in Biological Progress, including 'GOBP_ACETYLCHOLINE_METABOLIC_PROCESS', 'GOBP_L_KYNURENINE_METABOLIC_PROCESS', and 'GOBP_N_ACYLETHANOLAMINE_METABOLIC_PROCESS' according to the GSEA and GSVA results. Therefore, we established a classifier that can divide different HCV-related HCC patients into 4 subgroups, including EphA2+/Meta+, EphA2-/Meta-, EphA2-/Meta+, EphA2-/Meta-. The scatter plot map shows different genes expression of different subtypes. Moreover, it's obvious the 'EphA2+/Meta+' subtype has the lowest median survival and overall survival ($P < 0.01$). **Conclusion** Our work revealed that there is another important role of EphA2, except for the migration, adhesion, proliferation, and differentiation, it's also metabolism-related. It helps us to understand more comprehensively the function of EphA2 in the cancer cells and the carcinogenesis of HCV. Both of them will improve the understanding the HCV-related hepatocellular carcinoma and the development of anti-cancer treatment.

P039 STANDARD-VOLUME PLASMA EXCHANGE IN ACUTE LIVER FAILURE: ASSESSMENT OF LABORATORY PARAMETERS AND CLINICAL OUTCOMES

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10.1136/gutjnl-2021-BASL.48

Background Acute liver failure (ALF) is a life threatening syndrome defined by hepatic encephalopathy and an International Normalised Ratio greater than 1.5 in a patient with no underlying chronic liver disease. Plasma Exchange (PEX) is an extracorporeal procedure separating plasma constituents from cellular blood components by centrifugation and replaces it with stored plasma. A large randomised controlled trial in ALF demonstrated reduced mortality with high-volume PEX. The primary objective of this retrospective case-control study was to evaluate the effect of standard-volume (1.5 Total Blood volumes of plasma) PEX on clinical parameters and outcomes of ALF patients receiving PEX compared to those on standard medical treatment (SMT) only.

Methods This study compared clinical parameters, organ failure scores, and outcomes in patients with paracetamol-induced ALF receiving PEX ($n=16$) and those not receiving PEX ($n=68$). Parameters were recorded at admission to the intensive care unit and then 24 hours after the last cycle of PEX, and at similar timepoints for non-PEX patients. Data was collected for all ALF patients admitted to St James's University Hospital in Leeds, UK between 2017 and 2020. To further investigate the effects of different aetiologies of PEX and treatment options received, admission and outcome data was collected for a further 34 ALF patients admitted between 2011 and 2016 who did not receive PEX.

Results Analysis of results in 16 PEX and 68 non-PEX patients found significant improvements in biochemical parameters in patients 24 hours after receiving PEX (INR, PT, ALT, Bilirubin; $P < 0.01$), compared to those who were on SMT only. The admission Sequential Organ Failure Assessment (SOFA) mortality predictive scores were significantly higher in the PEX group than non-PEX ($P < 0.01$), which may explain the difference in mortality rates found in this study (37% and 22% respectively).

Conclusions Standard-Volume PEX is effective in improving clinical parameters in individuals with ALF compared to SMT. Patients are at lower risk of transfusion-related acute lung injuries and it is more cost-effective than high-volume PEX. This intervention could be considered for liver support until recovery or liver transplantation.

P040 IDENTIFICATION AND FUNCTIONAL CHARACTERISATION OF A RARE MTTP VARIANT UNDERLYING HEREDITARY NON-ALCOHOLIC FATTY LIVER DISEASE

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10.1136/gutjnl-2021-BASL.49

Background and Aims Non-alcoholic fatty liver disease (NAFLD) is a complex trait that has a global prevalence estimated as 25%. We aimed to identify the genetic variant underlying a four-generation family with progressive NAFLD leading to cirrhosis, decompensation and development of hepatocellular carcinoma in the absence of common risk factors such as obesity and type 2 diabetes.

Methods Exome sequencing and genome comparisons were used to identify the likely causal variant. We extensively characterised the clinical phenotype and post-prandial metabolic responses of family members with the identified novel variant in comparison to healthy non-carriers and wild type patients with NAFLD. Variant-expressing hepatocyte-like-cells (HLCs) were derived from human induced pluripotent stem cells generated from homozygous donor skin fibroblasts. The phenotype was assessed using imaging, targeted RNA analysis and molecular expression arrays.

Results We identified a rare causal variant in MTTP, c.1691T>C p.I564T (rs745447480) encoding microsomal triglyceride transfer protein (MTP) associated with progressive non-alcoholic fatty liver disease, unrelated to metabolic syndrome. Although other described mutations in MTTP cause abetalipoproteinemia, neither homozygotes nor heterozygotes exhibited characteristic manifestations of this severe disease. HLCs derived from a homozygote donor had lower lipoprotein ApoB secretion, compared to wild type cells. Cytoplasmic triglyceride accumulation in HLCs triggered endoplasmic reticulum stress, secretion of pro-inflammatory mediators and production of reactive oxygen species.