than 10 is significant PH above which the complications like variceal bleed and ascites develop. Currently proposed classification of cirrhosis is based on the degree of PH and associated clinical features. Development of ascites, variceal bleed and hepatic encephalopathy is considered to be decompensated cirrhosis. PH results from increase in the intrahepatic resistance which has dynamic and fixed components and it is coupled with increase in the portal blood flow. Therapeutic interventions which can reduce the HVPG like non selective beta blockers and Transjugular intrahepatic porta systemic shunt (TIPS) can be helpful in combating complications of cirrhosis. And they have been shown to improve survival. Bacterial infection is common in cirrhosis with one month mortality of 30%. Oral prophylactic antibiotics or bowel decontamination have shown to improve long term outcome in patients with decompensated cirrhosis. Malnutrition is common in all patients with cirrhosis. Now it is clear there is no need of restricting the proteins in these patients. In fact nutritional therapy can improve survival, reduce the rate of infections, stay in ICU and hospital, and reduce post operative complications. Screening for hepatocellular carcinoma (HCC) can pick up very early disease and survival can be improved in these patients by offering curative treatment. Therapeutic modalities can reverse the cirrhosis. These modalities according to the etiology are (1) abstinence for alcoholic cirrhosis, (2) antiviral therapy for hepatitis B, (3) immunosuppression for autoimmune hepatitis, (4) relieving biliary obstruction in patients with secondary biliary cirrhosis, (5) antiviral therapy for hepatitis C and (6) relieving obstruction in patients with budd Chiari syndrome. Future therapies like antifibortic, antiangiogenic and anti coagulants may have potentials reducing fibrosis, reversing cirrhosis. Stem cell therapy may be helpful in patients with liver cirrhosis.

CS16.3 New concept in nomenclature, classification and diagnosis of liver failure

Y.M. Wang*. *Chongqing, China*

Abstract not available

CS16.4 Treatment strategy developments of hepatitis B with liver failure

Z.L. Gao*. *Guangzhou, China*

Abstract not available

Free Paper Presentation 1: Hepatitis C

Friday, July 15, 2011, 15:30–17:00
Meeting Room 310

PL-001 USP18 stimulates HCV production in vitro: a novel mechanism for HCV resistance to interferon therapy

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Background: The molecular mechanisms of interferon resistance in almost 50% of the HCV infected patients remain unclear. We have previously identified that upregulation of interferon stimulated genes (ISGs), such as Interferon Stimulated Gene15 (ISG15) and Ubiquitin Specific Protease 18 (USP18) in hepatocytes, predicts treatment failure. Moreover, silencing USP18 potentiates IFN anti-HCV activity and increased expression of ISG15 promotes HCV production. In this study we investigate the role of USP18 in HCV production.
Methods: We studied the effect of over-expression of wild type (catalytically active) USP18 or an enzymatically inactive mutant form of USP18 on HCV RNA replication and viral production in JFH1 culture system. Levels of various ISGs and of the critical miRNA 122 were assessed by real-time PCR, and surface expression of the key HCV entry receptor, CD81, were quantified by FACS.
Results: Over-expression of wild type and mutant USP18 increases HCV production at baseline (without IFN) and blunts the anti-HCV activity of IFNa in the JFH1 infectious system. While neither ISG expression nor miRNA 122 levels were unaffected by overexpression of USP18, whether in the presence or absence of IFNa, surface expression of CD81 was increased following USP18 over-expression in Huh7.5 cells.
Conclusions: These data indicate that USP18 overexpression leads to increased HCV production independent of its catalytic activity, and in concert with increased surface expression of CD81. Thus, USP18, one of the ISGs increased in chronic HCV infection, stimulates HCV production and likely contributes to treatment failure by promoting HCV cell entry and blunting IFN anti-HCV activity.

OL-001 Clinico-epidemiological profile of patients with hepatitis C virus infection seen in private practice clinics in Metro Manila

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Background: Hepatitis C virus (HCV) infection is a major public health problem worldwide. In the Philippines, there are few published data on the clinico-epidemiological profile of patients with HCV infection.
Methodology: Out-patient charts of patients seen from October 2005 to November 2010 in private practice clinics of 3 gastroenterologists were reviewed. All patients with a positive anti-HCV and/or HCV-RNA were included. Clinical and epidemiologic information were collected and analyzed.
Results: Of 49 patients included, 27 (55%) were males. Mean age at diagnosis was 48.5 years. 26 patients had HCV genotype data – genotype 1 in 16 (61%) patients, genotype 2 in 8 (31%), genotype 4 in 2 (8%). The most common risk factor was blood transfusion before 1990 identified in 18 (37%) patients. Other risk factors identified: injection drug use (IDU) 7 (14%), hemodialysis (HD) 7 (14%), unknown 11 (23%), others 5 (12%). At presentation, 17 (35%) patients had advanced HCV-related liver disease – 13 cirrhosis only and 4 hepatocellular carcinoma (HCC). Among 37 evaluable treatment-naïve patients, 16 (43%) were ineligible for treatment with advanced HCV-related liver disease (69%) as the most common reason.
Conclusion: In this study, blood transfusion before 1990, IDU, and HD were the most common risk factors for HCV infection. Many patients had advanced liver disease precluding eligibility for therapy. Screening for HCV among those with a history of blood transfusion before 1990, IDU, and HD may help identify HCV-infected patients early allowing institution of antiviral therapy to prevent progressive liver disease.

OL-002 Could faluvastatin affect the sustained virological response in chronic hepatitis C virus treatment?

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Background: Hepatitis C viral (HCV) infection is the leading cause of death due to liver disease. Additional agents are

needed to increase the cure rate. In vitro experiments show strong antiviral effects of fluvastatin against HCV.
Aim of the study: To asses the clinical outcome of fluvastatin addition to the standard regimen for treatment of chronic HCV in Egypt.
Subjects and Methods: The study included 80 patients with chronic hepatitis C virus infection fulfilled clinical, laboratory and histo-pathological criteria to be ready for interferon therapy, divided into two groups: Group I (n = 40) received standard treatment for HCV (pegylated interferon and ribavirin) and group II (n = 40) received standard treatment plus fluvastatin (80 mg/daily). Before and after 6 months of treatment liver function tests and HCV-RNA were evaluated.
Results: Addition of fluvastatin to the standard HCV treatment (pegylated interferon and ribavirin) significantly increased SVR from (55% to 62.5%; P < 0.01) and significantly decreased viral load in relapser patients (P < 0.001). No significant differences and correlations were found between serum levels of LDL-cholesterol and viral load before and after treatment in both groups.
Conclusion: Fluvastatin can be used to increase SVR when added to standard treatment (pegylated interferon and ribavirin) of chronic HCV.

OL-003 Genetic changes in the interferon sensitivity determining region of hepatitis C virus during the natural course of chronic hepatitis C 3a may lead to non-response to interferon therapy

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Background: We have found 70% response rate in Pakistan for Genotype-3a patients with combinationtherapy of interferon and ribavirin. There is need to individualize the treatment to minimize the side effects.
Methods: For the current study five G3 patients, nonresponder of 24 weeks interferon-alpha-2b plus ribivirin therapy, withalmost equal levels of viremia (1.8×10^7 IU/ml) at the end of treatmentwere selected. Mean viral load at week 36 was 2.6×10^6 IU/ml, atweek 48 raised to 2.0×10^7 IU/ml. All samples were quantified on RotorGene3000™. Interferon sensitivity-determining region (ISDR) innon-structural region-5A was studied to link any genetic changes in virus genomewith therapy esistance. ISDR was amplified using genotype 3aspecific ISDR primers followed by sequencing and bioinformatics tools.

Table 1. Mutations in Interferon sensitivity determination region of responder (R) and non responder (NR) Genotype 3a cases

```
R    CCGTCGTTGAAGGCCACTTG-CGGAACGCAT-TGGCCTCATCTAGACACTGAGCTAGTGG  58
     ||||| |||||||||  | || ||| |||| |  |||| | || |||| ||||||||||||
NR   CCGTCATTGAAGGCCTCCTGCCGG-ACGCCTCAGGCC-CCTCCAGACGCTGAGCTAGTGG  58
R    ATGCCAACTTGTTGTGGCGGCAAGAGATGGGCAGCAACATCACACGGGTAGAGTCTGAGA  118
     | ||||||||||||||||||||||||||||||||||| |||||||||||||||| ||||| |
NR   ACGCCAACTTGTTGTGGCGGCAAGAGATGGGCAGTAACATCACACGGGTAGAATCTGAAA  118
R    CAAAGGTTGTGATCCTTGATTCATTCGAACCTCTGAGAG  157
     |||||||||||| |||||||||||||||| |||||||
NR   CAAAGGTTGTGATTCTTGATTCATTCGAACCACTGAGAG  157
```

Sequence homology between the responder (Naïve) and Non responders was found with a Score of 191 bits (103), Identities = 141/159 (88%), Gaps = 4/159 (2%)

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R    PSLKATCGTHWPHLDTELVDANLLWRQEMGSNITRVESETKVVILDSFEPLR
NR   PSLKASCRTPQAPPDAELVDANLLWRQEMGSNITRVESETKVVILDSFEPLR
     ***** * *     * **********************************
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Amino acid comparison of responder and non responder with 84.6% identity in 52 amino acid residues overlap; Score: 212.0; Gap frequency: 0.0%

Result: A157bp ISDR product corresponding to 52 aminoacid protein, when compared with responderHCV patient naïve genome [Table 1], eight amino acid mutations were detected includingdeletions and substitutions affecting the molecular weight of protein. Gly, Trp, Pro, Leu. His, Thr were substituted by Arg, Gln, Ala, Pro, Pro, Ala respectively.
Conclusion: Mutations in ISDR region may have role in virus-resistance and high viremia, influencingthe therapy response. Screening will help in deciding treatment plan makingit cost-effective.

OL-004 Sequence analysis of hepatitis C virus 5′ non-coding region

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Objectives: Our aim was to identify the prevalence of hepatitis C virus (HCV) genotype and investigate genetic mutation of HCV 5′ non-coding region (5′NCR) sequences in Shandong province of China.
Methods: Serum samples from 118 chronic hepatitis C patients hospitalized in Jinan Infectious Disease hospital were collected. Serum samples were amplified from 5′NCR by RT-PCR and PCR products were sequenced by Sangon Biotech (Shanghai) Co., Ltd. Sequences of 5′NCR of the patients were compared with reference HCV strains from Genebank and phylogenetic tree analysis was performed.
Results: The cases among genotype 1b, 2a, 1a, 3a, 3b, 6a were 65 (55.1%), 45 (38.1%), 2, 1, 2 and 3, respectively. Sequences of 5′NCR in 42 genotype 1b patients were identical. Compared to reference HCV 1b strains, 23 genotype 1b patients have 1–2 bases mutation with two characteristic nucleotide mutation sites (120 C-T and 204 C-T). The homology of 5′NCR among genotype 2a patients was 97.8%-100% with characteristic nucleotide mutation sites (site 222 C-T and 247 C-T). The homology of genotype 1a, 3a, 3b and 6a with the same genotype HCV stains from Genebank was high, only with 1–3 bases mutation.
Conclusions: The predominant genotype of chronic hepatitis C patients in Shandong province is 1b, followed by 2a and a small amount of 1a, 3a, 3b, 6a. Genotype 3a and 6a are not reported before. Sequence of HCV 5′NCR is highly conservative and accords to HCV strains worldwide. Both genotype 1b and 2a have characteristic nucleotide mutations.

OL-005 A higher correlation of HCV core antigen with CD4+ T cell counts in HCV/HIV coinfected patients

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Background: Development of HCV infection is typically followed by chronic hepatitis C (CHC) in most patients, while spontaneous HCV viral clearance (SVC) occurs in only a minority of subjects. With the development of techniques for direct detection of the HCV virus (RNA or core protein), it is expected that HCV infectious status can be evaluated better if the results of HCV antibodies and virus detection were