methods for in vitro, ex vivo and in vivo testing of immunogens, with the emphasis on HIV enzymes: reverse transcriptase/RT, protease/PR, and integrase/IN.

Materials & methods: The consensus humanized HIV enzyme genes, wild-type and with primary resistance mutations were created. Respective genes were designed, synthesized (Evrogen) and cloned into plasmids for DNA-immunization. Eukaryotic expression was confirmed by PAGE of the plasmid-transfected cells with subsequent Western blotting. Inactivation of enzymes was carried by site-mutagenesis yielding prototype DNA-immunogens. Gene immunogenicity was tested in BALB/c mice, injected with respective plasmids with subsequent electroporation employing flat or multi-needle electrodes (BEX). Immune responses were assessed by IFN-g/IL-2 Flourospot, and multiparametric FACS after stimulation of murine lymphocytes with HIV-derived peptides. Two *in vivo* challenge systems were developed, one based on co-delivery of HIV-1 and reporter genes with follow-up of reporter expression using bioluminescent imaging (Spectrum CT), and the other utilizing challenge with tumorigenic reporter-labelled murine cell lines expressing HIV antigens.

Results: Panel of HIV-1 enzyme genes were synthetised and their expression was confirmed by PAGE with Western blotting. Delivery protocols for plasmid DNA were optimized to support strong in vivo immunogen expression required for a potent immune response. Classical immunological tests demonstrated PR gene to be a potent Th1 immune; IN — a moderate mixed Th1/Th2-; and RT, a potent Th2 immunogens. Prime with their genes was sufficient to reduce the expression of the reporter gene in vivo, when the latter was introduced in a boost mixed with any of the given HIV genes. The latter phenomenon, dubbed «antigen challenge», turned to be useful for testing lytic capacity of HIV specific cellular response in rodents. In absence of straight-forward models to test the protective capacity of anti-HIV responses in small animals we suggested also a cancer-cell based model. We set such model of HIV challenge where mice received syngenic tumor cells (here of murine adenocarcinoma 4T1) expressing HIV proteins. In model experiments, expression of a foreign (reporter) protein prevented 4T1 cells from establishing tumours in immunocompetent mice pre-immunized with the reporter gene. Murine adenocarcinoma cell lines expressing nine variants of HIV proteins were already obtained, and shown to form tumors in immunocompetent mice. Models are currently used to assess of immune response against HIV enzymes can protect immunized mice against a challenge with HIV enzyme expressing 4T1 cells.

Conclusions: Promising immunogens inducing an immune response against HIV enzymes responsible for drug resistance in HIV-1 infection were obtained, and shown to be highly immunogenic in mice. In vivo challenge systems were established to assess the protective capacity of the immune response, which are of use in other immune therapy applications.

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Psychosocial aspects of comorbidity of HIV infection and dependence on psychoactive substances in pregnant women

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Russian Federation since the beginning of the XXI century is one of the first places in the world for the registration of people with HIV/AIDS and is one of the most involved in the epidemic process of European regions. Over 80% are in active reproductive age, which led to an increase in the number of pregnancies and births, including on the background of drug addiction.

The most pronounced emotional factor in a woman's life that causes change in its mental state, attitude to life, self-esteem is pregnancy. The diagnosis of HIV infection is lifelong and requires mental adaptation of personality to the new conditions of life. Psychic disadaptation in HIV-infected patients reduces the patient's motivation to treatment, which is especially important when carrying out chemo prevention of HIV transmission from mother to child during pregnancy. Related addiction may have a significant impact on the psychoemotional status of pregnant woman. Objective: to examine the psychosocial aspects of comorbidity of HIV infection and dependence on psychoactive substances during pregnancy.

Materials and methods. On the basis of specialized obstetric Department (Department № 16) City infectious diseases hospital № 30. S.P.Botkin surveyed 160 HIV-infected women in the third trimester of pregnancy: 72 women with heroin dependence (study group) and 88 women without addiction (comparison group). Age of women ranged from 17 to 34 years (mean age of 22,6±2,2 years). Used clinical-anamnestic and experimental-psychological methods, including a set of psychological techniques: the method «life style Index», test Kheima, the scale of anxiety Spielberg. Statistical analysis was performed using the statistical software package. A comparison of statistical samples and their parameters was performed using t-test and χ^2. Correlation analysis was conducted with calculation of correlation coefficients Spearman and Pearson. The critical confidence level of null statistic hypothesis is of 0,05.

The results of the study and their discussion.

All pregnant drug addicts have been infected with HIV by the parenteral route, in the comparison group in 81,8% of cases were sexual transmission and 18,2% of women could not definitely indicate the route of infection. 66,7% of drug addicts the experience of HIV is 1–5 years, and 72,7% of pregnant women without addiction the diagnosis of HIV infection was confirmed only during this pregnancy. Remission of drug dependence in the anamnesis was observed only among women married to men without drug dependence (r=0,62; p=0,036), possibly in connection with the support and positive influence from the spouse and family. 44,4% of drug-addicted HIV-infected pregnant women spontaneously refused from taking drugs during pregnancy, 11,1% — from an early time and at the time of the survey and testing the addictive behavior was not observed. For 77,8% of the drug addicts pregnancy is wanted. At the same time in the control group 18,2% of women admitted that the pregnancy became desirable only after the appearance of objective signs of pregnancy (fetal movements, ultrasounds).

Personal and psychological characteristics of drug-addicted HIV-infected pregnant women was characterized by a moderately pronounced disturbing radical (77,8%). A high measure of trait anxiety was observed in every fifth pregnant (22,2%, p<0,001). The level of trait anxiety was significantly lower in drug-addicted women who use drugs during pregnancy (r=-0,71; p=0,017). In the comparison group identified more than 59% of pregnant women with severe anxiety radical (p<0,001), however the average significant differences in comparison with drug-addicts had not. Indicator reactive (situational) anxiety in a group of drug addicts 55,6% was moderate, and in 33,3% (p<0,001) of cases was low, which was probably due to the low cognitive level assessment. These data are reliable the correlation between the index of reactive anxiety and level of education (r=-0,66; p=0,027) and can, obviously, be determined directly by the addiction. Among women from the comparison group in 30% of cases the level of situational anxiety was high (36,4%, p<0,001), but was mainly characterized by a moderate degree of severity.

The obtained data of activity of indicators of psychological defense «projection», «compensation», «negation» and «substitution» indirectly indicate the trend in drug-addicted women to extrapunitive response with removing the blame from herself. It should be noted that a number of indicators of psychological defense drug addicts have reliably correlated with patterns of drug, experience of drug addiction and drug use while in the hospital and testing: «projection» — r=0,64, p=0,031 inch; «substitution» — r=0,59, p=0,049; «overcompensation» (or «reactive formation») — r=0,86, p=0,002. In the group of pregnant women without addiction the most intense there was a mechanism of psychological protection «denying», in this group is it correlated with attitudes of spouse/sexual partner about pregnancy (r=-0,61; p=0,04) and level of education women (r=-0,61; p=0,04); and «displacement» related to the attitude of the woman to the pregnancy (r=-0,61; p=0,04). Constructive emotional coping strategy according to the type of «optimization» is more than half of surveyed drug addicts (55,6%), which is known for persons with addiction and therefore does not have the opportunity to consider this option as a constructive coping coping behavior. At a cognitive level and behavioral continues to be the most typical for drug addicted patients with non-constructive coping-strategy «ignoring» and «active avoidance» of the problem, promote further drug use.

In the comparison group on the emotional level prevails constructive coping strategy of «optimism» (63,6%), however, there are also ineffective as such «self-blame» (9,1%) and «aggressiveness» (9,1%), which is obviously connected with sexually transmitted HIV in this group. Noted in the behavioral sphere, 27,3% of surveyed «cooperation» and «treatment» give hope to the possibility of timely medical and psychological care to these patients.

Conclusions. Psychoemotional background in drug addicts are associated with derealization caused by taking drugs and the presence of a characteristic for persons with addiction behavior on the principle of «optimization», which can be considered as favorable, since focused on the possibility to avoid the problem. Tensions psychological protection shows the relevance of the process of mental adaptation. Assessment of emotional status showed a significant association with many indicators of addictive behavior, making the need for a differentiated approach to the management of HIV-infected pregnant women depending on the presence or absence of drug.

Strategies of the computer-aided design of HIV-1 reverse transcriptase inhibitors

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Millions of people are currently living with human immunodeficiency virus type 1 (HIV-1), which causes acquired immunodeficiency syndrome. Despite several protocols of the HIV/AIDS treatment currently exist, to find an effective treatment for HIV-1 infection is still a great challenge.

HIV reverse transcriptase is one of the key viral targets for HIV-1 inhibition.

Large-scale databases and scientific publications are important sources of training sets for various quantitative structure-activity relationship (QSAR) modeling approac-