mal control group and HCV-related chronic hepatitis regarding the HGFA H-score and TGF-β1 H-score.

Conclusions: Parallel expression of HGFA and TGF-β1 with the grade of activity and stage of fibrosis in HCV-related chronic hepatitis could make HGFA as an activity and regenerative marker.

**PP-138** Screening and cloning of gene of hepatocyte protein interacting with HCV NS5ATP4A protein

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Objective: We screen proteins of hepatocyte protein interacting with hepatitis C virus NS5ATP4A protein to clarify the signal transduction pathway of HCV.

Methods: "Bait" plasmids of hepatitis C virus NS5ATP4A were constructed. After verifying that hepatitis C virus NS5ATP4A protein could be steadily expressed in AH109 yeast strain, yeast-two "Bait" plasmids of hepatitis C virus NS5ATP4A were pre-transformed with liver cDNA library plasmids pACT2, and the diploid yeast cells were plated on quadruple dropout (QDO) medium and assayed for X-α-gal activity. Nineteen yeast colonies that could grow on QDO and had α-gal activity were obtained, then the library plasmids were extracted and sequenced.

Results: 7 genes were screened out and one of them was unknown gene. These genes were associated RNA synthesis, protein translation, cell cycle and tumor immune.

Conclusion: NS5ATP4 binding proteins were successfully screened, which offer new clues to the signal transduction pathway of NS5ATP4A and the pathogenic mechanism of HCV.

**PP-139** The evaluation of the hepatic fibrosis and its progression rate in chronic hepatitis C

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Aim: The evaluation of fibrosis through Ishak and Metavir scoring systems and its progression rate.

Methods: We studied 242 naïve patients with chronic hepatitis C, admitted between 2003 and 2006, who performed liver biopsy for diagnosis, being evaluated according two scoring systems. The evaluation of the fibrosis progression rate was performed only in 55 patients with a previous history of transusions, using the ratio between the fibrosis stage and the estimated infection duration (years).

Results: The mild and moderate fibrosis lesions predominated, with a concordance between the scoring systems. The mean fibrosis progression rate of 0.23 ± 0.34 units/year was 0.31 ± 0.51 units/year - Ishak system. The age at the time of infection and it's estimated duration correlate with the Metavir fibrosis progression rate (p < 0.005). MxA protein expression had a similar cell-specific activation patterns: ISG15 and MxA protein expression were correlated with response status. We previously reported that treatment nonresponders have marked pre-treatment upregulation of a subset of interferon stimulated genes (ISGs) in their livers, including ISG15 (Chen, et al. Gastroenterology 2005). Here, we study the source of the ISG expression signature and uncover the cellular basis of the phenotype through ISG15 and MxA protein expression.

Methods: ISG15 and MxA immunohistochemistry was performed on a subset of 31 liver biopsies and the expression pattern was correlated with response status.

Results: Using a simple histology scale scored from 0 to 3 (0: no staining in any cell, 3: staining in every cell), we found significantly more hepatocyte ISG15 expression in treatment non-responders versus responders (2.4 ± 0.6 vs 1.1 ± 0.6, p < 0.0001), but less macrophage ISG15 staining (0.2 ± 0.4 vs 0.8 ± 0.6, p < 0.005). MxA protein expression had a similar cell-specific pattern of expression. Treatment response was linked to cell-specific activation patterns: ISG15 and MxA protein upregulation was more pronounced in hepatocytes in treatment nonresponders, but in Kupffer cells in responders.

Conclusions: Our previously defined differential gene expression pattern in the livers of HCV responders and nonresponders is driven by activation of different cell types: hepatocytes in treatment nonresponders, and macrophages in treatment responders.

**PP-140** The occult HCV infection

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Aim: evaluating the presence and localisation of the HCV antigens (NS3, NS5, NS5A) in patients with chronic hepatitis C and undetectable versus detectable serum HCV-RNA.

Methods: 93 patients with chronic hepatitis C were included in the study, 55 with detectable viremia. Using immunohistochemical techniques involving monoclonal and polyclonal antibodies, we analysed the presence, localisation and semiquantitative grading of coloured cells.

Results: All untreated patients with detectable viremia presented hepatocyte expression of viral proteins, especially in the hepatocyte cytoplasm and less in the nucleus. The untreated subjects with undetectable viremia had similar detection rate as the untreated patients with detectable viremia, 92.3% respectively 92.4% and 84.61% for NS3, NS5, NS5A.

In treated patients with undetectable viremia, the proportion of positive results were comparable for NS3 (92%) but lower for NS5 and NS5A (80% and 60%). The positive immunohistochemical reaction was observed in fewer hepatocytes (< 30%), with focal lobular distribution and mild/moderate intensity in treated subjects with undetectable viremia, respectively moderate/important in the rest of patients.

The patients with undetectable viremia were found to have correlations between the presence of NS3 and NS5 antigens and the fibrosis level. The presence of steatosis correlated with NS3 and NS5 only in untreated patients with undetectable viremia. The portal space involvement was observed especially at macrophages.

Conclusions: Identifying the presence of viral antigens in the liver tissue in patients with undetectable viremia, who have either received antiviral therapy or not, can bring into discussion the occult HCV infection.

**PP-141** Predicting treatment response in hepatitis C virus infected patients: from gene to protein expression

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Objectives: Chronic hepatitis C virus (CHC) infection is treated with interferon/ribavirin, but only a subset of patients respond. We previously reported that treatment nonresponders have marked pre-treatment upregulation of a subset of interferon stimulated genes (ISGs) in their livers, including ISG15 (Chen, et al. Gastroenterology 2005). Here, we study the source of the ISG expression signature and uncover the cellular basis of the phenotype through ISG15 and MxA protein expression.

Methods: ISG15 and MxA immunohistochemistry was performed on a subset of 31 liver biopsies and the expression pattern was correlated with response status.

Results: Using a simple histology scale scored from 0 to 3 (0: no staining in any cell, 3: staining in every cell), we found significantly more hepatocyte ISG15 expression in treatment non-responders versus responders (2.4 ± 0.6 vs 1.1 ± 0.6, p < 0.0001), but less macrophage ISG15 staining (0.2 ± 0.4 vs 0.8 ± 0.6, p < 0.005). MxA protein expression had a similar cell-specific pattern of expression. Treatment response was linked to cell-specific activation patterns: ISG15 and MxA protein upregulation was more pronounced in hepatocytes in treatment nonresponders, but in Kupffer cells in responders.

Conclusions: Our previously defined differential gene expression pattern in the livers of HCV responders and nonresponders is driven by activation of different cell types: hepatocytes in treatment nonresponders, and macrophages in treatment responders.
This finding will help to develop diagnostic tools that can be used to predict treatment response before interferon-based therapy. It also provides insights into the molecular mechanism of interferon resistance in HCV-infected patients.

**PP-142** The predictive value of viral response during treatment to sustained viral response obtaining in chronic hepatitis C personalized treatment programs

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The antiviral effects of interferon in chronic hepatitis C is influenced by many factors, among which the personalized interferon and RBV dose, treatment course were the most important. The viral response during treatment was the composite expression of factors associated with treatment effects, and the very important predictive for sustained obtaining.

In this paper, the enrolled patients with chronic hepatitis C were given the intensive treatment doses of interferon and ribavirin according to their basic clinical condition. In the treatment of 0, 4, 12, 24 weeks, the end of treatment and 24 weeks after treatment stop, the serum HCV RNA were determined, and according the viral response on-treatment the individuation course was given, and the value of viral responses, including rapid viral response, (RVR), defined serum HCV RNA undetectable at 4 week, and complete early viral response (cEVR), serum virus undetectable at 4 week, on-treatment was anylsied predictive for SVR obtained. Given the personalized therapeutic program, 84.2% of patients obtained RVR, among which 90.7% obtained SVR. The RVR was not associated with HCV genotypes ($\chi^2=6.00$, $p=0.112$), but significantly with serum HCV RNA load baseline ($t=2.15$, $p=0.034$), which in RVR was $lg 5.883 \pm 1.246$ copies/ml, and $lg 6.502 \pm 0.693$ copies/ml in non-RVR. The RVR rate (87.8%) of naive patients interferon-$\alpha$ was higher than that of retreatment patients (65.0%) significantly in pegylated interferon treatment group ($\chi^2=6.651$, $p=0.031$). 92.4% (122/132) of patients obtained cEVR, those in pegylated interferon-$\alpha$ 180mg, 135mg and standard interferon group were 90.5%, 95.0% and 90.4%, and the difference among the three groups was not significant difference ($\chi^2 = 0.981$, $p = 0.640$). The SVR rate of patients with cEVR was SVR was 90.8% (108/119), which was significantly higher than that, 55.6% (5/9), of patients with no cEVR rate (Fisher’s exact test, $p = 0.007$). The SVR rate between naive and retreatment patients was not difference ($\chi^2 = 1.993$, $p = 0.158$), which were 94.7% (90/95) and 85% (17/20) respectively, and the difference of cEVR rate between genotype 1 and non 1 group was not significance aslo ($\chi^2 = 6.000$, $p = 0.112$), 91.22% (52/57) and 96.29% (26/27) respectively. This study showed that, RVR and cEVR were significantly related to SVR, and personality therapy can improve the obtaining probability of RVR, cEVR and the SVR.

According to the clinical characteristics of patients, given intensive doses of interferon and RBV, adjusted drug dose timely, and extended treatment of HCV RNA-negative course based on patient response were important in chronic hepatitis C personalized treatment.

**Poster Presentation – HIV/AIDS**

**PP-143** APOBEC3G/B/F mRNA levels in PBMC of HIV-infected patients and there correlation with CD4+ T cell counts

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Background: Apolipoprotein B mRNA-editing enzyme, catalytic polypeptide-like 3G/B/F (hA3G/B/F) showed anti-HIV activity in vitro, though there correlation with HIV disease progression is not clear. Our aim is to quantitative investigate hA3G/B/F mRNA levels in HIV-infected patients, then analyze there correlation with CD4+ counts.

**Methods:** Peripheral blood samples were collected from 21 HIV-infected subjects not taking antiretroviral therapy (ART) and 21 HIV-infected subjects receiving ART, and 10 HIV-uninfected controls. hA3G/B/F mRNA levels in PBMC were determined by real-time fluorescent quantitative PCR. Flow cytometry was used to detect CD4 counts.

**Results:** There was no correlation between hA3G/B/F mRNA levels and CD4 counts in either ART+ or ART- HIV-infected subjects. hA3G mRNA level in HIV-infected subjects was lower than that in HIV-uninfected controls ($p<0.05$), but no statistical difference between ART+ and ART- groups ($p>0.05$). However, significant difference were found in hA3/F mRNA levels between the three groups ($p<0.05$): ART- HIV-infected subjects < ART+ HIV-infected subjects < HIV-uninfected controls. hA3G/B/F mRNA levels were positively correlated with one another in ART+ HIV-infected subjects and HIV-uninfected controls, while not in ART- HIV-infected subjects.

**Conclusion:** hA3G/B/F gene expression levels do not directly correlate with HIV-1 disease progression. Host hA3G/B/F expression levels tend to decrease after HIV-1 infection, and ART may elevate hA3/F mRNA levels, but not for hA3G. The function of hA3 family proteins in anti-HIV infection needs further study.

**PP-144** Substitution treatment implementations in Ukraine – impact on HIV prevalence

Dmitry Metlitsky*. All-Ukrainian Network of PLWHAs

Substitution treatment is recognized as effective part of biomedical prevention and one of the main tools of HIV/AIDS epidemic control among IDU’s. ST admitted as essential choice for IDU if ones fail rehabilitation programs.

Although Ukraine has the highest HIV-prevalence in Eastern Europe regions (large portion of vulnerable populations consists of IDU’s), ST implementation was under the major focus of donors (Global Fund, Sunrise, Clinton Foundation).

By the reason ST was quit new activity for Ukraine vertical model of implementation – from center to regions were chosen. It meant that advocacy for needed decrees from Ministry of Health, drugs regulation authorities was made on the national level. Then a number of regional sites were opened.

In result regional medical authorities asked for help in meeting of requirement in ST sites, they started to participate in project competitions for sites financing, they realized advantages of new model of work with IDU’s.

As conclusion it should be mentioned that central advocacy work saved time and made regional implementation of program much easier. As the second phase – regions begun plan their activities accordingly needs of the regions. Governmental authorities were satisfied with decreasing of HIV transmission among IDU, more social reliability of patients and lower mortality rate among them.

Statistic data is available.

**PP-145** P53 and mitochondrial toxicity induced by AZT

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The mitochondrial toxicity of nucleoside reverse transcriptase inhibitors (NRTIs) is due to the inhibition of mitochondrial DNA (mtDNA) polymerase $\gamma$ (Pol $\gamma$), resulting in a blockade of mtDNA replication and subsequent disruption of cellular energetics. Previous study showed that p53 play a direct role through interaction with DNA Pol $\gamma$ or mitochondrial transcription factor.

**Poster Presentation – P53**