HIGH EXPRESSION OF APO-1 (CD95) ON T LYMPHOCYTES FROM HUMAN IMMUNODEFICIENCY VIRUS-1–INFECTED CHILDREN

To the Editor:

Advanced stages of human immunodeficiency virus-1 (HIV-1) infection and acquired immunodeficiency syndrome (AIDS) are characterized by progressive depletion of T lymphocytes, particularly the CD4+ subset of T cells. Experimental evidence suggests that depletion of CD4+ T cells may be mediated, at least in part, by apoptosis.¹ In peripheral T cells, apoptosis may be triggered by the APO-1 (CD95) receptor, a member of the nerve growth factor/tumor necrosis factor (NGF/TNF) receptor superfamily, identical to the...
Infection in Children. In were observed polymerase chain reaction, and (3) absence of clinical symptoms for

3102 CORRESPONDENCE

...T-cell accumulation is probably caused by the inability of these mice to properly delete their peripheral T cells by T-cell receptor-induced apoptosis. In addition, agonistic anti-APO-1 antibodies induce apoptosis in activated peripheral human T cells. We previously found that APO-1 is not expressed on the majority of naïve resting T cells in cord blood and shows only low expression on resting adult T cells. Therefore, in an initial attempt to define the putative role of APO-1 in T-cell depletion by apoptosis in AIDS, we studied APO-1 expression on T cells of HIV-1+ children compared with that on T cells from age-matched uninfected controls. The cohort of HIV-1+ children was part of the German Multicenter Study on HIV-Infection in Children. In this study, children born to HIV-1 mothers were observed for a 3-year period. Children with a positive anti-HIV-1 enzyme-linked immunosorbent assay (ELISA) and Western blot beyond 18 months of age were considered to be infected. Criteria for HIV-1+ children were (1) complete seroreversion by the age of 18 months, (2) no evidence for the presence of HIV-1 in culture and polymerase chain reaction, and (3) absence of clinical symptoms and immunodeficiency.

APO-1 expression was investigated on isolated peripheral blood lymphocytes by two-color immunofluorescence using fluorescein isothiocyanate (FITC) labeled anti-APO-1 (lg G3, K) and phycoerythrin (PE)-labeled anti-CD4 or anti-CD8 (Dianova, Hamburg, Germany). We found that, although APO-1 expression was highly variable, it was significantly increased in CD4+ and CD8+ T cells from HIV-1+ children in comparison to HIV-1- controls (P < .001 for CD4 T cells and P < .001 for CD8+ T cells using the two sample Wilcoxon rank sum test; Fig 1). Thus, APO-1 expression on T cells of the CD4+ and the CD8+ subset is increased in HIV-1 infection. The mechanism of this increase may be directly related to HIV-1 infection or stimulation by HIV-1 products or may be caused by a general stimulation of T cells in this disease. It is interesting that the increase of APO-1 expression is observed in both CD4+ and CD8+ T cells from HIV-1+ children. Assuming a role of the APO-1 receptor and its ligand in apoptotic depletion of CD4+ T cells in AIDS requires, therefore, that sensitization of the APO-1 pathway is mainly directed at the CD4+ subset of T cells. Sensitization may involve stimulation of CD4 on these cells by gp120. Our data provide a first interesting potential link between APO-1-mediated apoptosis and T-cell depletion in AIDS. Therefore the contribution of APO-1-mediated apoptosis in the course of this disease warrants further detailed analysis.

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REFERENCES

4. Watanabe-Fukunaga R, Brannan CI, Copeland NG, Jenkins ...
NA, Nagata S: Lymphoproliferation disorder in mice explained by defects in Fas antigen that mediates apoptosis. Nature 356:314, 1992
Enhanced thromboxane biosynthesis in patients with Mediterranean spotted fever [letter; comment]

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