will complete four assessments: 1 — the first day of detoxification; 2 — the peak of opioid withdrawal; 3 — the last day of detoxification; 4— the last day of stabilization. The assessment protocol consists of gathering structured information on patient demographic characteristics, drug abuse history, and medical history, followed by physical examination, neurocognitive assessment, mood and withdrawal severity assessment, comorbidities (viral hepatitis, syphylis) and blood sampling for biomarkers of interest. In addition, we will collect the data from the medical cards.

The specific measures of HPA dysregulation will include:

1) plasma ACTH;

2) cortisol;

3) DHEA, DHEA-sulfate.

The specific measures of SAM dysregulation will include:

1) plasma neuropeptide Y;

2) plasma epinephrine;

3) norepinephrine.

The specific measures of impaired viral regulation and potential underlying mechanisms will include:

1) HIV RNA;

2) T-cell subsets: activated CD4+ cells (HLA-DR+) and activated CD8+ cells (HLA-DR+, CD38+);

3) SCD14 (evidence of microbial translocation);

4) MCP-1 (CCL2; evidence of monocyte activation);

5) IL-6 (acute phase response & chronic inflammation indicator).

Results: Preliminary results demonstrate an HPA/SAM dysregulation during the peak of opioid withdrawal. In addition, the extent of this dysregulation correlated with level of immune impairment. HPA/SAM systems and neurocognitive functions were normalized at 4 weeks of opioid abstinence in comparison with the last day of detoxification. The primary hypothesis is dealing with immediate effect of HPA and SAM dysregulation during the 1-day period of detoxification on progress HIV viral load and worse neurocognitive performance. We will estimate the changes in measures of HPA dysregulation and SAM axis perturbation during the 1-day period and use them as predictors. This approach will help to answer on question on immediate effect of neuroendocrine dysregulation on viral regulation, immune activation and neurocognitive processes. Further analyses will investigate potential underlying mechanisms of impaired viral regulation (SCD14; MCP-1; IL-6) by linking HPA and SAM axis perturbation to immune activation measures.

Conclusion: This study will provide data about clinical and immunological dynamics during detoxification at the medical settings and after in-patient treatment. The data could inform future policy on pharmacotherapy which focused on immune therapy during detoxification.

Modified HIV-1 Env proteins in VLPs enhance induction of neutralizing antibodies

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Introduction: Broadly neutralizing antibodies can prevent HIV-1 infection via binding to envelope (Env) glycoprotein complexes on the virion surface. The HIV-1 envelope glycoprotein exhibits a number of features that help the virus to evade humoral immunity including variable loops, extensive N-linked glycosylation, and conformational flexibility. Purified Env proteins as well as virus-like particle (VLP) vaccines presenting membrane-anchored HIV-1 spikes have been explored, but none have yet demonstrated a high potential to induce neutralizing antibodies even against moderately sensitive (tier 2) strains of HIV-1

Purpose of research: To investigate the effects of specific modifications of the transmembrane spanning (TMS) and cytoplasmic tail (CT) domains on assembly and antigenic properties of HIV-1 clade C transmitted/founder (T/F) ZM53 Env glycoprotein.

Materials and Methods: To generate modified Env proteins we used plasmid pBlueSF162 containing the SF162 *env* gene (accession number EU 123924) and plasmid pcr3.1−53M21-env containing the ZM53 *env* gene (accession number AY 423984). HIV-1 *env* coding sequences were modified by replacing the TMS-CT domains with domains from the mouse mammary tumor virus (MMTV) Env glycoprotein with or without a GCN4 trimerization sequence in the cytoplasmic (CT) domain. Standard HIV VLPs (Env/Gag VLPs) were produced by coinfection of insect cells (Spodoptera frugiperda Sf9 cells) with rBVs expressing Gag and modified Env proteins for immunization studies. Female guinea pigs were obtained from Charles River Laboratory (Wilmington, MA) and immunized (four animals in each group) two times with SF162 or ZM53 pCAGGS DNA vaccines (50 μg per guinea pig) separately followed by two boosting immunizations by the intramuscular (I.M.) route with VLPs using doses containing 10 μg Env. Env-specific antibody (Ab) titers in immune sera were determined by enzyme-linked immunosorbent assay (ELISA) using recombinant ZM53 or SF162 Env gp120 proteins (5μg/ml) as coating antigens. Neutralization activity was determined using the JC53-BL indicator cell assay. The avidity index values of serum antibodies for the native viral envelope were determined by measuring the resistance of antibody-envelope glycoprotein complexes in the ConA ELISA to treatment with 1,5 M sodium thiocyanate (NaSCN).

Results: We investigated the effects on assembly and antigenic properties of specific modifications of the transmembrane spanning (TMS) and cytoplasmic tail (CT)

domains of HIV-1 Env from a transmitted/founder (T/F) ZM53 Env glycoprotein. A modified protein containing a short version of the TMS domain derived from the mouse mammary tumor virus (MMTV) Env with or without a GCN4 trimerization sequence in the CT exhibited the highest levels of incorporation into VLPs and induced the highest titers of anti-Env IgG immune responses, compared with native glycoproteins. Sera from guinea pigs immunized by VLPs with high Env content, and containing the CT trimerization sequence, had increased neutralization activity and antibody avidity. A cross-clade prime-boost regimen with clade B SF162 or clade C ZM53 Env DNA priming and boosting with VLPs containing modified ZM53 Env further enhanced these immune responses.

Findings: Virus-like particles (VLP) containing Env-trimers with modified CT domains are able to induce antibodies with broad spectrum neutralizing activity and high avidity and have the potential for developing an effective vaccine against HIV.

Examination of inflammatory markers in HIV-infected person with heavy alcohol consumption.

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Introduction. Currently, the mechanisms of internal organ impairment due to the risky alcohol consumption which lead to serious diseases, such as heart attack, are poorly understood. The purpose of this study is to investigate the impact of risky alcohol consumption among a cohort of HIV-infected patients on cellular immunity in particular, a cellular component of innate and acquired immune response. This project will allow gathering important data about effects of alcohol and HIV-infection on mechanisms of formation of chronic diseases, including atherosclerosis and as a consequence of heart attack and fatal outcomes. The planned work will help to develop new diagnostic and therapeutic approaches to solving the problem of high mortality among HIV-infected patients with alcohol abuse.

Methods. The study will enroll 150 patients with HIV infection with high-risk alcohol consumption. We plan to enroll ART naïve patients; we have the opportunity to study the effect of alcohol consumption on the innate and acquired immunity before the start of ART.

The study design calls for tests to determine the number of CD4 cells, plasma biomarkers of inflammation (IL-6, D-dimer and C-reactive protein), indicators of microbial translocation (of sCD14, 16SrDNA, LPS) and disease progression markers (CD4 counts, HIV-1 RNA, hemoglobin, platelets, eGFR, HCV Ab, HCV Ag, AST/ALT), measures of alcohol consumption (self report and PEth), and immune senescence biomarkers (CD4 and CD8 memory, naïve, CD28- and CD57 cells) and cells types involving adaptive immune function (i.e., T Helper (TH) 1,2,17 and Fox P3T regulatory cells); innate immune function (i.e., M1,M2, M3 monocyte cells) and both adaptive and innate immune function (i.e., δγ T cells and natural killer cells). The study is planned to study cellular immunity, which plays an important role in the formation of chronic diseases. Blood sampling will be performed at baseline and every 6 months for 12 months, which will examine the changes in biomarkers of innate immune system. Participants also will estimate the interview, which contains questions about the use of alcohol in the last 12 months and the number of alcohol consumed during the last 30 days, the presence of symptoms of anxiety and depression. Hypothesis. Heavy alcohol consumption will be associated with higher number of cell types involving adaptive and innate immune function. To determine the cross sectional association between heavy alcohol consumption and cells types involving adaptive immune function (i.e., T Helper (TH) 1,2,17 and Fox P3T regulatory cells); innate immune function (i.e., M1, M2, M3 monocyte cells) and both adaptive and innate immune function (i.e., δγ T-cells and natural killer cells).

The unique opportunity to measure additional immune cells in the context of this cohort will add greater understanding of the roles of the innate and adaptive immune system in HIV, alcoholism and microbial translocation which may prove useful, not only for the disease management of HIV or alcoholism, but potentially to other diseases that result from altered immune status or increased microbial translocation.

Prospects for Internet-Based HIV Prevention Programs

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According to the Federal AIDS Center, the prevalence of HIV in Russian Federation remains high, the number of people living with HIV (PLWH) grows, and the epidemic goes beyond vulnerable populations to the general population. Modern prevention technologies with proven efficacy are needed to stop the spread of the epidemic. Remote HIV prevention could be implemented using computer programs, Internet programs and Smartphone applications. Remote prevention allows involve more people with fewer expenses. The possibility of anonymous participation is especially beneficial for HIV prevention given the stigmatization associated with it. As far as we know, any publications concerning implementation and efficacy of remote HIV prevention in Russia do not exist, while in English scientific journals this research direction is actively developing.

We have implemented a review of publications, describing the processes of development and testing of