

Results: Real Time PCR confirmed the increased expression of eSip-L in NASH. Western blots demonstrated the expression of eSip-L in liver, HepG2 and Huh7 cell lines. Large fluorescent cytoplasmic lipid droplets were obtained in all lipid overloaded cells. Immunofluorescence analysis showed Sip-L to be localised in the nucleus and cytoplasm.

Conclusions: eSip-L mRNA expression is upregulated in NASH, highlighting the potential for eSip-L to be utilised as a biomarker for NAFLD.

723 DRUG INDUCED LIVER INJURY IN ASIA: THE IMPORTANCE OF ADULTERATED SUBSTANCES IN HERBS

C.T. Wai¹, B.H. Tan², M.Y. Low², B.C. Bloodworth², C.L. Chan², S.G. Lim¹. ¹Department of Medicine, Yong Loo Lin School of Medicine, National University of Singapore, Singapore; ²Health Sciences Authority, Ministry of Health, Singapore

Introduction and Aim: Our previous pilot study showed half the cases of drug induced liver injury (DILI) at our unit were due to traditional Chinese medicines (TCM), but their toxic components are unknown. This prospective study aims to evaluate presence of adulterated medications in the herbs in TCM-DILI. We achieved this through a collaborative study between a clinical hepatology unit and a government pharmacological laboratory.

Methods: All patients admitted to, or referred to our hepatology unit for suspected DILI from 1 Sept 2004 to 31 August 2005 were recruited and evaluated. Implicated TCMS were sent for further analysis. The test protocol categorized 208 commonly encountered drugs in adulterated herbs into 37 different pharmacological effect groupings. Depending on the volatility of the drugs, the screening protocol used Gas Chromatography/Mass Spectrometry or High performance liquid chromatography/Diode-Array Detector to screen for common adulterants. Any positive results from HPLC were further confirmed by using Liquid Chromatography/Mass Spectrometry.

Results: Twenty-four patients with suspected DILI were recruited over the 12 months period: median age 53 yrs (range 23–79), 12 (50%) male, 18 (75%) Chinese, 20 (84%) were related to TCM, 1 each related to anti-TB drugs, lovastatin, phenytoin, and ketamine. 19 had hepatocellular injury, 2 had cholestatic injury, and 3 had mixed injury. Adulterated substances were found in 5/24 (21%) preparations of TCM: toxic doses of mercury (1), phenylbutazone (1), berberine/codeine (1), berberine/metformin (1), and dexamethasone (1). 1 died from liver failure from anti-TB drugs related DILI, 1 who took herbs adulterated with toxic doses of mercury developed acute liver failure requiring living donor liver transplant, the other 22 (92%) survived. Of note was that 1 inactive hepatitis B carrier who took herbs adulterated with dexamethasone developed hepatitis B flare requiring lamivudine therapy; and another male patient who took herbs adulterated with phenylbutazone developed autoimmune hepatitis requiring steroids therapy.

Conclusion: TCMS could be adulterated with toxins to the liver. Further studies on the safety of TCMS including routine testing for adulterated substances should be considered.

724 GENE EXPRESSION IN HEPATIC AND WHITE ADIPOSE TISSUES OF PATIENTS WITH OBESITY-RELATED NON-ALCOHOLIC STEATOHEPATITIS (NASH)

R. Collantes^{1,2}, A. Baranova^{1,2}, K. Schlauch¹, S. Gowder², L. Del Giacco², H. Elariny^{1,2}, A. Van Meter², A. Afendy¹, J.P. Ong^{1,2}, Z. Goodman³, V. Chandhoke^{1,2}, Z.M. Younossi^{1,2}. ¹Center for Liver Diseases, Inova Fairfax Hospital, Falls Church, VA, USA; ²Center for the Study of Genomics in Liver Disease, George Mason University, Fairfax, VA, USA; ³Armed Forces Institutes of Pathology, Washington, DC, USA

NASH is commonly seen in patients with metabolic syndrome or associated conditions (obesity, diabetes, hyperlipidemia, and arteriosclerosis).

White Adipose Tissue (WAT) is a biologically active organ, secreting a number of factors associated with NASH.

Aim: To assess the gene expression profiles of patients with NASH in both hepatic as well as omental adipose tissue (WAT).

Methods: Snap-frozen liver biopsy and omental adipose tissue specimens were obtained from obese patients with biopsy-proven NASH as well as non-NASH controls (lean and obese). From each sample, total RNA was extracted, amplified, and reverse transcribed into cDNA probes with aminoallyl nucleotides and coupled with fluorescent cyanine 3 or cyanine 5 dyes. cDNA probes were hybridized with microarray chips containing 5297 common genes. For each patient, extensive clinico-demographic and laboratory data were available. Comparisons were performed using non-parametric Mann-Whitney tests. Genes deemed statistically significant (adjusted p-value <0.05) were extracted for further study.

Results: Hepatic gene expression was available for 27 NASH patients. Adipose tissue gene expression was available for 10 NASH patients. Additionally, expression data from 39 controls were available for comparison. In patients with NASH, fatty-acid-Coenzyme A ligase, long-chain 4 (FACL4) was over-expressed in both hepatic and adipose tissues, with a ratio of 2.5 and 2.2, respectively (p <0.05). FACL4 is potentially involved in both lipid metabolism as well as apoptosis. In assessing genes related to obesity, 11 genes were differentially expressed in both the omental adipose tissue and hepatic tissue of the obese patients. Genes up-regulated in obese patients included iodide transporter, sialyltransferase, sulfotransferase, and several genes involved in cell contacts. Concordant up-regulation of endothelin converting enzyme 1 (ECE-1) was also observed in obese patients in both tissues, providing a potential link between metabolic syndrome, arteriosclerosis, and NASH.

Conclusions: This study of gene expression in the omental adipose and hepatic tissue of patients with NASH shows up-regulation of a number of interesting genes associated with lipid metabolism and apoptosis. Additionally, up-regulation of ECE-1 may provide a link between NASH and arteriosclerosis.

725 LIVER INVOLVEMENT IN ACUTE VASO-OCCLUSIVE CRISIS OF PATIENTS WITH SICKLE CELL DISEASE: PREVALENCE AND PREDISPOSING FACTORS

N. Sevastos¹, J. Koskinas¹, G.H. Zacharakis¹, N. Galiatsos², E. Manesis¹, A.J. Archimandritis¹. ¹2nd Department of Internal Medicine, Athens University School of Medicine, Hippokraton General Hospital, Greece; ²Biochemistry Department, Hippokraton General Hospital, Greece

Background: Liver involvement is relative common in patients with sickle cell disease (SCD) and acute vaso-occlusive crisis, but predisposing factors and prevalence are largely unknown.

Objective: To study prevalence and predisposing factors of liver involvement in SCD patients in acute vaso-occlusive crisis.

Design: Prospective study of all SCD cases admitted in acute vaso-occlusive crisis during 36 months.

Setting: Medical Department of a University Hospital.

Patients: 41 consecutive patients: 44% males; 71% heterozygous (HbSA), 29% homozygous (HbSS) with median age 33 (17–58) and 42 (16–56) years, respectively.

Measurements: Severity of vaso-occlusive crisis was graded by in-house-modified APACHE score; presence of asplenia or functional hyposplenism also considered. Hematological and biochemical parameters including various relevant enzymes/isoenzymes followed daily.

Results: Nine (22%) patients presented with acute painful hepatomegaly (8 were HbSA). Overall, liver involvement was found in 16 (39%) patients; 1 had “hepatocellular”, 8 “cholestatic” and 7 “mixed” type of liver injury. The severity of vaso-occlusive crisis (score 20.6 vs 18.2) was not related to liver involvement, but the presence of normal spleen function (P <0.001) and platelet counts <500,000/mm³ (P <0.001) were. Patients with liver involvement, compared to those without, had higher total and