I-42 Regulation of a hepatitis C virus co-receptor claudin-1 in hepatocytes

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The polarization of hepatocytes involves formation of functionally distinct sinusoidal (basolateral) and bile canalicular (apical) plasma membrane domains that are separated by tight junctions. In murine livers, integral tight junction proteins claudin-1, -2, -3, -5, -7, -8, -12, -14 which can form tight junction strands are detected together with occludin, JAM, CAR and tricellulin, and claudin-1, -2, -3 are expressed in the bile canaliculus region of hepatocytes. In the livers (mouse, rat, human), claudin-1 and -3 are expressed in the whole liver lobule, whereas claudin-2 shows a lobular gradient increasing from periportal to pericentral hepatocytes. It is reported that downregulation of claudin-1 serves as a potential marker for a poor prognosis in HCC. More recently, it is found that the claudin-1 is a hepatitis C virus co-receptor with CD81. Thus, the study of regulation of claudin-1 in hepatocytes is very important for analysis of pathogenesis of hepatitis C virus infection.

We have been studied for the regulation of tight junction proteins including claudin-1 in hepatocytes in vivo and in vitro. In this lecture, we present the regulation in expression and function of hepatic claudin-1 by growth factors (EGF, TGF-beta), cytokines (IL-1beta, oncostatin M) and partial hepatectomy via distinct signal transduction pathways.

I-43 Assessment of specific antibodies to F protein in sera of Chinese hepatitis C patients treated with interferon plus ribavirin

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The hepatitis C virus alternate reading frame protein (ARFP/F) of the 1b genotype is a double-frameshift product of the HCV core protein. In order to assess the presence of anti-F specific antibodies and their clinical relevance in sera of HCV patients, we produced recombinant F protein and core protein of the 1b genotype in Escherichia coli. An ELISA assay was developed using purified recombinant HCV core, F protein, as well as a 99 residue synthetic F peptide. Sera-prevalence of anti-core, anti-F and anti-F99 peptide was 95%, 68% and 36% respectively in 168 HCV patients. The prevalence of anti-F antibodies did not correlate with viral load, genotypes, or ALT level. Interferon combination therapy induced a decline of the level of anti-F antibodies in 55 responders (p < 0.01). Thirteen responders (24%) lost their anti-F recombinant protein antibodies and 17 (31%) lost their anti-F synthetic peptide antibodies respectively, whereas no decrease was observed for the 17 non-responders. These changes were significant between responders and non-responders (p < 0.05). Meanwhile, no change was found in the anti-core antibody titer of these 72 treated patients. The percentage of anti-F protein negative patients (15/15, 100%) who obtained sustained virological response was higher than that of the anti-F positive patients (70%, p < 0.05). Based on these findings, HCV F protein elicits a specific antibody response other than the anti-core protein response. Our data also suggest that the presence and the level of anti-F antibodies response might be influenced by interferon plus ribavirin treatment and associated with SVR in Chinese hepatitis C patients.

I-44 Efficacy and relapse: peginterferon alpha-2a plus ribavirin combination therapy in Chinese patients with chronic hepatitis C in clinical practice

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Chronic hepatitis C virus (HCV) infection poses a challenge for a growing number of infected patients who exhibit disease complications, including cirrhosis, hepatocellular carcinoma, and liver failure in China. The combination treatment of peginterferon alpha (PEG-IFN alpha) plus ribavirin (RBV) is recommended as a standard care for HCV infections, which can improves hepatic markers and eradicates the virus in about 50% of patients. However, a significant number of patients do not respond to therapy or relapse following treatment discontinuation. Several viral, hepatic, and patient-related factors influence response to therapy.

In our clinical practice, a total of 77 interferon-naive patients (61% male; median age 47 years) with chronic hepatitis C include 11 cirrhotic patients (no genotyping) received PEG-IFN alpha-2a 180 mcg/week plus RBV 900–1200mg/day for 48 weeks and follow up 24 weeks. The results show that the patients have more RVR and EVR rate (54% and 90.9% respectively). While the SVR (undetectable HCV-RNA 24 weeks after treatment completion) rate is only 51.5%

In conclusion: Comparing with the data of clinical trail, the RVR, EVR and EOTR were higher, while SVR was the same in Chinese patient with chronic hepatitis C patients received the combination therapy of PEG-IFN plus RBV. The reason of high relapse was still unknown. Although optimal duration of retreatment and benefits and safety of maintenance therapy have not been determined, an extended duration is likely needed, even for the patients who achieved EVR.

Concurrent Session 8 − Nosocomial Infection and Public Health

I-45 Rational management of community-acquired pneumonia

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Pneumonia is the commonest cause of fever world-wide and accounts for considerable morbidity and mortality, and for a large proportion of the workload for the frontline doctors. Not all patients with community-acquired pneumonia must be managed as inpatients. A number of prediction rules have been developed to help clinicians to identify predictors of poor prognosis and some are relatively easy to use. Empirical therapy must be started as soon as possible based on knowledge of the most likely infective organism(s) and its likely anti-microbial sensitivity. Treatment success depends on the accuracy of the diagnosis with a sound understanding of the underlying microbiology. Clinical parameters should be used to assess treatment outcome. Treatment failure is usually due to incorrect diagnosis, incorrect/inadequate therapy or development of complications.