dependent-magnetic resonance imaging (BOLD-MRI) was used to quantify changes in renal oxygenation. Tissue expression and distribution of RLN receptor (RXFP1) was determined by qPCR and immunofluorescence. Expression of vasoconstrictor genes was quantified by qPCR array.

Results RXFP1 was detected on glomerular podocytes, renal pericytes, and endothelial cells of the renal, segmental and interlobar arteries of cirrhotic rats. In CCl_4 cirrhosis, acute i.v. RLN (4μg) induced a 50% increase in RBF after 60 minutes ($p < 0.01$ vs. placebo, $n = 6$). BOLD-MRI showed increased tissue oxygenation at the same timepoint in renal cortex and medulla. Extended s.c. RLN increased RBF by 54% in CCl_4 ($p < 0.01$ vs. placebo, $n = 8$) and 57% in BDL ($p < 0.001$ vs. placebo, $n = 5$) and increased GFR by 138% in CCl_4 ($p < 0.01$ vs. placebo, $n = 8$) and 103% in BDL ($p < 0.05$ vs. placebo, $n = 5$). Mean arterial pressure was unaffected by RLN. L-NAME (250mg/L) orally (p.o.) abrogated the effect of RLN on RBF and GFR. The relative expression of vasoconstrictor genes in the kidney was markedly reduced by RLN treatment.

Conclusion RLN increases RBF in experimental cirrhosis. Crucially, RLN also improves renal function and oxygenation but does not induce systemic hypotension even in decompensated disease. The effects of RLN are mediated via augmentation of NO and downregulation of vasoconstrictor genes known to be important in the pathogenesis of HRS. RLN has potential as a treatment for HRS and further translational studies are warranted.

Disclosure of Interest None Declared.

PWE-147 HUMAN HERPESVIRUS AND ADENOVIRUS UNIQUE GENETIC SEQUENCES DETECTED IN HEPATOCELLULAR CANCER GENOMES

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Introduction Hepatitis C virus (HCV) is the most common cause of hepatocellular cancer (HCC) in the western world. HCV is an RNA virus that does not integrate with human DNA and so the oncogenic mechanisms of HCV remain unclear. Next generation sequencing (NGS) provides a flexible platform and generates large amounts of data at a relatively small time and constantly reducing costs. The role of viral infection is well established in the aetiology of a wide range of tumours. In this study we investigate DNA of HCV driven HCC for the possibility of integration of all known viral genomes.

Methods Bar-coded DNA libraries from 41 samples of various stages of development of HCC from 6 different patients were sequenced in parallel using NGS. One to two million 74bp reads per genome were generated. The reads were aligned to all known viral genomes downloaded from the National Center for Biotechnology Information using Burrows-Wheeler Aligner (BWA). Reads with mapping scores of < 37 were discarded. Basic Local Alignment Search Tool (BLAST) was used to test if the sequences that aligned to viral genomes belonged to the human genome or any other viruses apart from the identified virus. Only those reads were the BWA alignment matched the leading BLAST hit were considered

Results Six test samples mapped to unique sequences from Human herpesvirus 6. The test samples included a single HCC and 5 premalignant nodules from 2 different patients. Six test samples mapped to unique sequences of Human Adenovirus (6/41). The test samples in this case included 4 HCCS and a 2 premalignant nodules from 2 different patients. A single dysplastic nodule mapped to Human papillomavirus.

Conclusion DNA from HCV driven HCC was searched for all viral genome sequences only Human Herpes 6, Human Adenovirus and Human pappilomavirus were found in a small number of cases. Further studies are needed to understand their relation to HCV hepatocarcinogenesis.

Disclosure of Interest None Declared.

PWE-148 HEPATOTOXICITY FROM ANABOLIC ANDROGENIC STEROIDS MARKETED AS DIETARY SUPPLEMENTS: CONTRIBUTION FROM ATP8B1/ABCB11 MUTATIONS?

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Introduction In the United Kingdom (UK) it is illegal to produce, supply, or possess androgenic anabolic steroids (AAS) with intent. Despite this, non-prescription use of AAS, often marketed as dietary supplements, persists. We encountered drug-induced liver injury (DILI) associated with use of AAS and attempted to elucidate underlying mechanisms.

Methods We describe two patients with cholestatic DILI following ingestion of the dietary supplement massdrol ("Celtic Dragon") containing the AAS 2a-17a-dimethyl-etiocholan-3-one,17b-ol.

Results Two Western European males (aged 25 and 45 years) presented to our institute between July, 2011, and March, 2012, with jaundice and intractable pruritus following use of massdrol acquired from fellow gym users. Screening found no other causes of hepatobiliary disease. Despite significant hyperbilirubinaemia (respective peaks: 614 and 229 μmol/L), peak gamma glutamyl transferase activities were within "normal range". Besides "bland" intralobular cholestasis, consistent with DILI, liver biopsy in both found deficiency of canalicular expression of the ectoenzymes neutral endopeptidase (CD10), alanyl aminopeptidase (CD13), GGT, and carcinoembryonic antigen (CD66). This suggested generalised abnormality in ectoenzyme trafficking to, or retention within, canalicular membranes, as seen in *ATP8B1* disease (familial intrahepatic cholestasis 1 [FIC1]). The younger patient showed normal expression of bile salt export pump (BSEP, encoded by *ABCB11*) and of multidrug resistance protein 3 (MDR3; encoded by *ABCB4*); in the older BSEP but not MDR3 marking was focally diminished. While this may have been due to AAS-induced inhibition of expression of normal *ATP8B1*/*ABCB11*, it also raised the intriguing possibility of mutation in either of these genes – in effect, that AAS exposure had triggered initial episodes of benign recurrent intrahepatic cholestasis type 1/2. On sequencing, *ATP8B1* was normal in both patients; the younger was heterozygous for the mutation c.2093G > A mutation in *ABCB11*, a known polymorphism previously encountered in association with intrahepatic cholestasis following antibiotic exposure (personal communication, R Thompson). Morbidity from cholestasis and pruritus was substantial, necessitating use of multiple antipruritic agents and consideration for extracorporal albumin dialysis (*MARS*). At last follow-up, however, jaundice was resolved in both.

Conclusion AAS marketed as dietary supplements remain a cause of serious DILI in the UK; underlying mechanisms remain speculative but may include unmasking of genetic cholestatic syndromes.

Disclosure of Interest None Declared.

PWE-149 THE EFFICACY AND SAFETY OF TREATING HEPATITIS C IN PATIENTS WITH A DIAGNOSIS OF SCHIZOPHRENIA

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