

Abstracts

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Acute Liver Failure

Oral Presentations

Abstract # 371

MicroRNA-181c potentially relieved fulminant viral hepatitis by targeting TNF- α

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Objectives: The relationship between circulating microRNAs (miRNAs) and HBV associated acute-on-chronic liver failure (HBV-ACLF) need to be further investigated. The purpose of our study was to identify the aberrant expression of miRNAs in HBV-ACLF and to investigate its potential role during the progression of HBV-ACLF.

Methods: miRNA expression profile by miRNA microarray analysis was performed on Peripheral Blood Mononuclear Cell (PBMC) obtained from patients with mild chronic hepatitis B (CHB) or HBV-ACLF, respectively. Selected unnormal expressed miRNAs were verified in more clinical samples by quantitative real-time PCR (qRT-PCR). A luciferase reporter assay was conducted to confirm direct target of miR-181c. mmu-miR-181c agomir was delivered by tail vein injection into mouse hepatitis virus-3(MHV-3)-infected BALB/cJ mice to evaluate its interference effect in fulminant viral hepatitis mouse model.

Results: 7 kinds of miRNAs were down-regulated and 9 kinds of miRNAs were up-regulated in the PBMC of HBV-ACLF patients compared with that of patients with mild CHB. Among the deregulated miRNAs, the expression of Hsa-miRNA-181c was significantly down-regulated in HBV-ACLF by qRT-PCR. While serum TNF- α significantly increased in HBV-ACLF. A luciferase reporter assay was conducted to confirm TNF- α was verified as a target of miR-181c. miR-181c significantly improved fulminant viral hepatitis mice survival rate.

Conclusion: These data suggested that miR-181c might have potentially therapeutic potential for the treatment of fulminant hepatitis.

Abstract #689

Amphiregulin alleviated conA induced acute liver injury by anti-apoptosis and interrupting neutrophil infiltration

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Introduction and objective: Amphiregulin (Areg) has a well-documented protective role in tissue injury, however, its effects on immune-mediated liver injury are still unclear. Here we used concanavalin A (conA) induced acute liver failure (ALF) model to explore the effects of Areg on immune-mediated acute liver injury.

Methods: C57BL/6 mice were administrated with conA at a dose of 20 mg/kg as the hepatitis mice, part of them received 5 μ g Areg as the treated mice. Then survival rates were analyzed within 36 h. After 5 h treatment, liver function, hepatic histology and apoptosis of liver tissue were investigated, cytokines levels, chemokines expressions, neutrophil infiltration and activity in livers were also detected.

Results: Our data showed that Areg treatment obviously increased mouse survival rates, markedly alleviated liver damage and improved liver function. Moreover, Areg administration raised the expression of anti-apoptotic proteins Bcl-2 and Bcl-xL, and down-regulated apoptosis molecule Caspase3 in livers. There were fewer neutrophils infiltration, lower MPO activity and less CX3CL1 expression in livers from the Areg treated mice than those from the untreated mice. Interestingly, these changes were concomitant with significantly enhanced IL-22 levels and IL-22-producing T cells in livers, whereas neutralization of IL-22 in vivo completely abolished the hepatoprotective effects of Areg.

Conclusions: Areg treatment revealed direct protective mechanisms against conA induced acute hepatitis, which provides the potential therapeutic strategy for Areg in immune-mediated acute liver injury.

Abstract #1263

A nomogram to predict mortality in patients with hepatitis E virus-related acute liver failure

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sequencing covering 72 significantly mutated genes (SMGs) associated with HCC, spanning 285,470 nucleotides.

Results: Genomic analysis in all HCCs revealed frequent genetic mutations in TERT promoter, TP53, CTNNB1, ALB, ARID1A. In multinodular HCC, MC was identified in 3 cases without common genetic alterations, while IM was diagnosed in 9 cases with at least one common mutation. In IM cases, 5 cases possessed only TERT promoter as a sole common mutation regardless of tumor size, while multiple common alterations were detected in others. In one IM case, all 3 nodules harbored 3 common oncogenic mutations including TP53 and NFE2L2. As for postoperative recurrence, MC cases had longer recurrence-free survival (RFS). IM cases harboring TERT promoter as a sole common mutation had better RFS compared to other IM cases. Meanwhile, very early multiple intrahepatic recurrence was detected in an IM case with multiple common oncogenic mutations.

Conclusion: Genomic analysis in multinodular HCCs can possibly stratify patients at risk for early postoperative recurrence. Patients with multiple common oncogenic mutations in all HCC nodules are at high risk of aggressive recurrence, implying requirement of intensive additional treatment such as with TKIs.

Abstract #316

Serum miRNA-320 as a potent diagnostic biomarker for human hepatocellular carcinoma irrespective of etiology

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Introduction: Hepatocellular carcinoma (HCC) is one of the leading causes of cancer death worldwide. MicroRNAs (miRNAs) play a pivotal role in the pathogenesis and progression of HCC.

Objectives: The present study was designed to identify a markedly downregulated circulating miRNA to diagnosis HCC irrespective of etiology.

Methods: Over 20 miRNAs with expected aberrant expression were screened in around 100 serum samples from HCC patients with different etiology along with healthy controls. The total miRNAs were isolated using Qiagen miRNeasy kit. About 200 nanogram of isolated total miRNA was hybridized with respective oligo for a particular miRNA in 96-well plates and the hybridized product with a biotinylated tag is detected using chemiluminescence technique as counts, which is a very sensitive and specific method to quantify miRNAs.

Results: The microarray data demonstrated that miRNA-320 is dramatically downregulated in all the serum samples from HCC patients irrespective of etiology. About 8–10 fold reduction ($P < 0.0001$) was observed in the serum levels of miRNA-320 compared to healthy controls. There was no significant difference in the mean miRNA-320 levels in serum samples between HCC patients with different etiology such as alcoholic liver cirrhosis, liver cirrhosis due to other reasons, chronic hepatitis due to hepatitis C virus (HCV) and HCC developed from other unknown causes.

Conclusion: The results of the present study demonstrated that there is a remarkable reduction in the serum levels of miRNA-320 in all

HCC patients irrespective of etiology. Therefore, the circulating miRNA-320 could be used as a diagnostic biomarker for HCC along with other clinical parameters.

Abstract #345

Impact of laparoscopic liver resection for hepatocellular carcinoma on the development of postoperative complication

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Aim: This study was aimed to compare the postoperative complication rate between laparoscopic and open liver resection.

Methods: From January 2008 to June 2018, 384 patients underwent curative liver resection for hepatocellular carcinoma (HCC) within 5 cm in size without macroscopic vascular invasion. The subjects were 321 patients who underwent limited resection or segmentectomy. Of these, laparoscopic liver resection was adopted in 191 patients (Lap group) and open liver resection was done in 130 patients (Open group). Propensity score matching (PSM) was conducted to adjust potentially confounding factors. Postoperative complication rate (Clavien-Dindo classification ≥ 2) were compared between Lap and Open groups after PSM. In addition, subgroup analysis was performed between subphrenic HCC (segment 7, 8) and non-subphrenic HCC subgroups.

Results: After PSM, the study group of 206 patients were well matched. Postoperative complications (27.2% vs. 7.8%, $p < 0.001$), abdominal abscess (7.8% vs. 1%, $p = 0.035$), bile leakage (5.8% vs. 0%, $p = 0.029$) were more frequently observed in Open group than Lap group. The blood loss volume was significantly lower in Lap group than Open group (100 ml vs. 355 ml, $p < 0.001$), and the length of hospital stay was significantly shorter in Lap group (9 days vs. 13 days, $p < 0.001$). In the subgroup analysis, among subphrenic HCC patients, abdominal abscess (14.6% vs. 0%, $p = 0.012$) were more frequently observed in Open group than Lap group, whereas among non-subphrenic HCC patients, no statistical significance was confirmed between the both group.

Conclusions: Compared to open liver resection, laparoscopic liver resection might reduce the development of postoperative abdominal abscess, especially for subphrenic HCC.

Abstract #528

Post-treatments of lenvatinib in patients with advanced hepatocellular carcinoma

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Introduction: Lenvatinib has been the second frontline systemic therapy for patients with advanced hepatocellular carcinoma (HCC) in Japan. However, post-treatments of lenvatinib have not been standardized yet.