administration. Phenobarbital (0.35 g/L) was given in drinking water. BT was defined as the growth of bacteria in MLNs culture. T cells were isolated from the intestinal lamina propria and analyzed by flow cytometry.

Results: In the cirrhotic rat with BT, there is marked submucosal edema, organization structure disorders and inflammation of the intestines. BT to MLNs did not occur in any of the normal control rats. BT was detectable in 46% of cirrhotic rats with ascites. Intestinal bacterial can translocate to liver and ductus thoracicus to circulatory system. In addition, in the cirrhotic rat with BT, $CD3^+$T and $CD4^+$T cells were significant reduced in the small intestine and colon, $CD8^+$T cells were increased. Intestinal bacterial translocation in rats with cirrhosis is related to the Th17/Treg imbalance in Gut-associated lymphoid tissue.

Conclusions: Compromised gut immunity seems to predispose to BT in experimental rat cirrhosis. Understanding this gut associated lympatic tissue immunity including the underlying mechanisms could help us to find new treatment avenues.

FRI-010
DETERMINATION OF STAGE SPECIFIC MARKERS FOR LIVER FIBROSIS IN HEPATITIS B: A COMPARATIVE TISSUE PROTEOMIC STUDY

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Background and Aims: Chronic Hepatitis B infection is one of the major causes of liver cirrhosis and around 600,000 people die annually worldwide. The virus itself is non-cytopathic and the liver damage is due to host immune reaction. Thus liver damage pathways might differ in chronic HBV and comprehensive tissue proteomic analysis is missing in literature. To estimate which patient with chronic hepatitis B will develop rapidly fibrosis or cirrhosis is yet a thorny issue and requires a vast recognition of cellular pathways involved in fibrosis. The aim of this study is to enlighten pathways associated with liver fibrosis in HBV infection for leading up to new therapeutic targets and diagnostic biomarkers.

Methods: Tissue samples from 47 HBV infected patients classified according to Ishak's classification (F1: n = 7, F2: n = 20, F3: n = 12, F4: n = 3, F5: n = 2, F6: n = 3) were enrolled for two dimensional difference gel electrophoresis (2D-DIGE) proteomic screening. Proteomic profiles were analyzed between different fibrotic stages by univariate analysis ($p < 0.05$) and validated by western blotting. Differentially expressed proteins were subsequently identified by mass spectrometry. Protein functional association and expression profiles were analyzed using the EnrichNet application and String database.

Results: The differentially expressed proteins in tissue samples along fibrogenesis were annexin A4, apolipoprotein A1, immuglobulin kappa chain C region, aldehyde dehydrogenase 2, retinal dehydrogenase 1, phenazine biosynthesis-like domain-containing protein, transferrin, glutamate dehydrogenase I, pyruvate kinase PKM, peroxiredoxin 3, glyceraldehyde 3-phospahate dehydrogenase. Data mining of the Reactome and KEGG databases using EnrichNet and String analysis highlighted the possible involvement of platelet release, glycolysis and HDL mediated lipid transport pathways in HBV related fibrosis.

Conclusions: This proteomics study showed that significant alterations in platelet release, glycolysis and HDL mediated lipid transport pathways are associated with the progression of liver fibrosis in HBV infected patients. Previous invitro studies investigating HBx interactome pointed interaction of HBx with phoshoenolpyruvate and apolipoprotein A1. Here it is shown that these interactions are in play during progression of fibrosis invivo and these interactions may be important in the search of new therapeutic targets and noninvasive diagnostic biomarkers.

FRI-011
NORADRENALINE POTENTIATES PORTAL HYPERTENSION THROUGH THE ALPHA 2A ADRENERGIC RECEPTOR – A TARGET FOR THERAPY IN PORTAL HYPERTENSION

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Background and Aims: Portal hypertension (PH) is a serious complication in cirrhosis and current therapy with beta-blockers is ineffective in more than 50% of patients. Plasma noradrenaline (NA) in cirrhosis patients is elevated and correlates with Child Pugh score, SIRS, and HVPG. In a sepsis model, specific Alpha 2a adrenergic receptor subtype (Adra2a) antagonism inhibits the inflammatory response of Kupffer cells. In this study we used the bile duct ligation (BDL) rat model of cirrhosis to investigate a possible mechanism for the effect of elevated NA on portal pressure (PP) and to determine whether specific Adra2a antagonism ameliorates the rise in PP.

Methods: Male Sprague Dawley rats underwent BDL or sham surgery. Treatment with BRL44408 (BRL; 10 mg/kg, i.p.) or saline was given on the final 2 study days. Haemodynamic measurements were performed under anaesthesia, and plasma and tissue samples were collected for analysis 28 days after surgery.

Results: Plasma NA was higher in BDL than sham rats ($p = .006$) and correlated with PP ($r = 0.677$, $p = 0.001$). Adra2a expression was higher in BDL than sham rats. PP was higher ($p < 0.001$) and hepatic arterial blood flow (HABF) lower ($p = 0.009$) in BDL than sham rats. BRL treatment reduced PP ($p < 0.001$) and increased HABF ($p = 0.032$). Mean arterial pressure (MAP) was lower ($p = 0.009$) and plasma renin activity (PRA) higher ($p < 0.001$) in BDL than sham rats. BRL treatment did not significantly change MAP or PRA. Activated phosphorylated eNOS expression (p(S117)-eNOS) was considerably lower in BDL than sham rats whilst caveolin-1 expression (inhibitor of eNOS activity) was increased. BRL increased p-eNOS and decreased caveolin-1. Expression of the activated myofibroblast marker αSMA was higher in BDL than sham rats and was decreased by BRL treatment. In vitro stimulation of rat hepatic stellate cells (HSCs) with an Adra2a agonist (guanfacine; 50 μM) increased 3D collagen gel contraction.

Conclusions: We demonstrate for the first time that a relevant PH rat model replicates the correlation between plasma NA and disease severity seen in cirrhotic patients and that specific Adra2a antagonism significantly improves hepatic haemodynamics without deleterious effects on systemic haemodynamics. Our data suggest that both a reduction in eNOS activity and an increase in HSC activation contribute to the mechanism of NA-induced PH. Specific Adra2a antagonism represents an attractive therapeutic strategy for PH and warrants further investigation.

FRI-012
CHRONIC OPIOID THERAPY IS ASSOCIATED WITH GUT DYSBIOSIS IN CIRRHOSIS INDEPENDENT OF CIRRHOSIS SEVERITY

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Background and Aims: Chronic opioid therapy is epidemic in cirrhotic patients. Due to their impact on gut motility, opioid therapy could impact gut microbiota composition in cirrhosis. However the effect of opioids on gut microbiota in cirrhosis is unclear. To define the effect of chronic opioid therapy on gut microbiota composition in cirrhotic patients.