899

SIGNIFICANCE OF MICRO RNA-122 IN PATIENTS WITH CHRONIC HEPATITIS C ON INTERFERON THERAPY

Y. Kamo, H. Miyaaki, T. Ichikawa, S. Uchida, E. Yoshimura, Y. Kubota, T. Yamaguchi, H. Shibata, T. Honda, N. Taura, H. Isomoto, F. Takeshima, K. Nakao. *Department of Gastroenterology and Hepatology, Graduate School of Biomedical Sciences Nagasaki University, Nagasaki, Japan*
E-mail: wildduck1214@yahoo.co.jp

Aim: Peg-interferon (IFN) and Ribavirin therapy is a curative treatment for chronic hepatitis C and virological response to IFN therapy have been strongly associated with genetic variation in IL28B SNPs. Recently, micro-RNA122 (miR-122), that is most abundant micro-RNA in the liver, is reported to be important factors for replication of HCV-RNA. We investigate the correlation between miR-I22 andvirological response to IFN treatment and other clinical data.
Method: Subjects are 46 patients with hepatitis C who received the IFN therapy in our hospital from 2006 to 2011. We investigate the correlation of miR-122 expression by liver biopsies specimen with viral response and other predictor of IFN therapy including IL28 SNPs. We extract total RNA from liver biopsies specimen (RecoverAll Total Nucleic Acid Isolation Kit) and amplification for RT-PCR, and measured miR-122 expression by Real-time PCR. MiR-122 expression is normalized by RNU6B expression.
Results: MiR-122 expression showed no significant difference between both IL28B SNPs (rs8099917) (TT 2.237±2.828 : TG 5.594±14.013, P = 0.70605). Regarding virological response, there is no significant difference between sustained virlogicag response and non-response group (SVR 3.728±9.951 : NR 2.763±3.792, p = 0.62814). On the other hand, the decline rate of the virus in 2 weeks (P = 0.04498), 4 weeks (P = 0.03907), 8weeks (P = 0.02937) showed an inverse correlation between miR-122 expression. Sensitive indicator of β-cell insulin secretion were associated with miR-122 (P = 0.01278).
There are no significant correlation between miR-122 and other predictive factors of IFN therapy (age, gender, viral load, LDL, genotype, fibrosis).
Conclusion: In this study, miR-122 was independent factor to other predictor of IFN therapy. Regarding virological response to IFN therapy, miR-122 expression showed significant collelation with early phase decline rate by IFN treatment. This result suggested that miR-122 might act on the first phase of IFN treatment.

900

CORE AMINO ACID 70 SUBSTITUTION IN DIFFERENT HCV GENOTYPES AND ASSOCIATION WITH IL28B POLYMORPHISMS

H. Sharafi[1], A. Pouryasin[1,2], S.M. Alavian[3], B. Behnava[3], S.R. Rozehi[1], M. Keshvari[4], M. Zareiy[1], L. Mehrnoush[3], O. Kheradvar[1], S. Salimi[3], S. Mahinrousta[1], M. Gholami Fesharaki[5]. *[1]Armin Pathobiology Laboratory, Tehran, [2]Department of Genetics, Islamic Azad University-Arsanjan Branch, Arsanjan, [3]Baqiyatallah Research Center for Gastroenterology and Liver Disease, Baqiyatallah University of Medical Sciences, [4]Iranian Blood Transfusion Organization, [5]Department of Biostatistics, Tarbiat Modares University, Tehran, Iran*
E-mail: a.pouryasin@gmail.com

Introduction: It is obvious that heterogeneous responses to IFN-based treatments in chronic hepatitis C patients are due to variations in host and viral factors. Recently three different genome wide association studies (GWAS) reported the Polymorphisms of IL28B as a strong predictor of SVR. Viral factors such as HCV Core gene variations can also influence hepatitis C outcome. The aims of this study were to determine:
1. rate of Core 70 substitution in different HCV genotypes,
2. association of IL28B as a host predictor of SVR with HCV Core 70 amino acid substitution as viral predictor of SVR.

Patients and Methods: In this study, 459 chronic hepatitis C patients were enrolled. For IL28B genotyping, genomic DNA was extracted from peripheral blood using QIAamp DNA Mini Kit. Two common IL28B polymorphisms (rs8099917 and rs12979860) were genotyped by PCR-RFLP method. HCV RNA was extracted from plasma using QIAamp Viral RNA mini Kit and Core gene of HCV was amplified by QIAGEN Onestep RT-PCR Kit followed by direct-sequencing procedure and phylogenetic analysis for genotyping of HCV. Also, according to the HCV Core gene sequence, Core 70 substitution evaluated.
Results: The Core 70 substitution was observed in 32 (57.1%) HCV-1b infected patients, 7 (2.8%) HCV-1a infected patients and 8 (5.4%) HCV-3 infected patients. This mutation significantly found more in HCV-1b than other genotypes ($P < 0.001$). In HCV-1b infected patients, Core 70 amino acid substitution more frequently found in rs12979860 T/T genotype than non-T/T genotypes (85.7% vs. 47.6%) ($P = 0.02$). We didn't observe such association between Core 70 substitution and IL28B polymorphisms in patients infected with other genotypes of HCV.
Conclusion: Here we found coexistence of unfavorable viral variants and unfavorable host genetic variation. We observed higher distribution of rs12979860 T allele and also Core 70 substitution in HCV-1b infected patients, which all together can explain the possible cause of unfavorable outcome of HCV-1b infected patients.

901

VITAMIN D STATUS AND LIVER HISTOLOGY IN CHRONIC HEPATITIS C GENOTYPE 1 INFECTION: ANALYSIS OF THE AUSTRALASIAN CHARIOT STUDY COHORT

M.T. Kitson[1], G.J. Dore[2], P. Button[3], G. McCaughan[4,5], D. Crawford[6], W. Sievert[7,8], M. Weltman[9], W. Cheng[10], S.K. Roberts[1], CHARIOT. *[1]Alfred Hospital, Melbourne, VIC, [2]Kirby Institute, University of New South Wales, [3]Roche Products, [4]Royal Prince Alfred Hospital, [5]Centenary Research Institute, Sydney, NSW, [6]Greenslopes Hospital, Brisbane, QLD, [7]Monash Medical Centre, [8]Monash University, Melbourne, VIC, [9]Nepean Hospital, Sydney, NSW, [10]Royal Perth Hospital, Perth, WA, Australia*
E-mail: m.kitson@alfred.org.au

Background and Aims: Vitamin D status is reportedly associated with liver fibrosis stage and necroinflammatory activity grade in chronic hepatitis C. We therefore analyzed the relationship between vitamin D status and liver histology, and identified independent predictors of liver histology in a large Australasian cohort with HCV genotype 1 (HCV-1) infection.
Methods: Demographics and baseline laboratory values, including 25-hydroxyvitamin D level [25(OH)D], of 274 treatment-naïve Australasian patients with HCV-1 infection from the CHARIOT study who had a liver biopsy and received up to 48 weeks of therapy with PEG-IFN plus RBV were evaluated. The relationship of vitamin D status, as assessed by the reference LC-tandem MS assay, with liver histology was analyzed with Kruskal-Wallis, ANOVA and Chi-squared tests. Independent predictors of METAVIR liver fibrosis stage and necroinflammatory activity grade were determined by multivariate analysis.
Results: METAVIR fibrosis stage prevalence was: F0 7.1%, F1 39.5%, F2 36.9%, F3 10.5% and F4 6.0%. 47% had low (0/1) and 53% had high (2/3) activity grade. 48% and 16% had 25(OH)D <75 nmol/L and <50 nmol/L respectively. Mean 25(OH)D level did not significantly differ between fibrosis stage (F0–4), advanced vs non-advanced fibrosis (F0–2 vs F3/4) or activity grade. However, 25(OH)D level <50 nmol/L was more prevalent in those with high activity grade (21% vs 11%, P = 0.03). Variables associated with fibrosis stage are shown in Table 1. Variables associated with activity grade are shown in Table 2.