

samples (79.1%). The phylogram showed that the strains of one genotype divided into three subgenotypes: D1 — 1 (2.9%), D2 — 15 (44.2%) and D3 — 18 (52.9%). The genotype C was detected in 7 (16.3%) patients and four of them formed a cluster with Chinese samples that were registered in the GenBank database. Genotype A was isolated in 2 (4.6%) samples and formed a cluster with strains isolated in Poland and Belgium.

HBV genotype D comprised out of subgenotypes D1, D2, D3 and prevailed among the CHB patients living in the Nanaysky District of the Khabarovsk Territory. The second prevalent strain was genotype C. Genotype A was detected in individual cases.

7.9

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THE OCCURENCE OF HEPATITIS C MARKERS AMONG RESIDENTS OF THE KINDIA PREFECTURE OF THE REPUBLIC OF GUINEA AND THE KHANH HOA PROVINCE OF VIET NAM

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Hepatitis C virus (HCV) infection plays an important role in liver diseases. The burden of HCV infection continues to be significant in low- and middle-income countries, especially in Asia and Africa. The global elimination of HCV by 2030 is possible with the advent of effective diagnostic methods available to the majority of the population. The aim of the study was to estimate the prevalence of serological and molecular HCV markers among the apparently healthy people in Kindia region of the Republic of Guinea and Khanh Hoa region of Viet Nam.

Serum blood samples were obtained from apparently healthy adults of the Kindia prefecture (n = 248, the average age was 41.59±9.89) of Republic of Guinea and Khanh Hoa province (n = 256, the average age was 41.98±11.73) of Viet Nam. The presence of total anti-HCV and the specific antibodies to the core, NS3, NS4, NS5 HCV proteins were determined using ELISA-kits (Diagnostic Test Systems LLC, Russia). RNA HCV in the serum samples was detected by real-time PCR using the “AmpliSens HCV-FL” kit (FBIS “CRIE”, Russia). The confidence interval (95% CI) was calculated by the Wilson method.

Totally, anti-HCV was detected in 9 (3.63%; 95%, CI 1.92–6.75) of 248 adults from Kindia; in 3 (1.17%; 95%, CI 0.40–3.39) of 256 adults from Khanh Hoa. The uncertain results of the anti-HCV were obtained in 6 (2.42%; 95%, CI 1.11–5.18) of 248 residents of Kindia; one (0.39%; 95%, CI 0.07–2.18) of 256 residents of Khanh Hoa. RNA HCV was detected only in one (0.39%; 95%, CI 0.07–2.18) of 256 adults from Khanh Hoa, while RNA HCV was not detected in serum blood samples from Kindia.

The results of the occurrence of HCV markers in apparently healthy residents of both Kindia Prefecture and Khanh Hoa province do not differ from the available estimated metaanalysis data on the HCV prevalence in West Africa and South-East Asia. In order to assess the dynamics of the epidemic process, it is necessary to study HCV infection in different ethnic groups throughout the territory of both countries.

7.10

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POLYMORPHISM THE CCR2 GENE IN THE ST. PETERSBURG POPULATION

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HIV infection is one of the main socially significant diseases of the world population. Resistance/susceptibility to HIV-1 infection is different. Chemokine receptors such as *CCR2* play an important role during infection with HIV-1. The gene for the chemokine receptor *CCR2* locates in the short arm of chromosome 3. The replacement of nucleotide *G* by nucleotide *A* at position 190 in the *CCR2* gene results in the replacement of the amino acid valine by isoleucine at position 64 (*CCR2-V64I*) in the primary sequence of the protein. This replacement slows the development of AIDS in HIV-infected. In Europeans the allele frequency of *CCR2-V64I* is 8–10%, blacks — 15–17%, Mongols — 20–25%. Knowing the frequency of polymorphic allele distributions can help predict the epidemic situation in the region. The aim of the work was to study the frequency of alleles of the *CCR2* gene in St. Petersburg.

The study examined a group of 411 conditionally healthy donors aged 0 to 95 years living in St. Petersburg. Genomic DNA was isolated from biological samples using commercial kits (Interlabservice, Russia). *CCR2* genotype polymorphism was detected by pyrosequencing on the PyroMark Q24 instrument (Qiagen) using primers of our own design.

Factors “sex” and “age” had no a significant influence on the frequency of distribution of the studied alleles. The distribution of genotype frequencies in the studied population does not differ from the Hardy–Weinberg Equilibrium. Wild-type genotype (*GG*) was detected in 320 people. 6 people were carriers of the genotype *AA*, and 85 people were heterozygotes (*GA*). Frequency genotype of the *CCR2* wild-type (*GG*) was 77.9%. Heterozygotes (*GA*) were 20.7%, homozygotes *AA* were 1.4%. The frequency of allele *G* was 0.88, allele *A* was 0.12. Thus, more than 20% people of the population in St. Petersburg have a protective allele of the *CCR2* gene.

The high incidence of allele *CCR2* makes it reasonable to screen HIV-infected people and groups at risk for HIV infection. The obtained data can be used to predict the development of the AIDS epidemic in St. Petersburg.

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RECONSTRUCTION OF RECOMBINATION SITES IN GENOMES OF GENOTYPE 2 HEPATITIS C VIRUS STRAINS USING BIOINFORMATICS METHODS

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Hepatitis C virus (HCV) is an important human pathogen, causing an estimated 180 million chronic infections and annually 3–4 million new infections worldwide. Due to its genetic heterogeneity, HCV has been classified into seven major genotypes and about 80 subtypes. Although the different genotypes and subtypes share basic biological and pathogenic features they differ in clinical outcomes, response to treatment and epidemiology. HCV recombination raises many questions concerning its mechanisms and effects on the epidemiological and physiopathological features of the virus. The first natural recombinant strain of HCV was identified as recently as 2002. Since then,

there have been only a few more than a dozen reports including descriptions of HCV recombinants. However, the frequency of recombination may have been underestimated because not all known HCV recombinants are screened for in routine practice. However, the development of bioinformatics technologies allows for effective screening of genomic sequences for the presence of recombination signals.

Recombination analysis was performed with the Recombinant Detection Program (RDP) version 4.61. This tool provides statistical evidence for the breakpoint site by using six methods (RDP, Geneconv, maximum chi-square, Chimaera, SiScan and 3-seq). A recombination analysis was conducted on 237 complete genome sequences of genotype 2 HCV strains, extracted from the ViPR database. The analysis by the RDP was phylogenetically corroborated by NeighborNet method using the SplitsTree 4.14.1 program and statistically confirmed by the PhiTest method.

Using the RDP method, 116 unique recombination events with a high degree of reliability ($p < 0.01$) were found in the strains studied. The presence of recombination was confirmed by phylogenetic reconstructions. Some of these events occur in dozens of strains, including those belonging to several different subtypes, which may indicate their ancient origin. Furthermore, many strains contain more than one recombination site, and in some cases these areas can overlap. Analysis of parental strains showed that recombinations occur both within and between subtypes, and parental strains often come from different geographic regions. These results may indicate that genotype 2 hepatitis C virus strains have a higher potential for recombination variability than it was thought before.

7.12

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LOW HEPATITIS B VIRUS DNA BURDEN DOES NOT ALWAYS PROTECT FROM LIVER CANCER DEVELOPMENT

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Due to the considerable number of patients chronically infected with hepatitis B virus (HBV) worldwide (260 million), persistent infection with this agent still represents the principal etiology of the main form of primary liver cancer, hepatocellular carcinoma (HCC). Two decades ago, it has been shown in Far-Eastern countries, that the risk of HCC development increases considerably when high loads ($> 2.0E+04$ IU/mL) of circulating HBV DNA are measured in the plasma of the patients. This observation prompted the release of therapeutic guidelines recommending to treat the patients when HBV DNA exceeds $2.0E+03$ IU/mL. We recently conducted a molecular analysis on Peruvian patients with HCC infected with HBV genotype F ($n = 53$). Half of these patients were remarkably young (< 40 years) and their livers unscathed with cirrhosis. Two-third of them were carrying HBV surface antigen, while the remaining were occultly infected. Remarkably, a single patient was displaying HBV DNA loads above the threshold for mandatory treatment. In tumor and non-tumor liver tissues, HBV DNA copy number per cell was usually very low (0.1–10% of infected cells) and no clonal integration was detectable. HBV genome mutations usually observed at this stage of the liver disease (Stop pre-core, basal core promoter double mutations, pre-S deletions) were infrequent ($< 25\%$ of cases) in this series.

In tumor cells, innate immune response was inactive while most DNA repair systems were strongly activated. Our data suggest that for some populations such as American Indians, or in case of infection with specific HBV strains such as genotype F, the standard procedures of surveillance of patients at risk for HCC are ineffective. Our observations imply that the local patho-physiological context should prevail above guidelines generated from analyses conducted on populations with different geo-anthropological backgrounds. In addition, our observation is somehow reminiscent of the HCC presentation described in Yupik people from Alaska who are also infected with HBV genotype F, the endemic genotype of the Americas. It suggests that similar adverse situations might affect populations with American Indian ancestry. In that respect, research on populations living in Siberia, on the other side of Bering strait, might provide some interesting comparison points. Larger surveys should now be conducted to confirm and refine these preliminary observations.

7.13

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THE PREVALENCE OF HIV-1 DRUG RESISTANCE MUTATIONS IN PATIENTS WITH LOW ADHERENCE TO ANTIRETROVIRAL THERAPY IN THE LENINGRAD REGION

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Against the backdrop of an increase in the number of people embarking on antiretroviral therapy (ARVT), the manifestation of drug resistance of HIV is becoming an increasing obstacle to the fight against the epidemic.

Variants of the virus that have drug resistance are usually able to accumulate in the body in the event of interruptions in the intake of antiretroviral drugs. Therefore adherence to therapy is one of the most important factors in the formation of HIV resistance.

The aim of this work is to study the structure of mutations in the HIV genome associated with drug resistance in patients with low adherence.

Blood plasma samples from 269 patients were examined for the detection of mutations in drug resistance. Previously, the history of patients was studied: sex, viral load during therapy, adherence to the latter.

Among patients there are 139 (51.67%) people with low adherence to therapy. In the aggregate of patients with low adherence, men predominate (57.55%). This may be due to the peculiarity of the psyche, more typical for male patients. It is also important to note that majority of patients with low adherence belong to disadvantaged groups of people: people who use alcohol and drugs that do not have a permanent place of residence, etc. As a result of an unstable lifestyle, such patients most often interrupt therapy. This, in turn, leads to changes in ARVT regimens, which together with a high viral load (74% of patients with viral load exceeding 10 000 copies/ml) is a factor contributing to the formation of drug resistance.

One of the reasons for the drug resistance of HIV is the appearance of mutations in parts of the virus genome associated with the synthesis of viral enzymes, which are the main targets of therapy. Analysis of the results of studies on the presence of HIV drug resistance revealed several common mutations: M184V (51.08%), K103N (18.71%), L74V (12.95%), K101E (11.51%), A62V and G190S (10.79%), the remaining mutations occur in less than 10% of cases.