OL-024 **Genetic diversity and nucleoside analogues resistance mutations of hepatitis B virus in Russian Federation and Viet Nam**

E.A. Elpaeva[1], A.B. Komissarov[1], E.A. Poretskova[1], O.P. Dudanova[2], D.T. Tuyên[3], M.M. Pisareva[1], E.V. Esaulenko[1]*, M.P. Grudinin[1]. [1]*Research Institute of Influenza, Russian Academy of Medical Science, Saint Petersburg, Russia,* [2]*Petrozavodsk State University, Petrozavodsk, Russia,* [3]*Military Institute of Hygiene and Epidemiology, Hanoi, Vietnam*

Objectives: To reveal HBV genetic diversity in chronic hepatitis patients from 4 regions of Russia, to determine the structure of HBV DNA polymerase gene fragments responsible for nucleoside analogues treatment.
Methods: HBV genotyping by original PCR method. Sequencing of polymerase gene fragment. Real time PCR – to determine viral load in patients' blood and liver biopsy. Disease severity evaluated by clinical-laboratory markers and morphology.
Results: In 2008–2010 HBV genotypes were determined in 381 patients with chronic hepatitis B from Saint Petersburg region, Karelia (Petrozavodsk), 2 districts from Central part of Russia (Perm and Kazan) and Vietnam. HBV D genotype was revealed in 77% of cases in Saint Petersburg region, 86% in Petrozavodsk, 67% in Perm and 83% in Kasan. In the rest of cases A genotype was determined in these regions. In Vietnam samples two HBV genotypes were detected: genotype B – 86% and C – 14% of cases. As reported previously more severe disease was diagnosed in Russian patients with HBV A genotype. 98% of patients with HBV D genotype were HBeAg-negative.
HBV polymerase gene fragment sequencing from 62 patients revealed high diversity of this fragment. YMDD-motif in all cases was characteristic for wild type (lamivudin susceptible). Russian patients have been successfully treated by talbivudine during 1 year in the absence of resistance mutations. However, lamivudin/adefovir resistance mutation rtA181T and entecavir resistant mutation rtS202N were revealed in 3 and 4 sequences from Vietnam patients, correspondingly. Interestingly that the entecavir resistance mutation was observed in patients not treated with entecavir.
Conclusion: Comparing with the period of 2004–2008 HBV genotypes distribution in Saint Petersburg region in 2008–2010 considerably changed as the result of active migration of population from Central Russia. HBV sequencing analyses obtained in this study allowed to justify the therapy selection.

OL-025 **Research on the immunological mechanism of one new type adjuvant for therapeutic hepatitis B vaccine**

P. He[1]*, X.C. Zhang[1], Z.Y. Hu[1], X. Fang[1], S.H. Qiu[1], Z.L. Liang[1]. [1]*National Institute for the Control of Pharmaceutical and Biological Products, China*

Background: Recently, studies showed that bacterial DNA and synthetic non-methylated CpG containing Oligonucleotide (CpG-ODN) can stimulate the immune response, promoting the proliferation and differentiation of immune cells. Hepatitis B vaccines with CpG as adjuvant are under phase II clinical studies abroad. At present, studies on CpG-ODN mainly focused on humoral immune responses. In this paper, study on the cellular immunology of a new type CpG-ODN (BW006) was carried out.
Methods: Spleen MNCs of BALB/c mice were separated aseptically and added into cell culture plates accompanied by BW006 after cell concentrations were adjusted. Plates were incubated under 37°C for different time. Expression levels of mRNA of IL-12p35, IL-12p40 and IFN-γ inducing protein (IP-10) in MNCs were detected by bDNA kit from Panomics. Expression level of IL-12 was detected by Luminex 100™ analyzer. Level of IP-10 in peripheral blood of BALB/c mice inoculated subcutaneously with 200 μg BW006 was detected with IP-10 detection kit (R&D) 3 hours after inoculation.
Result: Three hours after stimulation with BW006, IL-12p35 and IP-10 mRNA levels increased by 2.2 times and 2.8 times, respectively; 6 hours after stimulation, IL-12p40 mRNA level increased by 26 times. Expression of IL-12 reached peak level 48 hours after stimulation (9198.71pg/ml). IP-10 level of mice inoculated with BW006 was significantly higher than that of control group (14001.31pg/ml, 300.78 pg/ml; $P < 0.01$).
Conclusion: BW006 can induce high level expressions of IL-12 and IP-10 both at transcriptional and translational levels in early phase after in vitro stimulation. Elevated levels of IL-12 and IP-10 in mice after stimulation with BW006 implies that BW006 has strong ability in inducing Th1 type cellular immune response, which provides new clues for the development of new therapeutic hepatitis B vaccines.

Free Paper Presentation 6: Bacterial Infections
Saturday, July 17, 2010, 16:45–17:45
Convention Hall 2A

PL-006 **Myeloid-derived suppressor cells act as a key immune regulator in the CSF of patients with bacterial meningitis post-neurosurgery**

G.Z. Shi[1], J.Y. Han[2,3]*, G. Liu[4], Y. Hao[2,3], B.B. Wang[2,3], Y.A. Liu[5], Y. Mao[2,3], J.Z. Zhao[6], J.X. Zhou[1], H. Zeng[2,3]. [1]*Intensive Care Unit, Beijing Tiantan Hospital, China Capital Medical University,* [2]*Institute of Infectious diseases, China Capital Medical University,* [3]*Institute of Infectious diseases, Beijing Ditan Hospital,* [4]*Department of infectious diseases, Beijing Children's Hospital, China Capital Medical University, Beijing,* [5]*Department of Laboratory Medicine, Beijing Tiantan Hospital, China Capital Medical University,* [6]*Department of Neurosurgery, Beijing Tiantan Hospital, China Capital Medical University, China*

Bacterial meningitis is one of the common and serious complications after neurosurgery. In bacterial meningitis, peripheral blood leukocytes migrate into CSF through a series of cytokines and chemokines, and then regulate the local inflammation responses. On the other hand, compensatory anti-inflammatory mechanisms are necessary to avoid excessive inflammatory responses. Regulatory T cells (Tregs) and myeloid-derived suppressor cells (MDSCs) have been considered two major immune suppressive cells. We therefore investigated whether Tregs and MDSCs could be involved in immune responses in adult bacterial meningitis post-neurosurgery. In our study, we found the frequencies of Tregs and MDSCs elevated within the CSF compared with that in peripheral blood in patients with bacterial meningitis post-neurosurgery. MDSCs in CSF consisted of immature granulocytes mainly, which were capable of exerting a T cell suppressive effect in vitro. Furthermore, they could also induced resting Treg (rTreg) to activated Treg (aTreg). In the migration assay, rather than Treg-specific, but MDSC-specific chemotactic activity increased in CSF supernatants. In conclusion, both Tregs and MDSCs, especially MDSCs, should play important roles in bacterial meningitis as negative regulatory cells. And MDSCs would migrate into the CSF along a series of cytokines and chemokines. These