

JOURNAL OF HEPATOLOGY

ABSTRACT BOOK

THE INTERNATIONAL
LIVER CONGRESS™

19-23 APRIL, AMSTERDAM, THE NETHERLANDS

2017

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11-15 April 2018

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VOLUME 66, SUPPLEMENT 1, PAGES S1–S858

CONTENTS

Acknowledgements	iv
Thursday, 20 April 2017	
General session I and opening ceremony	S1
Autoimmune and cholestatic liver disease I	S4
Acute liver failure and end-stage liver disease	S7
Liver tumours: From patient stratification to management	S12
Fatty liver disease: From pathophysiology to drug discovery	S16
HCV: Post SVR management and complications	S20
Hepatitis B and D: Emerging treatment options	S24
Viral hepatitis immunology	S28
Friday, 21 April 2017	
General session II and award ceremony I	S33
Liver immunology	S35
Liver transplantation: Clinical and experimental	S39
Fibrosis and regeneration	S43
Portal hypertension and hepatic encephalopathy	S46
NAFLD: Clinical progress	S50
Advances in the treatment of HCV	S54
Challenges in hepatitis B and E	S58
Saturday, 22 April 2017	
Gut liver axis: Clinical translation	S63
Non-invasive assessment of liver disease	S66
Public health issues in hepatology	S70
Autoimmune and cholestatic liver disease 2	S73
Liver tumours: Mechanisms and pathways	S76
Alcohol and drug-induced liver injury	S79
HCV: DAA resistance and retreatment	S82
General session III and award ceremony II	S85
Late breakers: Orals	S89
Posters Thursday, 20 April 2017	
Late breakers: Posters	S95
Alcoholic liver disease	S114
Cirrhosis and its complications: Clinical aspects	S118

Cirrhosis and its complications: Experimental and pathophysiology	S140
Fatty liver disease: Clinical aspects	S148
Fatty liver disease: Experimental and pathophysiology	S162
Genetic and pediatric liver diseases	S171
Liver transplantation/surgery: Clinical aspects	S183
Liver transplantation/surgery: Experimental and pathophysiology	S201
Liver tumours: Clinical (epidemiology, diagnosis) and management	S204
Liver tumours: Experimental and pathophysiology	S224
Non-invasive assessment of liver disease	S232
Viral hepatitis: Hepatitis A, B, D, E – Clinical (except therapy)	S246
Viral hepatitis: Hepatitis B and D – Clinical (therapy, new compounds, resistance)	S256
Viral hepatitis: Hepatitis C – Clinical (except therapy)	S267
Viral hepatitis: Hepatitis C – Clinical (therapy)	S280
Viral Hepatitis: Immunological aspects	S317
Posters Friday, 21 April 2017	
Acute liver failure: Clinical and experimental	S333
Alcoholic liver disease	S344
Autoimmune and chronic cholestatic liver disease: Clinical aspects	S352
Autoimmune and chronic cholestatic liver disease: Experimental and pathophysiology	S363
Cirrhosis and its complications: Clinical aspects	S368
Cirrhosis and its complications: Experimental and pathophysiology	S389
Drug-induced liver injury	S395
EU and public health	S403
Fatty liver disease: Clinical aspects	S416
Fatty liver disease: Experimental and pathophysiology	S429
Liver transplantation/surgery: Clinical aspects	S435
Liver tumours: Clinical (epidemiology, diagnosis) and management	S443
Liver tumours: Experimental and pathophysiology	S459
Viral hepatitis: Hepatitis A, B, D, E – Clinical (except therapy)	S468
Viral hepatitis: Hepatitis B and D – Clinical (therapy, new compounds, resistance)	S477
Viral hepatitis: Hepatitis B and D – Experimental and pathophysiology	S482
Viral hepatitis: Hepatitis C – Clinical (except therapy)	S488
Viral hepatitis: Hepatitis C – Clinical (therapy)	S500
Viral Hepatitis: Immunological aspects	S537
Posters Saturday, 22 April 2017	
Autoimmune and chronic cholestatic liver disease: Clinical aspects	S543
Autoimmune and chronic cholestatic liver disease: Experimental and pathophysiology	S553
Cirrhosis and its complications: Clinical aspects	S558
Cirrhosis and its complications: Experimental and pathophysiology	S579
Fatty liver disease: Clinical aspects	S586
Fatty liver disease: Experimental and pathophysiology	S598
Liver transplantation/surgery: Experimental and pathophysiology	S612

Liver tumours: Clinical (epidemiology, diagnosis) and management	S616
Liver tumours: Experimental and pathophysiology	S633
Molecular and cellular biology: Cell cycle control/apoptosis	S641
Molecular and cellular biology: HSCs and fibrosis	S648
Non-invasive assessment of liver disease	S657
Viral hepatitis: Hepatitis A, B, D, E – Clinical (except therapy)	S677
Viral hepatitis: Hepatitis B and D – Clinical (therapy, new compounds, resistance)	S687
Viral hepatitis: Hepatitis B and D – Experimental and pathophysiology	S696
Viral hepatitis: Hepatitis C – Clinical (except therapy)	S702
Viral hepatitis: Hepatitis C – Clinical (therapy)	S715
Author Index	S751
Disclosures: no commercial relationships	S807
Disclosures: commercial relationships	S851

Registration of Clinical Trials

The *Journal of Hepatology* endorses the policy of the WHO and the International Committee of Medical Journal Editors (ICMJE) on the registration of clinical trials. Therefore, any trial that starts recruiting on or after July 1, 2005 should be registered in a publicly owned, publicly accessible registry and should satisfy a minimal standard dataset. Trials that started recruiting before that date will be considered for publication if registered before September 13, 2005.

More detailed information regarding clinical trials and registration can be found in *New Engl J Med* 2004; 351:1250–1251 and *New Engl J Med* 2005; 352:2437–2438.

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POSTER PRESENTATIONS

progression and monitored apoptosis *in vivo* using fluorescence molecular and micro-computed tomography (FMT, μ CT).

Results: Single dose injection (0.2 mg/kg body weight) revealed a significant reduction of *Jnk2* on mRNA and protein levels in wildtype mice after 1 week. Moreover, 4 week *sjnk2* treatment had no influence in JNK1^{Δhepa} livers. Next, we sought to investigate the effects in an acute model of Nemo^{Δhepa} mice. Treatment with *sjnk2* caused hepatocyte hypertrophy, mitotic catastrophe, karyomegaly, exacerbated cell infiltration, hepatic fibrogenesis and ductular proliferation. These effects were evident by high alkaline phosphatase levels, cleaved caspase-3 positive cells alongside with increased compensatory proliferation. Furthermore, our data indicated that proinflammatory monocytes massively infiltrate the liver after hepatocyte-specific *Jnk2* inhibition. Interestingly, decreased compensatory proliferation, cleaved Caspase-3 protein levels and markers of hepatic stellate cell activation/matrix deposition were observed in a chronic model of Nemo^{Δhepa} mice injected over 8 weeks.

Conclusions: *sjnk2* therapy successfully depleted the levels of *Jnk2* both *in vivo* and *in vitro*. *Jnk2* knockdown induced significant changes in liver parenchyma and a therapeutic option by reducing HCC progression. These results open new opportunities for precision medicine of CLD treatment with potential translation into humans.

FRI-113

Histological subtypes of hepatocellular carcinoma are related to gene mutations and molecular tumor classification

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Background and Aims: Our increasing understanding of hepatocellular carcinoma (HCC) biology holds promise for personalized care, however its translation into clinical practice requires a precise knowledge of its relationship to tumor phenotype. We aimed at investigating molecular-phenotypic correlations in a large series of HCC.

Methods: Surgically resected HCC (n = 343) were investigated by pathological review, immunohistochemistry, gene expression profiling and sequencing.

Results: *CTNNB1* (40%) and *TP53* (21%) mutations were mutually exclusive and defined two major groups of HCC characterized by distinct phenotypes. *CTNNB1* mutated-tumors were large (P = 0.001), well-differentiated (P < 0.001), cholestatic (P < 0.001), with microtrabecular (P < 0.001) and pseudoglandular (P < 0.001) patterns and without inflammatory infiltrates (P < 0.001). *TP53* mutated-tumors were poorly-differentiated (P < 0.001) with compact pattern (P = 0.02), multinucleated (P = 0.01) and pleomorphic (P = 0.02) cells and frequent vascular invasion (P < 0.001). World Health Organization (WHO) histological subtypes were also strongly related to molecular features. The scirrhous subtype was associated with *TSC1/TSC2* mutations (P = 0.005), epithelial-to-mesenchymal transition and a progenitor expression profile. The steatohepatic subtype showed frequent IL-6/JAK/STAT activation without *CTNNB1*, *TERT* and *TP53* pathway alterations (P = 0.01). Pathological review identified a novel subtype, designated as “macrotrabecular-massive” associated with HBV infection (P = 0.01), poor overall survival (P < 0.001), high alphafoeto-protein serum level (P = 0.01), angiogenesis activation (P = 0.007), *FGF19* amplifications (P = 0.02), *TP53* (P < 0.001) and *ATM* (P = 0.03) mutations. Finally, integration of HCC pathological characteristics with the transcriptomic classification showed phenotypically distinct tumor subclasses closely related to G1-G6 transcriptomic subgroups.

Conclusions: HCC phenotypes are tightly associated with gene mutations and transcriptomic classification. These findings may help in translating our knowledge of HCC biology into clinical practice.

FRI-114

Nanovesicle mediated delivery of combination of anticancer agents effectively induced cell death in Hepatocellular carcinoma cell lines

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Background and Aims: Hepatocellular carcinoma (HCC) is a primary malignant hepatic tumor and highly resistant to treatment owing to tumor heterogeneity. The current treatment modalities for HCC are not effective due to lack of efficient and organ specific drug delivery system. We studied the efficacy of milk-derived nanovesicles (MNV) to deliver the anticancer agent doxorubicin into HCC cells in culture as well as intrahepatic tumors induced in immunodeficient mice.

Methods: MNVs were isolated from skim milk using ultracentrifugation and characterized with nanoparticle tracking analysis (NTA) and electron microscopy. MNVs were loaded with doxorubicin (dox-MNV), purified by ultracentrifugation, and characterized using spectrophotometry and NTA. HepG2, Hep3B, and PLC/PRF/5 HCC cells in culture were treated with dox-MNV and evaluated the rate of cell death. Intrahepatic tumors induced in nude mice were injected with dox-MNV through tail vein and assessed tumor regression using *in-vivo* imaging system.

Results: Cellular uptake studies depicted plain and dox-MNV attained saturation within 4 h of treatment. Cell toxicity studies on HepG2, Hep3B, and PLC/PRF/5 HCC cells with MNV-dox at 1 μ M depicted around 20% cell death at 24 h, 50% at 48 h, and 80% at 72 h. HepG2 cells treated with fluorescent-tagged dox-MNV exhibited nuclear disintegration and apoptosis within 24 h. Treatment of intrahepatic tumors with dox-MNV resulted in significant regression and increased survival rate in nude mice.

Conclusions: Our studies demonstrated that MNVs could be effectively used for successful delivery of anticancer agents into HCC cells and intrahepatic tumors. MNV mediated delivery of anticancer agents through intravenous system would be an effective method for the treatment of primary hepatic tumors.

FRI-115

Genetic and epigenetic bases of the relationship between reduced OCT1 expression and poor response to sorafenib in hepatocellular carcinoma and cholangiocarcinoma

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Background and Aims: The organic cation transporter-1 (OCT1, *SLC22A1* gene) plays a key role in sorafenib uptake and interaction with its molecular targets. Its expression has been found decreased both in hepatocellular carcinoma (HCC) and cholangiocarcinoma (CCA). Here we have aimed at characterizing the genetic and