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 cells type, 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 cell 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.

Basic Hepatology

IDDF2021-ABS-0145 TURNING IMMUNOLOGICALLY COLD TUMORS INTO HOT ONES BY ACTIVATING HEPATOMA-INTRINSIC FADD/NF-KB/CCL5 PATHWAY

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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 exosome 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,