UMP. 782

HBX plays a potential role in developing hepatocellular carcinoma in chronic HBV carriers, a series of evidences suggesting plausible oncogenic factor

N. Arshad[1,*], M. Khemani[2]

[1] *Federal Urdu University of Arts, Science and Technology, Microbiology, Karachi, Pakistan*
[2] *University of Karachi, Biochemistry, Karachi, Pakistan*

Background: Chronic Hepatitis caused by HBV is one of the principal causative agent for incidence of hepatocellular carcinoma around the world. In this respect, HBV viral protein HBX is possibly the most probable target that reinforces the prevalence of HBV mediated HCC. In this study HBX is used to delineate the molecular pathway it follows to develop oncogenesis.

Methods & Materials: Around 500 complete genome sequences of HBV and respective HBX sequences were extracted from NCBI and UNIPROT database. They were subjected to multiple sequence alignment. Using maximum likelihood method the phylogenetic tree was reconstructed, engaging 1000 bootstrap replicates. Representative sequence from each genotype was selected to develop molecular model of HBX. By means of structural and thermodynamic refinements HBX dimers were constructed on basis of geometrical complementarity. Evidences suggests that longitudinal positioning of residues may lead to variations in the dimerization of HBX among different genotypes and subsequently their related functions. However, the dimer interaction region showed a region which could further be exploited for designing disruptor/small inhibitor. Moreover, selected sequences were predicted for post translational modifications analyses by different kinases to associate their molecular and biological functions.

Results: HBX is intrinsically disordered protein structurally, providing justification for subsequent multiple molecular and biological roles including HBV associated carcinoma. HBX contains a Zinc Finger domain, which is an unambiguous evidence of protein-nucleic acid interaction. Structural variance is observed in molecular models inferring varying role in HBV associated hcc. Conformation of dimerization and variations in the post translational modification profile strengthens this fact further. PTM analysis exhibited 14 different kinases involved in the cell cycle regulation, regulate gene expression, signal transduction, apoptosis, cell metabolism, immune response and neuron differentiation tends to alter most of the sequences of HBX pointing towards their role in carcinogenesis.

Conclusion: This study delineates the structural and functional polymorphism of HBX and provides enough evidence, suggesting HBX a plausible oncogene. HBX gene is found to be associated with development of hepatocellular carcinoma. This may also augment in understanding the molecular pathway followed by HBX in development of oncogenesis. Amplified with the further studies the present investigation may elucidate potential targets for therapeutic intervention.

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Influenza and influenza-like illnesses in risk groups: evaluation of antiviral therapy with umifenovir in hospitalized patients

V. Bulgakova[1], N. Pshenichnaya[2,*], A. Grekova[3], E. Selkova[4], N. Lvov[5], I. Leneva[6], I. Shestakova[7], V. Maleyev[8]

[1] *Children's Health Research Centre, Department of Forecasting and Planning of Scientific Research, Moscow, Russia*
[2] *Rostov State Medical University, Infectious diseases department, Rostov-on-Don, Russia*
[3] *Smolensk State Medical University, Department of Infectious diseases, Smolensk, Russia*
[4] *G.N. Gabrichevsky Moscow Research Institute of Epidemiology and Microbiology, Scientific department, Moscow, Russia*
[5] *S.M. Kirov Military Medical Academy, Infectious diseases department, Saint-Peterburg, Russia*
[6] *I.I. Mechnikov Research Institute of Vaccines and Serum, laboratory of experimental virology, Moscow, Russia*
[7] *A.I. Evdokimov Moscow State University of Medicine and Dentistry, Infectious diseases department, Moscow, Russia*
[8] *Central Research Institute of Epidemiology, Scientific Department, Moscow, Russia*

Background: Bacterial complication and prolonged course of influenza and influenza-like illnesses (ILI) are often observed among patients with risk factors for severe course of disease.

The aim of study was to evaluate the efficacy of antiviral therapy with arbidol (umifenovir) in hospitalized patients with influenza and ILI who had risk factors for severe course of disease.

Methods & Materials: 3285 medical charts of patients with influenza and ILI who treated in 2010-2015 years in 80 hospitals in Russia have been retrospectively reviewed. Laboratory confirmation of disease was available in 31.0% patients; of these, influenza viruses were found in 60.7% samples (influenza A/H1N1 - 48.8%, A/H3N2 - 16.3%, influenza A subtype–10.6%, influenza B - in 24.3%, other respiratory viruses - 39.7%).

Patients were divided into 2 groups depending on therapy. Antivirals were not administered to patients in the 1th group. 2th group of patients was treated with umifenovir from the first 24-48 hours after symptom onset. Additionally each of group was divided into 2 subgroups. Patients in subgroups 1a (n = 183) and 2a (n = 2319) had no risk factors for severe course of influenza and ILI. Patients in subgroups 1b (n = 155) and 2b (n = 628) had risk factors (children younger than 2 years old and adults over 65, pregnant women, people with chronic somatic diseases and obesity). Duration of clinical symptoms and frequency of bacterial complications were evaluated.

Results: Duration of fever and frequency of complications in patients without risk factors were significantly lower in 2a group versus 1a group: 2.86 ± 1.57 days and 3.76 ± 2.83 days, $13.1 \pm 1.3\%$ and $20.0 \pm 3.2\%$, accordingly. Duration of fever and frequency of complications in patients with risk factors were significantly lower in 2b group versus 1b group: 3.0 ± 1.48 days and 4.1 ± 2.2 days, $9.9 \pm 1.2\%$ and $42.6 \pm 3.6\%$, accordingly.

Conclusion: The efficacy of antiviral therapy was higher in patients with risk factors than in patients who are not at risk. In patients treated with umifenovir the duration of fever and frequency of complications were lower than in patients who did not receive antiviral therapy.

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UMP. 785

CCL5-dependent replication of human cytomegalovirus is inhibited by tricin in vitro

T. Murayama*, H. Sadanari, M. Takemoto, T. Daikoku

Hokuriku University, Kanazawa, Japan

Background: Human cytomegalovirus (HCMV) infection is a widespread opportunistic pathogen in immunocompromised individuals. So, HCMV infection is still associated with severe morbidity and mortality. HCMV can enhance the expression of a CC chemokines. HCMV infection is presumed to contribute to atherosclerosis, where chemokines may have a pathogenic role. Elevated levels of RANTES (CCL5) are observed in atherosclerotic plaques. HCMV and CCL5 may cooperatively contribute to atherosclerosis. Our recent study revealed that tricin (4′,5,7-trihydroxy-3′,5′- dimethoxyflavone) has anti-HCMV activity in a human embryonic lung fibroblast cells (HEL). In the present study, we revealed that HCMV-induced CCL5 expression further augments HCMV infection and that tricin exerts its anti-HCMV activity by targeting CCL5.

Methods & Materials: HEL cells were treated with tricin after HCMV infection. Total RNA was then extracted at 24 h after infection and subjected to detect *CCL5* mRNA or proteins were then extracted to detect CCL5 protein. HEL cells were infected with HCMV at 24 h after *CCL5* siRNA transfection. At 6 days after infection, supernatants were collected to determine virus titer.

Results: Tricin inhibited HCMV replication, with concomitant decreases in the levels of transcripts of the *CCL5* gene and in the accumulation of the CCL5 protein. We also found that the replication of HCMV was significantly lower in *CCL5* gene-knockdown cells.

Conclusion: These results suggested that CCL5 represents an attractive anti-cytomegalovirus target, and that tricin may be a good candidate for novel anti-HCMV agent.

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BK polyomavirus infections after hematopoietic stem cell transplant – a single center experience

A. Tanase[1,*], O. Craciun[1], L. Stefan[1], I. Constantinescu[2], L. Lipan[1], C. Orban[3], A. Colita[1]

[1] *Fundeni Clinical Institute, Bone Marrow Transplant Unit, Bucharest, Romania*
[2] *Fundeni Clinical Institute, Immunogenetics Laboratory, Bucharest, Romania*
[3] *Fundeni Clinical Institute, Bucharest, Romania*

Background: The BK virus is a member of the polyomavirus family, highly prevalent in healthy adults. When the immune system is compromised, as patients with hematopoietic stem cell and solid organ transplantation, the virus is reactivated, leading to important mortality and morbidity in these patients.

Methods & Materials: This study analyzes the incidence and outcome of BK virus infections and correlation with different symptoms in 171 adults patients receiving Hematopoietic stem cell transplantation (HSCT) and transplanted in BMT Unit, Fundeni Clinical Institute-Bucharest, Romania, between 01 2012 to 06 2017. All patients were monitorised with Nested PCR for BKV first year after allotransplant, in allogeneic cases, or if the clinical situation indicate such an infection in autologous stem cell transplants recipients.

Results: In our study 27 patients (15.8%) developed BK viremia, in which 7.4% of the patients underwent autologous transplantation. The median of BV viremia detection was 101 days (range, 7-496 days) after transplantation. Hemorrhagic cystitis (HC) was observed in 11 patients (40.8%), and urinary symptoms in 55.5% of the patients with BKV. Pancytopenia was associated in 19 patients (70.4%) patients with BK viremia, and association with CMV reactivation in 10 patients (37%). Renal impairment with creatinine level above upper limit in 2/27 patients.The platelet number had no impact on HC occurrance; the median number of platelets was 49000/mm3 for patient with HC and 59000/mm3 for patients without HC. 23 from 27 patients (85,2%) had a positive PCR viral load in first 180 days after allogeneic HSCT. Eight patients from 27 associated clinical signs of acute or chronic GVHD. Seven from eight patients with GVHD had high level of viremia (>10 × 106) and HC.

Conclusion: Although the role of the BKV reactivation is more common in allogeneic HSCT patients, its frequency is not exactly known in autologous HSCT patients. More studies are required to determine the frequency of BKV in HC with autologous HSCT. Even if BKV infection has been connected with the development of HC, this is not the only important symptom associated with BK viremia after HSCT. The most severe clinical aspects have been associated with severe immunosupresion for GVHD.

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