

Analysis of NK cell receptor-ligand expression in the prevention of AIDS-defining opportunistic infections in patients with low CD4+ T cell count

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Background: CD4+ T lymphocyte cell count is commonly used in the management of HIV infection. However, HIV infected individuals with low CD4+ cell counts may have dramatically different clinical evolutions, ranging from asymptomatic infection to AIDS. In this study, we investigated NK cell populations and the expression of NK cell ligands on CD4+ T cells in HIV-infected patients presenting with low CD4+ but different clinical features (AIDS versus non-AIDS).

Methods: We recruited 19 HIV-infected patients with a history of comparable CD4+ < 200/ml at presentation (11 AIDS and 8 non-AIDS at diagnosis) and 10 healthy subjects (HD). AIDS diagnosis was PCP in 9 cases and neurotoxoplasmosis in 2 patients. The mean duration of the antiretroviral treatment and CD4+ at sampling was similar in both groups. Multiparametric flow cytometry and specific mAbs were used to evaluate phenotypic and functional parameters of NK and T cells, including activating and inhibitory receptors, CD69, HLA-DR, CD107a and NK ligand expression by CD4+ (PVR, nectin-2 and MIC-A) either before or after *in vitro* activation. Statistical analysis included U-test and Spearman's test for correlation.

Results: CD4+ immune reconstitution was comparable among AIDS and non-AIDS patients. Expression of NKp46 as well as its density on CD56+ NK cells was significantly higher in non-AIDS when compared with AIDS ($p < 0.05$). A similar finding was observed also for the expression of NKp30. AIDS and non-AIDS patients had a substantial increase of CD69 expression on CD56+ NK cells ($p < 0.05$) and HLA-DR both on CD56+ NK ($p < 0.05$) and CD4+ ($p < 0.01$) T cells as compared to HD. The expression of NKp46 and CD107a positively correlated ($p < 0.05$). The expression of nectin-2 and MIC-A on *in vitro* activated CD4+ T-cells compared to receptor expression on NK cells (DNAM and NKG2D, respectively), was higher in non-AIDS patients compared to AIDS ($p < 0.05$).

Conclusion: The innate immune response of AIDS and non-AIDS patients differs despite similar CD4+ counts. NK cell activation and differences persist throughout treatment. Increased receptor-ligand expression in non-AIDS patients suggests an involvement of innate mechanisms, rather than CD4+ absolute counts alone, in preventing the occurrence of AIDS-defining opportunistic infections.