score; Hong Kong Score (2014); and Imperiale Score (2015).

Methods Patients scheduled for colonoscopy assessment, both with or without gastrointestinal symptoms, were recruited. FOBT positive patients were included, but those who had an examination of the colon, including colonoscopy, within the last five years were excluded. Univariate and multivariate logistic regression was applied to identify significant risk factors for advanced neoplasia. For each patient, the 3 different risk scores were applied and the performance of each score in the prediction of advanced neoplasia was compared by examining the area under the curve (AUC) value.

Results A total of 361 patients undergoing colonoscopy (48.2% male, median age 60 years) were prospectively recruited. The prevalence of adenomas was 31.6%, and 10.0% for advanced adenoma including 8 CRC (2.2%). Upon multivariate analysis, age and male sex were found to be significant risk factors ($P=0.001$, $P=0.002$). For predicting the prevalence of advanced neoplasia, the APCS score had AUC 0.71 (95%CI 0.63–0.79), Hong Kong Score 0.69 (95%CI 0.61–0.78), and Imperiale Score 0.68 (95%CI 0.59–0.77). Using a non-parametric comparison of the AUCs, there was no statistical significance between each of the scores for both symptomatic and asymptomatic populations ($P=0.37$ for APCS vs Hong Kong Score; $P=0.32$ for APCS vs Imperiale Score; $P=0.43$ for Hong Kong Score vs Imperiale Score).

Conclusions All three scores are equally effective in stratifying the population into low and high risk colorectal neoplasia groups, and may be used to prioritise patients for colorectal screening.

IDDF2019-ABS-0132

METACHRONOUS GASTRIC CANCER PREVENTION WITH ASPIRIN AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR EARLY GASTRIC CANCER: PROTOCOL OF A MULTI-CENTER RANDOMIZED CONTROLLED TRIAL

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10.1136/gutjnl-2019-IDDFabstracts.7

Background Epidemiological studies suggest that long term low-dose aspirin use reduces the risk of gastric cancer. However, no randomized control studies have been conducted to assess the role of aspirin in the reduction of occurrence of gastric cancer. This study aims to investigate the chemo-preventive effect of aspirin on the development of metachronous gastric cancer after endoscopic submucosal dissection (ESD) for early gastric cancer (EGC).

Methods A total of 1120 patients received ESD for EGC and *Helicobacter pylori* eradication at 33 institutions among Japan and Hong Kong will be enrolled in this study. Enrolled patients will be randomly assigned to either receive aspirin 81 mg once daily or nothing for 5 years at a 1:1 allocation ratio.

Patients will be examined endoscopically for metachronous gastric cancer at 12, 24, 36, 48 and 60 months after randomization. The primary outcome measure is the development of metachronous gastric cancer at 5 years. Metachronous gastric cancers will be confirmed through histological examination of samples obtained through biopsy, or endoscopic or surgical resection. A blinded adjudication panel consisting of three pathologists will diagnose all specimens. The histological criteria of gastric cancer will be defined as categories 4 and 5 with the Vienna classification.

Results This study was approved by Institutional Review Board of Nippon Medical School Foundation on February 25, 2019. The start of the recruitment is planned in April 2019 and will continue for a 3-year period.

Conclusions The findings of this study will be submitted to a peer-reviewed journal. Abstracts will be submitted to relevant national and international conferences. This study is registered with the University Hospital Medical Information Network (UMIN) Clinical Trials Registry (www.umin.ac.jp/ctr/; identification No.: UMIN000031302).

IDDF2019-ABS-0142

COMBINATION OF ERCP AND EUS-GUIDED BILIARY DRAINAGE (CERES) VERSUS PTBD FOR MALIGNANT HILAR BILIARY OBSTRUCTION: A MULTICENTER PROSPECTIVE COMPARATIVE COHORT STUDY (THE CERES STUDY)

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10.1136/gutjnl-2019-IDDFabstracts.8

Background Combination of ERCP and EUS-BD (CERES) including EUS-guided hepaticogastrostomy (EUS-HGS) and EUS-guided hepaticoduodenostomy (EUS-HDS) may provide complete BD in bismuth 3 and 4 malignant hilar biliary obstruction (MHBO). This study aims to prospectively compare the efficacy of CERES versus PTBD in MHBO.

Methods Patients with MHBO were recruited. Patients presented to endoscopy and interventional radiology service received CERES (group A) and PTBD (group B) as primary BD method, respectively. Technical and clinical success rate (TSR and CSR) and time to RBO (T-RBO = time from last successful BD to biliary reintervention procedure) were recorded. The study was conducted during March 2016 until October 2018 as a multicenter study of 3 Thai hospitals (King Chulalongkorn Memorial Hospital of Thai Red Cross Society, Tha-Bor Hospital, and Roi-Et Hospital) under the Thai Association for Gastrointestinal Endoscopy (TAGE) guidance.

Results 45 patients (23M, 22F) were recruited into group A (n=23) and group B (n=22). One patient from group A was withdrawn due to loss to follow up. Demographic data and results of both groups are shown in table 1. Overall TSR, CSR, and complication rate (CR) of group A versus B were 90.9% (20/22) vs 100% (22/22) (p =not significant (NS)), 81.8% (18/22) vs 86.4 (19/22) (p =NS), and 18.2 (4/22) vs