Abstracts

Infections in People Living with HIV and AIDS

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Immunophenotypic and Intracellular Cytokine Profile of Indian Patients with Human Immunodeficiency Virus-Infected and -Uninfected Patients with Tuberculosis
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Background: Tuberculosis (TB) occurs in more than 50% of HIV infected Indian patients. There is little information regarding intracellular cytokine profile of lymphocytic subsets among these individuals.

Objectives: This study was carried out to determine the immunophenotypic and intracellular cytokine profile of our patients with HIV/TB coinfection.

Methods: 15 patients with HIV/TB coinfection and 15 each with TB alone and healthy individuals were studied. Immunophenotypic analysis and intracellular cytokines were measured using appropriate antibodies on a flowcytometer.

Results: CD3 percentage did not differ significantly in the three groups. CD4:CD8 ratio was reversed among patients with TB and HIV/TB. CD19 and CD25 were present on fewer cells of healthy individuals but this was not statistically significant. Significantly higher percentage of cells of patients with TB and HIV/TB were CD69 positive. IL-10, IFN gamma and TNF alpha levels are significantly reduced in the CD4+ cells of patients with HIV/TB when compared with those with TB and healthy individuals. In CD8+ cells of patients with HIV/TB, levels of IL-10 are lower and TNF alpha higher when compared with the other two groups. IL-2 producing cells were not significantly different in any of the above subsets. Monocytes in individuals with HIV/TB had significantly higher IL-6 and TNF alpha.

Conclusions: T helper cells among patients with HIV/TB have significantly lower cytokine production. T suppressors and monocytes patients produce more TNF alpha. These findings may be significant in view of recent attempts to treat HIV/TB coinfected patients with anti-TNF therapy.

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Vascular Endothelial Cells Enhance HIV-1 Replication in CD4+ Memory T Cells and Provide their Apoptosis Resistance
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Background: We have discovered that vascular endothelial cells (ECs) can provide the HIV-replication in memory CD4+ T-lymphocytes in a Nef-dependent manner. We have also demonstrated that non-proliferating and minimally activated T-cells are the sources of HIV-1 replication in EC/T-cell culture. Moreover, productively infected T-cells in EC/T-cell culture exhibited the resistance to apoptotic cell death. Conversely, the bystander uninfected T-cells exhibited the increased apoptosis numbers even in cultures infected by derivative strain of HIV, containing the deletion of nef gene (Nef-). In contrast to EC/T-cell culture, in PHA-treated peripheral blood mononuclear cells (PBMCs) and HIV-1 permissive cell lines (CEMx174 and CEM-GFP) apoptosis occurred predominantly in HIV-infected cells and uninfected bystander T-cells exhibited the restricted possibilities to undergo apoptosis. The deletion of nef gene (Nef-) did not substantially influence on HIV-replication and apoptosis resistance of productively infected cells in PHA-treated PBMCs and cell lines. Since there is an emerging body of evidence indicating that cytokines are able to promote HIV-1 replication in T-cells with minimal effects on their phenotype, cell cycle and differentiation state, we proposed that apoptosis resistance of high viral producers in EC/T-cell culture could be due to their activation state.

Methods: To determine if bystander (cytokine-mediated) model was operative in EC/T-cell culture, we evaluated the effects of cytokines (IL-2, 6, 7, 15, TNF-alpha) on promoting resting T-cell infection of HIV-1 and apoptosis susceptibility of productively infected and bystander T-cells.

Results: We demonstrated that only IL-7 treated resting T-cells become productively infected and demonstrated the apoptosis resistance. Anti-IL-7 mAbs in EC/T-cell culture also decreased HIV-1
replication and numbers of productively infected T-cells.

**Conclusions:** Our data indicate that EC/T-cell model is relevant to specific depletion of CD4+ bystander T-lymphocytes and resistance of productively infected T-cells in HIV-infected patients. Furthermore, our data illustrate a novel mechanism for HIV-replication in vivo within the minimally activated and apoptosis-resistant memory CD4+ T-lymphocytes. Since this phenotype allows productively infected CD4+ T-cells to become resistant to antiretroviral (ARV) therapy and thereby serve as the viral reservoirs, the EC-T-cell interactions may contribute for renewed viral replication following cessation of ARV therapy.

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**Higher Cytotoxic Activity and Chemokine Secreting Natural Killer Cells in Asymptomatic HIV-2 than in HIV-1 Infected Individuals**


**Background:** Natural killer (NK) cells are the most potent effectors of natural immunity. Their ability to lyse virus infected cells and produce cytokine/chemokines without prior activation may be important in supporting adaptive immune response in HIV infection. Therefore, they may play a major role in slowing disease progression in HIV-2 infection. Uninfected control and HIV infected subjects at CD4 counts >500 cell/μl were studied to measure the frequency of NK cells secreting b-chemokine and, compare the cytolytic activity and IFN-γ secretion.

**Methods:** PBMCs were obtained from 30 HIV-1, 30 HIV-2 infected and 50 HIV uninfected control subjects. Lytic activity and IFN-γ secretion by NK cells were measured by chromium release and ELISPOT assays respectively after incubating with NK-sensitive cell line (K562). Chemokine secretion was also measured by Flow cytometry analysis of cells that produce Mip1b, Mip1a and RANTES through intracellular cytokine staining technique. Student T-test and Spearman rank correlation were used to compare activities between HIV-1 and HIV-2 in relation to the frequency of NK cells.

**Results:** Cytotoxic activity by NK cells was significantly higher in HIV-2 than in HIV-1 infections (p<0.05) but was similar to healthy controls. There was significant correlation between NK population and cytolytic activity in HIV-2 individuals (r=0.59, p=0.001). Interferon-gamma secretion in ELISPOT assay was similar in HIV-1 and HIV-2 infections. Mip1b, and RANTES secreting NK cells were also significantly higher (p<0.05) in HIV-2 than HIV-1 individuals. However, Mip1a secreting cells were similar in both infections.

**Conclusion/Recommendations:** The slow disease progression in HIV-2 individuals in early stage of infection may be influenced by effective cytolytic capacity of NK cells and also supported by potent chemokines secretion to control viral replication. Its therefore suggest that strategic immune-based therapy in enhancing these function could be very useful in controlling the disease.

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**The Impact of Treatment, Care and Support on People Living with HIV/AIDS in Mossaka Town, Republic of Congo**


**Background:** Mossaka is the 7th locality with the most HIV patients. To find out the impact of treatment, care and support on People Living with HIV/AIDS (PLWHAS) in Mossaka.

**Methods:** Research assistants randomly administered 60 questionnaires to a group of PLWHAS, clinical staff and community health workers, in Mossaka village. The period of this research was from November 2004.

**Results:** 9500 PLWHAS in Republic Of Congo are on antiretrovirals (ARV) of whom 32/545 are from Mossaka Town. Out of these, 80% developed short-lived side effects while 20% did not. ARV boosts the immunity of PLWHAS hence reducing the viral load, prolonging their lives. Here about 2000 PLWHAS access all the required care services free charge, thus improving their quality of life. Eighteen support groups have been established, which offer financial advice, care and support, through income generating activities, revolving fund, advocacy and outreach. This helps improve the living standards of PLWHAS, thus empowering them to be more productive. Finally, it was found out that in 70% of PLWHAS in other localities around Mossaka Town there was no access treatment care and support.

**Conclusion/Recommendation:** ARV has short-term side effects on some PLWHAS but boosts immunity thus reducing the viral load. PLWHAS respond positively to support groups and grow psychologically, economically and socially. More sensitization on treatment, care and support is required in Mossaka Town. Association Coeur Africain and other NGOs in collaboration with Ministry of Health have done a commendable job in treatment, care and support.