5 AALF patients sampled (Abstract P95 figure 3). Intra-hepatic levels of IL-10 (2 vs 0.6; p=0.05) 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 modulations 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.

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### P96 SERUM PROTEIN N-GLYCOSYLATION AS A BIOMARKER OF PAEDIATRIC NAFLD

**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 (DSA-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 NAFLD, peak 1 (NGA2F) was the most significantly raised N-glycan in paediatric NASH patients with peak 5 (NA2F) 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 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 undergalactosylation 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 multivariate 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.
FXR STIMULATION WITH INT-747 IN A RAT BILIARY DRAINAGE MODEL PROTECTS FROM HEPATOCellular INJURY AFTER LOSS OF ENTEROHEPATIC CIRCULATION

Aim: To assess the functional impact of Th17/Tc17 associated cytokines on hepatocellular cells.

Method: Primary human cholangiocytes, hepatocytes and sinusoidal endothelial cells were assessed for IL-17, IL-21 and IL-22 receptor expression. The effects of stimulation with recombinant IL-17, IL-21, IL-22, TNF-a or IFN-g alone or in combination were compared on apoptosis, proliferation and cytokine secretion using flow cytometry with annexin 7-AAD staining and in situ Ki67 staining and measurement of IL-1b, IL-6, IL-23 and TGF-b1 secretion by ELISA.

Results: All the parenchymal cell types expressed IL-21R and IL-22R. Th17 and Tc17 cytokines did not cause apoptosis but alone and in combination led to parenchymal cell proliferation. Cholangiocytes and hepatocytes responded best to IL-17, whereas sinusoidal endothelial cells were responsive to IL-22. Cholangiocytes responded to Th17/Tc17 cytokines by secreting high levels of IL-1b, IL-6, IL-23 and TGF-b1 all cytokines that support the survival of Th17 and Tc17 cells.

Conclusion: Liver parenchymal cells express IL-17, IL-21 and IL-22 receptors and proliferate in response to Th17/Tc17 cytokines. Cholangiocytes also respond to such cytokines by secreting Th17 polarising cytokines. Thus IL-17 related cytokines secreted by infiltrating lymphocytes may activate the epitheliome to generate a local environment characterised by cholangiocyte proliferation and Th17 cell survival. This response may contribute to the bile duct proliferation and persistent chronic inflammation that characterised many liver diseases.

LIVER TRANSPLANTATION (LT) RESULTS IN REDUCED RECIPIENT NATURAL KILLER (NK) CELL ACTIVATION WITH ASSOCIATED DOWN REGULATION OF ACTIVATING RECEPTORS NKP30 AND NKP46 BUT NOT NKG2D

Introduction: In solid organ transplantation, the effect of the allograft on recipient NK cell function is poorly understood. NK cells recognise self through inhibitory receptors for HLA class I, so that they

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