Background The outbreak of Coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 infection has become a global health emergency. We aim to decipher SARS-CoV-2 infected cell types, the consequent host immune response and their interplay in the lung of COVID-19 patients.

Methods We analyzed single-cell RNA sequencing (scRNA-seq) data of bronchoalveolar lavage fluid (BALF) samples from 10 healthy donors, 6 severe COVID-19 patients and 3 mild recovered patients. The expressions of SARS-CoV-2 receptors (ACE2 and TMPRSS2) were examined among different cell types. The immune cells infiltration patterns, their expression profiles, and interplays between immune cells and SARS-CoV-2 target cells were further investigated.

Results Compared to healthy controls, ACE2 and TMPRSS2 expressions were significantly higher in lung epithelial cells of COVID-19 patients, in particular club and ciliated cells. SARS-CoV-2 activated pro-inflammatory genes and interferon/cytokine signaling in these cells. In severe COVID-19 patients, significantly higher neutrophil, but lower macrophage in the lung was observed along with markedly increased cytokines expression compared with healthy controls and mild patients. By contrast, neutrophil and macrophage returned to normal level whilst more T and NK cells accumulation were observed in mild patients. Moreover, SARS-CoV-2 infection altered the community interplays of lung epithelial and immune cells: interactions between the club and immune cells were higher in COVID-19 patients compared to healthy donors; on the other hand, immune-immune cells interactions appeared the strongest in mild patients.

Conclusions SARS-CoV-2 could infect lung epithelium, alter communication patterns between lung epithelial cells and immune system, and drive dysregulated host immune response in COVID-19 patients.

IDDF2021-ABS-0210

ALTERED GUT METABOLITES AND BACTERIAL INTERACTIONS ARE IMPLICATED IN COLORECTAL CARCINOGENESIS AND CAN DETECT PRECANCEROUS AND CANCEROUS LESIONS

^{1,2}Olubisi Oluwabukola Coker*, ^{1,2}Changan Liu*, ^{1,3}William Ka Kei Wu, ^{1,2}Sunny Hei Wong, ⁴Wei Jia, ^{1,2,5}Joseph JY Sung, ^{1,2}Jun Yu. ¹State Key Laboratory of Digestive Disease, Li Ka Shing Institute of Health Sciences, CUHK Shenzhen Research Institute, The Chinese University of Hong Kong, Hong Kong, China; ²Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong, China; ³Department of Anaesthesia and Intensive Care, The Chinese University of Hong Kong, Hong Kong, China; ⁴School of Chinese Medicine, Hong Kong Baptist University, Kowloon Tong, Hong Kong, China; ⁵Lee Kong Chian School of Medicine, Nanyang Technology University, Singapore

10.1136/gutjnl-2021-IDDF.6

Background Gut microbiota contributes to colorectal cancer (CRC) pathogenesis through specific pathogens and their metabolites. We aim to determine gut microbiota-associated metabolites and their linkage to CRC.

Methods We performed metabolomics by gas chromatography coupled to time-of-flight mass spectrometry, and shotgun metagenomics analysis on fecal samples from 386 subjects [118 CRC patients, 140 colorectal adenomas (CRA) patients and 128 normal controls (NC)]. Stepwise logistic regression models

were used to identify metabolites and bacterial markers discriminating CRC stages. Associations among CRC-associated metabolites and bacteria were estimated with zero-inflated negative binomial regressions analysis.

Results Principal component analysis and partial least squares-discriminant analysis showed differences in the gut metabolite profiles among CRC, CRA and NC groups. Norvaline and myristic acid showed increasing trends from NC, through CRA, to CRC. CRC-associated metabolites were enriched in branched-chain amino acids and aminoacyl-tRNA biosynthesis pathways. Twenty metabolites classified CRC from NC subjects with an area under the curve (AUC) of 0.80, and CRC from CRA with AUC of 0.79. Combinations of metabolites and bacterial markers improved the diagnostic performances (CRC vs NC, AUC: 0.94; CRC vs CRA, AUC 0.92; CRA vs NC, AUC: 0.86), indicating a potential for early diagnosis of colorectal neoplasia. Moreover, relationships among CRC-associated metabolites and bacteria were altered across CRC stages; certain associations exhibited increasing or decreasing strengths while some were reversed from negative to positive or vice versa.

Conclusions Gut metabolites are altered in colorectal carcinogenesis. The combination of metabolites and bacterial species can increase the chance of a non-invasive diagnosis of colorectal neoplasia.

Basic Hepatology

IDDF2021-ABS-0145

TURNING IMMUNOLOGICALLY COLD TUMORS INTO HOT ONES BY ACTIVATING HEPATOMA-INTRINSIC FADD/NF-KB/CCL5 PATHWAY

Jiahuan Lu*, Jing Wang, Yalin Tu, Weiqin Yang, Wenshu Tang, Zhewen Xiong, Alfred Sze-Lok Cheng, Anthony Wing-Hung Chan, Ka-Fai To. Chinese University of Hong Kong, Hong Kong

10.1136/gutjnl-2021-IDDF.7

Background Lymphoepithelioma-like hepatocellular carcinoma (LEL-HCC) as a distinct variant of HCC displayed immunologically hot tumor features with prominent tumor-infiltrating CD8⁺T lymphocytes (TILs). Our whole exome sequencing data found an increased prevalence of chromosome 11q13.3 amplification in LEL-HCC, in which contains fas-associated death domain (FADD) that displayed a strongest positive correlation with differentially expressed genes function in TIL migration. We hence aim to elucidate the functional roles and molecular mechanisms of hepatoma-intrinsic FADD in regulating TIL abundance in general HCC patients.

Methods FADD-overexpressed HepG2 (FADD-oe) and FADD-knockdown huh7 cells (FADD-kd) were constructed to investigate cell growth rate by colony formation and MTS assay in vitro, subcutaneous tumor in immunodeficient nude and NOD/SCID mice in vivo. A co-culture model of human peripheral blood-derived- CD8⁺T cells and HepG2-oe or Huh7-kd in vitro, T cell adoptive transfer and humanized mice models in vivo were used to detect T migration preference. The downstream functional chemokines and molecular pathways controlled by FADD were determined by RT-qPCR, ELISA, western blot as well as gene modulation assays. Finally,