Basic Hepatology

IDDF2021-ABS-0073 CHARACTERISTICS OF BILIARY MICROBES IN PATIENTS WITH RECURRENT CHOLEDOCHOLITHIASIS

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Background To observe the characteristics of biliary tract microorganisms in patients with recurrent cholelithiasis, and to analyze the influence of biliary tract microorganisms on the recurrence of cholelithiasis.

Methods The clinical data of 40 patients with recurrent cholelithiasis who completed the operation and one-year follow-up in our hospital from March 2017 to August 2019 were retrospectively analyzed. The clinical data of 40 patients with non-recurrent cholelithiasis who were followed up for 1 year were regarded as the non-recurrent group. Observed and compared the characteristics of biliary tract microorganisms in two groups, and analyzed the effect of biliary tract microorganisms on the recurrence of cholelithiasis.

Results The number of biliary microbial pathogens in the relapsed group and the non-relapsed group were 37 and 33. The number of Gram-negative strains in the relapsed group was the same as that in the non-relapsed group. The relapsed group had more gram-positive bacteria and fungi than the non-relapsed group ($P=0.449$). *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus*, and *Propionibacterium acnes* were higher in the relapsed group than in the non-relapsed group ($P<0.05$); Logistic regression analysis showed that *Escherichia coli*, *Staphylococcus aureus*, intestine Proliferation of cocci and *Propionibacterium acnes* were the influencing factors for recurrent cholelithiasis ($P<0.05$); By drawing ROC curve found that the EUC of *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus*, *Propionibacterium acnes* for the prediction of recurrent common bile duct stones were: 0.813, 0.809, 0.807, 0.806, which have certain predictive value.

Conclusions Patients with recurrent cholelithiasis have significant changes in biliary microorganisms, and the detected pathogenic microorganisms are more significant than non-recurrent ones, such as *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus*, *Propionibacterium acnes*, etc. The proliferation of these pathogenic microorganisms may be related to the occurrence and recurrence of cholelithiasis. It is recommended that patients with cholelithiasis who are treated for the first time can pay close attention to the changes of biliary tract microbes after treatment. For patients who have detected the above pathogenic microorganisms, timely measures should be taken to adjust, which may have a positive meaning in reducing the recurrence of cholelithiasis.

IDDF2021-ABS-0115 ENHANCER DYSREGULATION OF MYELOID-DERIVED SUPPRESSOR CELLS IN HEPATOCELLULAR CARCINOMA

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Background Though immune checkpoint blockade (ICB) therapies have shown promise to treat HCC, the insufficient T cell infiltration to the non-inflamed tumor restricts the effectiveness of ICB therapy to a minority of HCC patients. As a key player in the tumor microenvironment (TME), myeloid-derived suppressor cells (MDSC) were reported to correlate with resistance to ICB and poor prognosis. Given the fact that enhancer reprogramming of MDSC is crucial to the MDSC identity and function, this study aims to identify the enhancer targets that are significantly contributing to MDSC immunosuppressiveness and to study the potential of myeloid targeting for improving immunotherapy efficacy.

Methods Single-cell RNA sequencing (sc-RNA-seq) of ICB-resistant patients was performed to understand the immune profile of patients and the heterogeneity of TME in HCC. The expression and immune profile of MDSC signature genes were determined by flow cytometry analysis in immune cells from tumor-bearing mice and HCC patients. FANTOM5 (Functional Annotation of the Mammalian Genome) database and JEME (Joint Effects of Multiple Enhancers) algorithm were used to identify enhancer RNA (eRNA) locations and expressions. Functional significance and molecular mechanisms of signature genes were conducted by gene knockdown in human blood-derived MDSCs, followed by mRNA and protein detection, q-ChIP-PCR and multi-colour flow cytometry.

Results MDSCs were negatively correlated with $CD8^+$ T cell proportion in ICB-resistant patients. A novel MDSC signature gene, EREG has been identified. Its expression is correlated with non-responsiveness in HCC patients. It is enriched in MDSCs of HCC patients and correlated with poor prognosis. Moreover, high EREG expression is correlated with increased tumor size and decreased tumor-infiltrating lymphocytes in ICB resistance mouse models. Mechanistically, it was found that eRNAs control the upregulation of EREG in MDSCs. Inhibition of eRNAs could reduce MDSC proliferation and T cell suppressive activity.

Conclusions Our data demonstrated the intricate interaction of enhancer regulation of EREG in MDSC and ICB resistance, delineating a new epigenetic mechanism underlying tumor immune evasion. Identifying this novel enhancer-regulated target might uncover new immunosuppressive mechanism and MDSC-directed strategy for improving HCC immunotherapy efficacy.

IDDF2021-ABS-0138 CIRCULATING NON-CODING TRANSCRIPTS SERVING AS BIOMARKERS FOR DIABETIC LIVER STEATOSIS

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Background Non-alcoholic steatohepatitis (NASH) as an advanced form of NAFLD is associated with excessive inflammation in the steatotic livers. Given the common comorbidity of NASH with diabetes mellitus (DM), we identified a set of circulating RNA transcripts as non-invasive