Methods All patients diagnosed with pancreatic adenocarcinoma over a 2-year period who underwent trial dissection or resection after routine staging with CT and EUS were included in the study. CT and EUS images were retrospectively reviewed by two radiologists in a double blinded manner and the findings were compared with operative findings and final histology in those patients who underwent radical resection. Sensitivity, Specificity, Positive Predictive value (PPV), Negative predictive value and Accuracy were determined for assessing major vessel involvement which in most cases preclude radical resection.

Results 23 patients (M:F=13:10; mean age=68; range=56–78) underwent trial dissection or radical resection over a 2-year period. 13 were inoperable (nine inoperable due to locally advanced tumour, 1 inoperable due to liver mets, three both locally advanced and liver mets) and 10 underwent radical resection (three resected with cuff of portal vein (all R1), seven resected with six of them R1). Predictably EUS had superior sensitivity and accuracy over CT for both major vessel involvement (88% vs 53%, 87% vs 65%) and nodal involvement (43% vs 10% & 56% vs 50%). However CT was superior to EUS in excluding major vessel involvement (specificity = 100% vs 86%) and comparable to EUS in ruling out nodal disease (specificity = 100%). Importantly, three patients declared as having major vessel involvement by either of the modality underwent radical resection, two of them with FV resection. One patient who was staged as resectable with no vascular involvement was found to have major vessel involvement and underwent resection (R1).

Conclusion Though CT and EUS have important role in staging of patients with pancreatic cancer, a significant minority of patients will still be amenable to radical surgery and should be offered trial dissection with a view to radical surgery as surgery is the only realistic curative therapeutic option.

Competing interests None declared.

Basic science (liver)

PMO-112 IS PRIMARY BILIARY CIRRHOSIS A STEROID SENSITIVE AUTOIMMUNE DISEASE?

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Introduction Primary biliary cirrhosis (PBC) is a classic T cell mediated autoimmune disease: an autoantigen has been described and high levels of antigen specific liver infiltrating auto-reactive CD4+ T cells found. However, unlike in other autoimmune conditions steroid therapy is not considered effective in PBC although there is existing evidence that it can improve histological and biochemical parameters.1 We sought further evidence that PBC is a steroid sensitive disease by using two in vitro measures of steroid sensitivity.

Methods We have applied an in vitro dexamethasone (Dex) inhibition of lymphocyte proliferation assay (DILPA), which correlates well with clinical steroid sensitivity and outcome in ulcerative colitis2 and alcoholic hepatitis,3 to 20 patients with PBC diagnosed by liver biochemistry, antibodies and liver histology (when performed). The DILPA assesses peripheral blood mononuclear cell (PBMC) sensitivity to treatment with steroids in vitro. We also performed a 1D Adams, 1S Afford.

FN14 IS EXPRESSED ON CHOLANGIOCYTES AND PROMOTES BILIARY DUCTULAR REMODELLING VIA APOPTOSIS AND REACTIVE OXYGEN SPECIES AFTER INTERACTION WITH TWEAK

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Introduction The mortality from chronic liver disease in the UK has increased by 50%.3 The prevalence of cholangiopathies, diseases of the bile ducts, has increased fourfold.2 These include primary biliary cirrhosis, primary sclerosing cholangitis and allograft rejection after transplantation.4 It is increasingly observed in livers donated for transplantation after cardiac death, a source of organs on which the NHS is becoming more reliant.5 6 It is characterised by inflammation and destruction of intrahepatic bile ducts.7 When sustained it may drive portal fibrosis to end-stage liver disease when the only therapeutic option for patients is liver transplantation.8 The novel TNF superfamily member TNF-like weak inducer of apoptosis (TWEAK) and its cognate receptor FGF-inducible protein 14 (Fn14) are implicated in hepatic inflammation and remodelling.9 10 TWEAK is mainly secreted as a soluble cytokine by myelomonocytic cells.11 Fn14-TWEAK interaction in other systems promotes cell growth, apoptosis, autophagy and transdifferentiation via activation of TRAF and NF-κB pathways.12

Aim To demonstrate the expression of Fn14 and TWEAK on cholangiocytes and the functional significance of Fn14/TWEAK interaction on biliary ductular remodelling.

Methods Human liver samples were obtained with consent from the Queen Elizabeth Hospital liver transplant programme. Sections were stained for Fn14 and TWEAK using immunohistochemical techniques. Expression of Fn14 and TWEAK on cholangiocytes stimulated with TNF-α, IFN-γ and FGF was established quantitatively using flow cytometry. Cholangiocytes stimulated with FGF were exposed to TWEAK for 48 h. Apoptosis and reactive oxygen species production at this time point were determined by flow cytometry using annexin and dichlorofluorescin assays respectively.

REFERENCES
**Results** Immunohistochemistry reveals Fn14 on the intra-hepatic small bile ducts of inflamed livers, especially around the Canals of Hering. Fn14 expression is increased on cholangiocytes in vitro by 26% after stimulation with FGF. Exposure of cholangiocytes to TWEAK for 48 h induces apoptosis and upregulation of reactive oxygen species in FGF-activated cholangiocytes.

**Conclusion** Fn14 is expressed on cholangiocytes in inflamed human livers. Activation of the Fn14/TWEAK receptor-ligand system induces apoptosis using a novel mechanism partly dependent on the generation of reactive oxygen species.

**Competing interests** None declared.

**REFERENCES**


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**PMO-115**

**ANTI-β1-INTEGRIN ANTIBODIES IMPROVE SURVIVAL OF ISOLATED HUMAN HEPATOцитES SIGNIFICANTLY INCREASING BOTH ADHESION TO HEPATIC SINUSOIDAL ENDOTHELIUM UNDER FLOW AND ENGRAFTMENT IN MURINE LIVER FOLLOWING TRANSPLANTATION**

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**Introduction** Hepatocyte transplantation is a potential alternative to orthotopic liver transplantation but is limited by poor survival of transplanted cells. This may be partly due to apoptosis of isolated hepatocytes following detachment from extracellular matrix with loss of β1-integrin-mediated survival signals. Anti-β1-integrin antibodies have been shown to reduce apoptosis of rat hepatocytes and improve their survival in allogeneic transplantation. The purpose of this study was to determine the effect of β1-integrin blocking antibodies on the survival and initial engraftment of transplanted human hepatocytes.

**Methods** Hepatocytes were isolated from tissue obtained with ethical approval from Queen Elizabeth Hospital Birmingham. Integrin expression was confirmed using flow cytometry. Cells were incubated in suspension with anti-β1-integrin blocking antibodies or isotype matched control for 1 h. Viability and caspase three activity were assessed using flow cytometry and cleaved caspase 3 ELISA respectively. A modified flow adhesion assay was used to investigate the resistance to flow of cells adherent to sinusoidal endothelium (HSEC). An FC blocking agent was used to exclude the possibility of antibody-treated cells binding via antibody-FC receptor interactions. 1×10⁶ fluorescently labelled cells were injected into C57BL/6 mice via the portal vein under general anaesthesia and the mice culled after 15 min. The livers were immediately frozen and sectioned and the number of fluorescent cells per field of view counted.

**Results** Mean surface expression of the β1-integrin subunit on human hepatocytes was 86.3% (MFI 46.8). Hepatocytes treated with β1-integrin antibodies showed increased viability (85.4% vs 79.0%, p = 0.02) and reduced caspase 3 activity as demonstrated by a decrease in cleaved caspase 3 (mean 450 nm absorbance 1.37 vs 1.90, p = 0.02). β1-integrin blockade significantly increased the mean percentage of cells remaining adherent to HSEC under flow compared to IgG control (50.6% vs 12.7%, p = 0.03) and significantly