

whether there is a “spill-over” of hepatic anti-inflammatory mediators into the systemic, circulatory, compartment.

Method Median levels (pg/ml) of hepatic IL-1 β , IL-4,-6,-10,-12,-17, IFN- γ , MCP-1, TNF- α , TGF- β 1 were measured using proteome arrays in 10 human AALF explants and 8 normal control liver tissue samples.

Hepatic and serum levels of IL-1 β , IL-4,-6,-10,-12,-17, MCP-1, TNF- α , TGF- β 1 were measured in 200mg/kg i.p. APAP treated male C3H/HeH mice (n=5 severe necrosis, n=5 moderate necrosis) and 5 control mice.

Regional levels (portal vein (PV)), hepatic vein (HV), arterial (art)) of TNF- α , IL-10 were determined using ELISA in 3 AALF patients at time of liver transplantation.

Results In human AALF, hepatic levels of IL-6 (115 vs 75; p=0.02), IL-10 (1.8 vs 0.6; p=0.03), TGF- β 1 (3009 vs 1323; p<0.0001) were elevated in AALF compared to controls while IL-1 β , IL-12, IL-17, IFN- γ and TNF- α were unchanged. Higher hepatic levels of IL-4 (37 vs 25; p<0.01), IL-10 (90 vs 66; p<0.01), IL-12 (11 vs 7.8; p<0.01) and TGF- β 1 (2521 vs 540; p<0.01) were detected in mice with severe hepatic necrosis compared to those with moderate necrosis and normal controls. Similar to human AALF, serum pro- (IL-6 (146 vs 13; p<0.01), IL-1 β (104 vs 62 (p=0.07)) and anti-inflammatory cytokines (IL-4 (3 vs 0.8; p<0.01), IL-10 (47 vs 1; p<0.01) were elevated compared to normal controls during murine AALF.

Conclusion We demonstrate a hepatic inflammatory microenvironment favouring resolution of inflammation/tissue repair processes. In vivo hepatic production and systemic “spill-over” of the immunosuppressive cytokines is observed and may account for functional monocyte deactivation and the marked predisposition to sepsis in AALF. The marked similarities in anti-inflammatory mediator profiles between human and murine models of AALF provide a rationale on which to base the studies examining evolution of disease and development of immunomodulatory strategies to ameliorate acute liver injury and promote tissue repair.

P101 FK STIMULATION OF HEPATITIS C VIRUS-SPECIFIC AND NONSPECIFIC PERIPHERAL BLOOD MONONUCLEAR CELL OF PATIENTS ON WAITING LIST TO EVALUATE AND TAILOR IMMUNOSUPPRESSION BEFORE ORTHOTOPIC LIVER TRANSPLANTATION

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Introduction We previously found that FK did not induce a severe reduction of immune response compared to other calcineurin inhibitor (ILTS 2009 oral presentation).

Aim We aimed to evaluate the in vitro effect of tacrolimus on hepatitis C virus (HCV)-specific immune response by ELISpot to establish early the possible effect of immunosuppression and so tailoring immunosuppressive schedule before OLTx to minimize or delay HCV recurrence.

Method Twenty-five HCV+ve patients (20 male and 5 female) on waiting list were enrolled. Blood samples were taken and at least on 2–2.5 \times 10⁵ cells per well ELISpot was performed to evaluate IFN-specific response after coculturing with 1 ng/ml or 5 ng/ml of FK for 24 h. CMV and a specific stimulation with PMI-Ionomycin were used as control on HCV patients. Ten healthy donors were used as control.

Results After 24 h of FK stimulation, PMA-Ion IFN-response was reduced in all patients (p<0.05) compared to basal values both with 1 ng/ml that 5 ng/ml while CMV- specific showed reduction only when cocultured with 5 ng/ml. Among patients on waiting list, we had that 8 out 25 had a major reduction of HCV and CMV specific

response (p <0.05) while 17 out 25 had no statistical significant changes in their IFN response.

Abstract P101 Table 1 Results

Results				
Patients parameters	HCV	CMV	PMI-Ion	HD-PMA-Ion
Age (y, mean SD)	55, 3	55, 3	55, 3	35, 6
Male	20/25	20/25	20/25	7/10
Female	5/25	5/25	5/25	3/10
HCV-RNA (IU/mL mean SD)	310 232 \times 10 ³	n.d.	n.d.	n.d.
Genotype				
1a/1b	23/25			
Non-1	2/25			
Immunological parameters				
IFN-ELISpot (SFC) in		25/25	25/25	10/10
TO without stimulation	65 25	192 103	225 100*	272 113*
FK stimulation 1 ng/ml	58 19	176 98	176 88*	200 126*
FK stimulation 5 ng/ml	52 50	128 42*	150 45*	133 23*
IFN-ELISpot (SFC) in	8/25 pts			
TO without stimulation	61 15*			
FK stimulation 1 ng/ml	41 7*			
FK stimulation 5 ng/ml	34 5*			

*p<0.05; p>0.05.

Conclusion Based on these results and our previous data, ELISpot assay before OLTx may useful to establish the impact of immunosuppressive schedule. In those having a major reduction of HCV specific immune response after CNI stimulation (FK) a different drug should be used to minimize or delay the possible HCV recurrence. Further studies are required to establish in vitro effects.

P102 THE UTILITY OF RADIOISOTOPE BONE SCANS IN THE LIVER TRANSPLANT ASSESSMENT FOR HEPATOCELLULAR CARCINOMA

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Introduction The incidence of skeletal metastases from hepatocellular carcinoma (HCC) is estimated to be 2–16%. It is well established that radioisotope bone scans can detect cancer earlier than cross sectional imaging. The role of bone scans in pre-transplant assessment has been discussed in the literature but its place in the assessment algorithm is not clearly established.

Aim The aim of this study is to determine the utility of radioisotope bone scans in patients with a diagnosis of HCC undergoing transplant pre-assessment.

Method Radioisotope bone scan results were reviewed for all patients undergoing liver transplant assessment for HCC at our unit from 1989 to 2009. Patients were initially selected for transplant assessment based on favourable HCC staging on cross sectional imaging. Patients undergoing bone scan had the result reviewed retrospectively as normal or abnormal. All abnormal scans we then reassessed against all available imaging and classified as showing benign or malignant changes. Patient outcomes were considered in relation to bone scan results.

Results During this period 216 patients with a primary or secondary diagnosis of HCC were assessed for liver transplantation. Two hundred and three patients were listed for transplant and 148 were eventually transplanted. The results of their bone scans are as below (Abstract P102 Table 1).