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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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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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.

Conclusion We have identified and characterized a rare causal variant in MTTP and homozygosity for MTTP p.I564T is associated with progressive NAFLD without any other manifestations of abetalipoproteinemia.

P041

TANDEM MASS TAG-BASED QUANTITATIVE PROTEOMIC PROFILING IDENTIFIES NOVEL PUTATIVE SERUM BIOMARKERS FOR THE DIAGNOSIS OF DRUG-INDUCED LIVER INJURY IN PATIENTS

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Background Diagnosis of drug-induced liver injury (DILI) remains a significant challenge in interventional clinical trials during drug development and in clinical practice. We aimed to discover novel diagnostic biomarkers using proteomics and to evaluate their performance characteristics in distinguishing DILI from acute and chronic liver injury from other etiologies.

Methods Adults with idiosyncratic DILI and acute non-DILI liver disease controls were recruited to the Prospective European DILI Registry. Case definitions and causality assessment were performed according to European Association for the Study of the Liver recommendations. Tandem Mass Tag (TMT) labelled quantitative proteomics was performed in serum samples from a discovery set of healthy volunteers (HV, n=10), patients with DILI at onset (DO) and recovery (DR) (n=10 each); acute non-DILI controls at onset (NDO) and recovery (NDR) (n=5 each) and patients with non-alcoholic fatty liver disease (n=10). The performance of top biomarker candidates was assessed in a confirmatory cohort with HV (n=60), DO (n=83), DR (n=85), NDO (n=35) and NDR (n=21) using peptide-based targeted mass spectrometry. Novel biomarkers and patient status were evaluated using univariate and multivariate models.

Results Global proteomic profiling of the discovery cohort revealed 2323 proteins, of which 12 novel biomarkers were chosen based on differential expression, liver specificity, and mechanistic relevance to liver biology/pathogenesis. In the confirmatory analysis, serum concentration of the novel biomarkers was significantly different at DO and returned to levels comparable to HV during recovery (DR). When the diagnostic performance of these 12 biomarkers was assessed

individually, along with the promising biomarker Cytokeratin 18 (CK18, Area Under the Receiver Operator Characteristic (AUROC) Curve = 0.96), the following biomarkers demonstrated the highest sensitivity/specificity (DILI vs HV): Cytoplasmic aconitate hydratase (ACO1, 0.99), Argininosuccinate synthase (ASS1, 0.98), Fumarylacetoacetase (FAH, 0.98), Carbamoyl-phosphate synthase (CPS1, 0.96), Fructose-bisphosphate aldolase B (ALDOB, 0.94), 4-Hydroxyphenylpyruvate dioxygenase (HPD, 0.94), Ornithine carbamoyltransferase (OTC, 0.92).

Conclusion A TMT-based quantitative proteomic profiling approach identified novel putative biomarkers, which are candidates for further evaluation of their role in the diagnosis and prognostication of DILI.

P042

AN AUDIT OF THE KNOWLEDGE OF THE DECOMPENSATED LIVER DISEASE BUNDLE AND ASCITIC TAPS ON PATIENTS PRESENTING ON THE MEDICAL TAKE

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Background The BSG-BASL decompensated cirrhosis care bundle seeks to optimise patient management during the first 24 hours of presentation. The pandemic has impacted on junior doctors' hepatology training, by reducing access to face-to-face teaching. We sought to redress this by assessing how a remote education programme could affect bundle implementation and awareness, shortly after the UK's first COVID-19 wave.

Methods A retrospective snapshot case-note audit was undertaken for 4 weeks (August 2020) at Bristol Royal Infirmary (BRI). Decompensated cirrhosis admissions were identified from coding and bundle usage and compliance with ascitic tap guidance were quantified. An online survey was conducted of BRI junior doctors (medical) to assess knowledge of the bundle and awareness of appropriate ascitic fluid tests. Subsequent quality improvement interventions were developed, with repeat audits in May-June 2021.

Results The baseline audit identified appropriate bundle completion in 50% (n=8/16) decompensated cirrhosis patients, none by foundation doctors, with 2 by hepatology consultants. Ascitic tap was attempted in only 50% of patients with detectable ascites (4/8), with recommended tests requested in 2 of 3 successful taps.

The online survey (40 participants 42% response) revealed good knowledge of when to use the bundle (85%) and how to access it (90%). For patients with new ascites, 46% of participants identified appropriate tests, however 39/40 also selected unnecessary options. Knowledge was poorer for patients with known ascites; 20% selected correct investigations and no participants knew the exact combination to request. Procedural skills varied, 49% of participants had performed an ascitic tap unsupervised, but 33% had never attempted one.

After these audits, remote teaching sessions and posters were used to improve prompting of bundle completion; paper copies were distributed to admission areas. Re-audit (May 2020) identified 15 hepatic decompensation admissions, of