5 AALF patients sampled (Abstract P95 figure 3). Intra-hepatic levels of IL-10 (2 vs 0.6; p=0.03) and SLPI (442 vs 116; p=0.004) were higher in patients with AALF compared to controls, whereas no difference in TNF-α (24 vs 19; p=0.3) concentration was detected. The percentage of monocytes phagocytosing *E. coli* was significantly reduced in AALF compared to HC (69 vs 92%; p=0.008).

**Conclusion** In AALF, circulating monocytes show modifications in intracellular signalling pathways compatible with ET and display reduced phagocytic capabilities. Our data also indicate that hepatic production of anti-inflammatory mediators, IL-10 and SLPI, may play a pivotal role in induction of ET monocytes and thus increase the risk of infection in AALF.

**P96**

**SERUM PROTEIN N-GLYCOSYLATION AS A BIOMARKER OF PAEDIATRIC NAFLD**

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**Introduction** Serum protein N-glycosylation has previously been shown to distinguish adult patients with simple steatosis from those with non-alcoholic steatohepatitis (NASH). The pattern of the disease in paediatric patients is distinct from adults.

**Aim** The aim of this study was to characterise the glycomic profile of children with varying degrees of NAFLD to identify potential biomarker profiles of disease.

**Method** Children with biopsy proven non-alcoholic fatty liver disease (n=51) were recruited from a tertiary paediatric hepatology unit. Liver biopsy was scored according to NAFLD activity score. Blood was taken on day of biopsy for analysis. Serum protein N-glycosylation patterns were assessed with DNA-sequence assisted fluorophore-assisted capillary electrophoresis (DFA-FACE) and compared with histology.

**Results** Median age at biopsy was 13.5 years (range 4.5–17.4). 31 were male. Median BMI z-score was 1.81. 23 children scored as simple steatosis/borderline NASH and 28 as true NASH. 18 children had no/minimal fibrosis (< F2) and 33 had significant fibrosis (≥ F2). Similar to previous work in adult patients with NASH, peak 1 (NGA2F) was the most significantly raised N-glycan in paediatric NASH patients with peak 5 (NA2) demonstrating the greatest decrease. The logarithmically transformed ratio of peak 1 to peak 5 (Glycomarker) was −0.85 (SD 0.22) in simple steatosis/borderline NASH and −0.75 (SD 0.12) in NASH (p=0.02). The biomarker correlated well with the amount of lobular inflammation with a consistent increase with ascending grade of inflammation. There was also a trend towards significance in differentiating patients with significant fibrosis ≥ F2: −0.74 (SD 0.15) from patients with no/minimal fibrosis < F2: −0.86 (SD 0.24), (p=0.06). Glyco-analysis of immunoglobulin G (IgG) confirmed the upregulation status with a significant increase in peak 1 (NGA2F: p=0.024) and a significant decrease of peak 6 (NA2F: p=0.01) on IgG. In multi-variate analysis of the Glycomarker, GGT, AST and INR, only the Glycomarker displayed a significant result for distinguishing simple steatosis from NASH (p=0.019).

**Conclusion** In conclusion, the findings in this study are novel in that they represent the first Glycomic analysis of paediatric NAFLD. They validate findings in adults in that a Glycomarker can serve reliably as a biomarker of severity of disease in NAFLD. The same N-glycosylation alterations are observed in paediatric NASH patients when compared to an adult population and therefore the same biomarker can be used. B cells play a dominant role in the N-glycan alterations of NASH patients, both in an adult and paediatric population.

**P97**

**LYMPHOCYTE-HEPATOCYTE INTERACTIONS: HEPATITIS C VIRUS CHANGES THE RULES**

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**Introduction** Hepatitis C Virus (HCV) is a major cause of liver disease worldwide. Innate and adaptive cellular immune responses play a critical role in resolving acute HCV infection. However, the majority of infections are not cleared, resulting in a progressive chronic liver disease consistent with inadequate immune control. Evidence from human and animal models suggest that T cells play a critical role in controlling acute HCV infection, yet the mechanism(s) behind their failure to control chronic HCV replication are unknown. HCV replicates predominantly in the liver and virus specific immune cells need to target infected hepatocytes to control virus replication. HCV specific effector cells have been reported to home to the liver, however, little is known on their subsequent trafficking and fate within the organ.

**Aim** Our aim is to investigate the role of HCV infection on lymphocyte-hepatocyte interactions, migration and immune cell effector function.

**Method** We used in vitro and ex vivo models to study the effect of HCV infection on lymphocyte–hepatocyte interactions. Primary lymphocytes and hepatocytes were used in combination with hepatoma cell lines and replication competent HCV clones. Ex vivo lymphocyte migration assays were performed using biopsy material and tissue from explanted liver. Results were confirmed by in vivo observations using tissue sections from patients with end stage liver disease of viral and non-viral origin. Experimental techniques included immunohistochemistry, flow cytometry, fixed and live cell time-lapse confocal microscopy.

**Results** We demonstrate: (1) A role for hepatocyte ICAM-1 in mediating T-lymphocyte adhesion and migration; (2) T-lymphocytes migrate spontaneously through hepatocyte monolayers via cell-cell junctions; (3) HCV enhances T-cell transmigration and pro-inflammatory cytokine expression. Our data demonstrate the existence of novel interactions between T-cells and hepatocytes that are modulated in HCV infection. The nature of the T-cell-hepatocyte interactions may have an impact on T-cell effector function and the outcome of anti-viral immune responses.

**Conclusion** Interaction with HCV-infected hepatocytes alters T-cell trafficking and cytokine expression, providing a novel mechanism for HCV to persist in the liver.

**P98**

**THE EFFECTS OF TH17 CYTOKINES ON LIVER PARENCHYMAL CELLS SHAPE THE MICROENVIRONMENT FOR LOCAL GENERATION OF TH17/TC17 IN INFLAMMATORY LIVER DISEASE**

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**Introduction** IL-17 secreting T cells (Th17/Tc17) in subsets of T lymphocytes that have been implicated in autoimmunity, inflammatory disease and provide a link between the innate and adaptive immune responses. High numbers of IL-17-producing T cells are found in close proximity to bile ducts in several liver diseases.
FxR stimulation with INT-747 in a rat biliary drainage model protects from hepatocellular injury after loss of enterohepatic circulation

Introduction
Enterocutaneous fistula are often associated with development of intestinal failure associated liver disease (IFALD), ultimately leading to liver damage. We hypothesise that this is caused by reduced farnesoid X receptor (FxR) stimulation, due to interruption of the enterohepatic circulation and consequent impact on bile acid synthesis.

Aim
We aimed at investigating the effect of specific stimulation of the farnosoid X receptor (FXR) with INT-747, a synthetic agonist, on bile acid synthesis.

Methods
Four groups of rats (n=6–8) were studied; two groups underwent bile duct cannulation and externalisation to achieve continuous biliary drainage, daily receiving either vehicle or INT-747 (Intercept Pharm LtD); two groups underwent laparotomy without cannulation also receiving either vehicle or INT-747. Loss of bile was recorded daily. After 7 days, plasma, serum and liver and intestinal tissue were collected. Alanine aminotransferase (ALT), alkaline phosphatase (AP), γ-glutamyl transpeptidase (GGT) and total bilirubin were assessed, along with histological scoring of necrosis, inflammation, bile duct proliferation, fibrosis and steatosis. Expression of genes involved in the FXR pathway, and lipid and cholesterol metabolism were quantified by qPCR.

Results
Loss of bile was significantly reduced in the INT-747 group compared to the vehicle group. Serum levels of ASAT, ALAT, AP, GGT, bilirubin (total and direct) were all significantly increased in the bile drainage group when compared to controls (p<0.05), suggesting hepatocellular damage. Interestingly, all parameters were significantly decreased in the bile drainage group receiving INT-747 (p<0.05). Histological analyses showed normal liver histology in both sham groups. In contrast, large necrotic areas were observed in the biliary diversion group receiving vehicle with a high number of infiltrating inflammatory cells, which decreased significantly in the biliary diversion group receiving INT-747 (p<0.05). Biliary diversion induced hepatic fibrosis and bile duct proliferation, which were both attenuated by INT-747 supplementation (p<0.05). Although genes involved in the FXR pathway (FXR, SHP, CYP7A1 and CYP8B1) were influenced by bile drainage, no significant change was observed when rats received INT-747.

Conclusion
The present data demonstrate that stimulation of FXR with INT-747 can attenuate hepatocellular damage in an experimental model of IFALD. The results suggest a role of FXR in the development of hepatocellular damage, hepatic fibrosis and necrosis during biliary diversion. FXR stimulation has the potential to be a novel therapy for patients with IFALD.

Abstract P100 Figure 1 Expression of activating receptors on NK cells.