SELECTIVE MODULATION OF B-CELL MARKERS OF ACTIVATION, INHIBITION AND EXHAUSTION WITH VASOACTIVE INTESTINAL PEPTIDE (VIP) IN ASYMPTOMATIC HIV INFECTION


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Background Chronic HIV-1 infection is characterised by immune activation and exhaustion. This study investigated B-cell subset distribution and novel markers of immune activation and exhaustion in an asymptomatic untreated HIV-infected cohort, and VIP’s effect thereon. The immunomodulator, VIP, is known to limit T-cell activation. No studies to date have examined VIP’s on B-cell activation in the context of HIV infection.

Methods HIV+ patients and matched HIV- controls were recruited at Emavudleni, a voluntary HIV testing and prevention clinic in Crossroads, Cape Town. B-cells were isolated via Rosette-Sep enrichment; cultured for 18h with either LPS, or R848 alone, or with VIP, and then analysed via BD FACS Canto II. B-cell subsets were as follows: activated memory (AM), resting memory (RM: CD212+CD27+), naive (MN: CD212+CD27-), or tissue-like memory (TLM: CD210CD2710). Surface expression of markers of activation (CD126, CD86, CD38, CD284) exhaustion (CD72, CD85), CD305, CD300a, CD307d), and apoptosis signalling (CD95) were measured. These were also compared to standard markers of immune activation (CD38+CD8+ T-cells) and HIV infection (CD4 count and plasma viral load).

Results RM was decreased, while TLM was increased (p < 0.01) with HIV-infection. CD126 & CD86 expression on AM & RM decreased by 20% with VIP inhibition; while AM, RM, TLM & MN CD72 expression decreased by 65%. CD85 AM & TLM expression decreased by 45%, & CD95 expression on RM, TLM, & MN decreased by 52% with VIP inhibition (all p < 0.001).

Conclusion Our data indicated that B-cells are in a more activated state and possibly more prone to apoptosis in untreated, asymptomatic HIV, and that addition of VIP resulted in a near complete down-regulation of markers associated with activation, exhaustion, and apoptosis. VIP is a potentially valuable novel immunomodulatory agent for the limitation of B-cell activation, alleviation of exhaustion and selective modulation of apoptosis in asymptomatic HIV infection.

TIM-3 AND PD-1 ARE DIFFERENTLY EXPRESSED ON EXHAUSTED T CELLS IN HIV INFECTED PATIENTS


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Progressive loss of T cell function is an important mechanism of chronic HIV-1 infection. PD-1 has been primarily used to describe exhausted T cells. Recently Tim-3 has been identified as additional marker for dysfunctional T cells. Tim-3 positive cells have not yet been defined in detail.

In this study we investigated the expression of PD-1 and Tim-3 on T cells from HIV-1-infected individuals.

We found that in the viremic patients only a small percentage of T cells expressed Tim-3 (mean: 4.1%). In contrast, a significant amount of T cells were PD-1 positive (mean 56.8%) and PD-1 was expressed at much higher levels than Tim-3. Nevertheless we found a trend to higher numbers of Tim-3 positive cells in viremic than in aviremic HIV-infected and even lower numbers in healthy individuals. When analysing CD8 T cells regarding CD45RA expression we found a striking difference between Tim-3 and PD-1 positive T cells: Tim-3 expressing cells were found in the CD45RA positive subset (p < 0.05) whereas PD-1 expression was nearly exclusively found on the CD45RA negative subset (p < 0.5). To further characterise the Tim-3 positive subset we performed multicolour staining using antibodies to various T-cell markers including CD28 and CD57. Although CD57 expression and loss of the CD28 molecule are both associated with T-cell senescence, Tim-3 expressing cells were exclusively found in the CD57 positive subset whereas is was not restricted to CD28 negative T cells.

In contrast to the PD-1/PD-1 pathway, blocking Tim-3 did not enhance HIV-specific T cell proliferation or IFN-γ secretion.

Furthermore, whereas PD-1 positive cells have previously been shown to be increased in HIV-infected patients with discordant immune response, Tim-3 expression did not differ between patients with or without immune restoration on HAART.

Taken together our data implicate that Tim-3 defines a novel subset of terminally differentiated T cells.

HIV DRUG-RESISTANCE MUTATIONS WITHIN HIV REVERSE-TRANSCRIPTASE AMONG PATIENTS RECEIVING HAART IN KAZAKHSTAN


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Introduction Drug resistance is very serious clinical problem, it is often cause of treatment failure among HIV-positive patients on HAART. Antiretroviral therapy (ART) was started in 2005. The aim of this study is to analyse of the prevalence of drug-resistance mutations (DRMs) within reverse-transcriptase (RT) among HIV-positive on first-line ART.

Methods 205 HIV-positive patients on (AZT/3TC + NVP or EVF) with viral load more than 1500c/ml, and 37 ART-naïve were examined. HIV RNA extraction, RT-PCR and sequencing pol gene were performed. These were also compared to standard markers of immune activation (CD38+CD8+ T-cells) and HIV infection (CD4 count and plasma viral load).

Results 205 HIV-positive patients on ART were identified M184V, T215F, and K219Q mutations. Among DRMs to NNRTI G190A/S, K103N, K101E/H mutations. Among DRMs to NRTI M41L, D67N, T215Y/F mutations were registered. Among ART-naïve patients M184V, T215F, and K219Q mutations were observed.

Conclusion In Kazakhstan the HIV resistance was determined in 3.9% among HAART treated patients and mostly to 3TC, NVP and EVF. It’s necessary to increase the variety of antiretroviral drugs used in the country.

WITHDRAWN BY AUTHOR

TRICHOMONAS VAGINALIS IN A MACACA NEMESTRINA MODEL: EVALUATING AGE AND DETECTION ASSAYS


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Poster presentations
Background Trichomonas vaginalis (TV) infection is a prevalent parasitic STD that may increase the risk of acquiring other STI including HIV. Trichomoniasis has been increasingly reported in older female populations. Detection methods include the InPouch culture system and GenProbe’s APTIMA Trichomonas vaginalis nucleic acid amplification test (NAAT). Both systems detect TV (viable or genetic material, respectively) from vaginal swabs. In addition to comparing TV detection technologies, this study attempted to look at infection status in younger versus older macaque populations.

Methods 24 sexually mature female pigtailed macaques were challenged with TV (ATCC S0148, human isolate), and followed weekly for five weeks, before metronidazole treatment. The reproductive age span for pigtailed macaques is approximately 4 to 18 years of age. Twelve animals aged 4–7 and twelve animals older than 13 years were enrolled. Paired vaginal swabs were collected weekly from each animal for culture and NAAT detection assays.

Results Each TV-challenged macaque developed trichomoniasis. Of 199 matched samples (culture and NAAT), 15 had discrepant results. Six of these were likely due to false culture results. Four samples represented the transition time from positive to negative status in three animals. It is plausible that organisms detected by NAAT were no longer viable (thus culture-negative). There is no obvious explanation for the three remaining discrepant results.

Trichomoniasis infection was self-limited (resolved prior to metronidazole treatment) in eight animals: two older and six younger macaques. Two of these younger macaques experienced intermittent discrepant results after testing negative by both methods for two consecutive weeks.

Conclusions NAAT detection appears to be more sensitive and less prone to erroneous results in this laboratory’s experience. There may be a trend for younger animals to self-clear TV infection faster than older animals, which might explain the increased TV infection rates noted in older women.

**P1.044**  A CROSS-SECTIONAL STUDY COMPARING SERUM VITAMIN D LEVELS IN HUMAN IMMUNODEFICIENCY VIRUS-INFECTED AND -UNINFECTED INDIVIDUALS


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Background Since the evolution of human immunodeficiency virus (HIV) infection, every effort has been made to increase the survival and quality of life of the infected patients. In this regard, metabolic/nutritional derangements are among the most important problems. So, we planned this study to evaluate the serum level of vitamin D as an essential micronutrient with known immunologic roles in HIV-infected patients and compare it with that of HIV- uninfected individuals, and to identify risk factors for possible hypovitaminosis D in the former group.

Methods This was a cross sectional study on 35 HIV-infected patients (cases) and 35 HIV-uninfected individuals (controls). All the participants were >18 years-old. Patients with conditions, like tuberculosis, or using drugs, with known effects on serum vitamin D level were excluded. The control group was matched for age, sex, nutritional habits and occupation (exposure to sunlight). HIV infection was confirmed in the cases with 2 positive HIV ELISAs and then a positive HIV Western Blot test. Serum level of vitamin D was measured by ELISA method. Chi-square and independent T tests were used for analysis of data.

Results Of the HIV-infected patients, 9 people (25.7%) were receiving antiretroviral therapy. Twenty-three HIV-infected patient (65.7%) had hypovitaminosis D (vitamin D < 30 ng/mL), comparing with only one person (2.8%) in controls (p value < 0.05). The mean level of vitamin D in the serum was significantly lower in HIV-infected patients (25.78 ng/mL) compared with HIV-uninfected individuals (41.4 ng/mL) (p value < 0.008). There was no association between hypovitaminosis D and sex, age, body mass index, CD4+ cell count, haemoglobin level and antiretroviral therapy in HIV-infected patients.

Conclusion This study shows the possible association of HIV-infection with vitamin D deficiency, and thus the evaluation of this group of patients for hypovitaminosis D seems reasonable.