JOURNAL OF HEPATOLOGY

VOLUME **73**, SUPPLEMENT **1**, PAGES **S1–S1001**

Abstracts of The Digital International Liver Congress™ 2020
August 27–29, 2020

Publication of this Abstract supplement was supported by the European Association of the Study of the Liver (EASL)

ELSEVIER

JOURNAL OF HEPATOLOGY

VOLUME **73**, SUPPLEMENT **1**, PAGES **S1–S1001**

CONTENTS

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.

derived neutrophils increased N1/N2 ratio and promoted NETs formation. These implied huc-MSC-EVs might regulated immunocompetence of the neutrophils via IRF4 signaling pathway.
Conclusion: In summary, huc-MSC-EVs alleviate HIRI by inducing neutrophil N2 subtype differentiation and reduces NETs. These findings provide a new theoretical basis to promote MSC-EVs based treatment in liver transplantation application.

THU302
Inhibition of gamma-glutamyl transpeptidase ameliorates hepatic/reperfusion injury in rats with fatty liver
Ryuichi Kubota[1], Nobuhiko Hayashi[1], Mutsumi Tsuchishima[1], Mikihiro Tsutsumi[1], Joseph George[1]. [1]*Kanazawa Medical University, Hepatology, Uchinada, Ishikawa, Japan*
Email: georgej@kanazawa-med.ac.jp.

Background and Aims: Fatty liver or steatosis is a condition of excessive fat deposition in the liver with increased γ-glutamyl transpeptidase (γ-GT) levels. Ischemia/reperfusion (IR) injury is a pathological condition with several deleterious effects. We evaluated the protective effects of a specific inhibitor of γ-GT in experimentally induced IR injury in rats with steatosis.
Methods: The portal vein and hepatic artery of left lateral and median lobes were clamped to induce ischemia. Before clamping, 1 ml of saline (IR group) or 1 ml saline containing 1 mg/kg body weight of GGsTop (γ-GT inhibitor) (IR- GGsTop group) was injected into the liver from inferior vena cava. The blood flow was restored at 30 min after the start of ischemia. Blood was collected before and at 30 min after ischemia, and at 2 h and 6 h after reperfusion. All the animals were euthanized at 6 h and the livers were collected.
Results: Treatment with GGsTop resulted in significant reduction of serum ALT, AST, and γ-GT levels and hepatic γ-GT, malondialdehyde, TNF-α, and 4-hydroxynonenal content at 6 h after reperfusion. Inhibition of γ-GT produced marked elevation of serum and hepatic glutathione levels. There was prominent hepatic necrosis in IR group, which is significantly reduced IR-GGsTop group.
Conclusions: Inhibition of γ-GT with GGsTop significantly increased serum and hepatic glutathione levels, reduced hepatic MDA and 4-HNE levels, and remarkably ameliorated hepatic necrosis after reperfusion. The results indicated that GGsTop might serve as an appropriate therapeutic agent to reduce IR-induced liver injury and related events in obesity.

THU303
Influence of PML, RASSF6 and NLRP12 on growth and recurrence of human hepatocellular carcinoma
Natalie Vogel[1], Katja Piras-Straub[1], Maike Busch[2], Nicole Dünker[2], Heiner Wedemeyer[1], Kerstin Herzer[1]. [1]*Essen University Hospital, Gastroenterology and Hepatology, Essen, Germany;* [2]*Essen University Hospital, Anatomy II, Neuroanatomy, Essen, Germany*
Email: natalie.vogel@uk-essen.de.

Background and Aims: Human hepatocellular carcinoma (HCC) is the third leading cause of cancer-related deaths worldwide. Limited therapy options are coupled with bad prognosis and for HCC recurrence post-liver transplantation, there is no cure. PML, RASSF6 and NLRP12 are tumour suppressor proteins involved in cell signalling pathways associated with tumour development and recurrence and for which we could show that they are reduced in expression in tumour tissue in the human HCC. We hypothesize, that their reduced expression impacts tumour growth positively what is investigated using CRISPR/Cas9 knockout in hepatoma cell lines and a chick chorioallantoic membrane (CAM) model. The CAM model is a modern system allowing to investigate tumour growth without a mouse model.
Method: Using CRISPR/Cas9, we generated heterozygote cancer cell lines with a knockout in exon 1 in PML, RASSF6 and NLRP12. Hepatoma cell lines Huh7, Hep3B and HepG2 were transfected and genotyping was performed via PCR and 2% gel electrophoresis. As yet, the Boyden chamber assay was performed in Huh7 by silencing PML to test for the influence on migration potential. These cell lines were further applied in the chick chorioallantoic membrane (CAM) model. Cell lines with and without the knockout generated tumours in the CAM model that were harvested, weighted and measured for tumour growth analysis and comparison of size and weight. The RNA expression was measured via rtPCR.
Results: PML, RASSF6 and NLRP12 expression is reduced in the human tumour tissue as well as *in vivo* in a murine model and *in vitro* in hepatoma cell lines. The generation of heterozygous PML, RASSF6 or NLRP12 knockout cell lines shows reduced expression of the respective genes. So far, functional assays were performed for PML and revealed that reduced PML expression favours cell migration 1.6-fold. PML expression was reduced to 24% in the cell line HepG2, to 27% in the cell line Huh7 and to 43% in the cell line Hep3B. Further in the CAM model, PML shows significant increase in tumour growth ($P \leq 0.02$) after knockout in the cell line HepG2. The relative RNA expression of PML was decreased by up to 73% in the CAM-tumours. Further research is currently being performed on RASSF6 and NLRP12.
Conclusion: Our findings reveal a relevant influence of PML on HCC tumour growth. The effect of the knockout of RASSF6 and NLRP12 on tumour growth, cell proliferation, migration and apoptosis is being further analysed and will be presented.

THU304
Serum glycomics early after liver transplantation relate to graft loss 3 months after liver transplantation independently of early allograft dysfunction
Verhelst Xavier[1], Anja Geerts[1], Helena Degroote[2], Roos Colman[3], Aude Vanlander[2], Luis Abreu de Carvalho[2], Frederik Berrevoet[2], Leander Meuris[4], Xavier Rogiers[2], Nico Callewaert[4], Hans Van Vlierberghe[1]. [1]*Ghent University Hospital, Gastroenterology and Hepatology, Gent, Belgium;* [2]*Ghent University Hospital, Hepatobiliary and Transplant Surgery, Gent, Belgium;* [3]*Ghent University Belgium, Biostatistics Unit, Gent, Belgium;* [4]*VIB, Center for Biomedical Technology, Ghent, Belgium*
Email: xavier.verhelst@uzgent.be.

Background and Aims: Graft loss during the first year after liver transplantation (LT) affects up to 15% of liver grafts, mainly in the first 3 months. Prediction of outcome early after LT is limited by the lack of robust clinical predictors. Early allograft dysfunction (EAD) is related to early graft loss but is not a strong predictor in individual patients. The goal of this work was to define a serum glycomic signature early after LT that is associated with graft loss at 3 months after LT.
Method: A prospective study in an experienced liver transplant center was performed between 1/1/2011 and 28 February 2017. Glycomic analysis using DSA-FACE was applied to serum samples on postoperative day 7. Using Lasso regression, an optimal serum glycomic signature was identified, associated with 3 months graft survival.
Results: A total of 117 patients were included. Graft loss at 3 months occurred in 14 patients (11.9%). The cohort was split in a training (82 without, 9 with graft loss) and a validation set (35 without, 5 with graft loss). The glycomic signature contains 13 glycans, using Lasso regression an optimal model was fitted yielding an AUC of respectively 0.95 and 0.94 in these sets for graft loss at 3 months ($p < 0.001$). Based on the Youden index an optimal cutoff of this biomarker was defined at 0.773. In the complete sample, this showed a sensitivity of 94% (95% CI: 0.891–0.981) and a specificity of 93% (95% CI 0.661–0.998). PPV and NPV were respectively 99.1% (95% CI 0.943–0.997) and 68% (95% CI : 0.491–0.989). Graft loss was associated with increased undergalactosylation (a marker of inflammation) and an increased presence of fucosylated and triantennary glycans, both signs of liver regeneration. According to this cut-off, multivariate logistic regression analysis showed a odds ratio of 70.211 (95% CI