Retrovirology

Poster presentation

Antiretroviral compounds affect the granule-dependent mechanisms of lysis in CD8 T cells

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Background

Cytotoxic T-lymphocytes (CTLs) are essential for suppression of viral replication and, in particular, they have a pivotal role in control of progression of HIV infection. It has been demonstrated that HIV-specific CTL responses are defective in HIV-infected patients undergoing highly active antiretroviral therapy (HAART). In this study we investigated the effects of antiretroviral compounds on the granule-dependent mechanisms of lysis in peripheral blood mononuclear cells (PBMCs).

Materials and methods

PBMCs of 10 HCs were incubated with 3 different antiretroviral drugs combinations: combination A: AZT (NRTI) + 3TC (NRTI) + IDV (PI); combination B: d4T (NRTI) + ddI (NRTI) + NFV (PI); combination C: 3TC (NRTI) + EFV (NNRTI) + TDF (NRTI). To evaluate the CTLs function we measured: production and release of granule-dependent effector molecules (perforin, granzyme B); production and release of granule-independent effector molecules (IFN-gamma, TNF-alpha); degranulation markers (LAMP1 and LAMP2). To assest the immunomodulant effects of IL-15, PBMCs were also incubate in presence of this cytokyne.

Results

Antiretroviral compounds reduce the granzyme B and perforin production (while they don't affect the IFN-gamma and TNF-alpha production). Moreover, one of the 3 tested combinations of antiretroviral compounds (combination B) reduces the granzyme B release and affects the degranulation in CTLs. IL-15 increases the levels of granzyme B and perforin.

Conclusion

Antiretroviral compounds mainly affect the expression of genes encoding for Pfp and GranzB, and deteriorate the mechanism of degranulation in CD8+ T cells. L-15 restores both the granule-dependent and the granule-independent cytotoxic mechanisms. Basd on these data, IL-15 seems to be useful in overcoming the negative effects of antiretroviral compounds on the cytotoxic function.