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SLE apoptosis and hyporesponsiveness to gammac-chain cytokines

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Sylvie Fournel,[Aff1]

Aff1 Universite Louis Pasteur, Strasbourg

Keywords

apoptosis, gamma-c cytokines, lupus

Context

A recent hypothesis suggests that dysregulation of apoptosis explains the development of autoimmune disease. Indeed, various authors have described an excess of apoptotic bodies in lupus patients after, for example, UV-irradiation. To explain this, two mechanisms have been proposed: (i) an increase in apoptosis, and (ii) a decrease of apoptotic-cell clearance. The dysregulation of apoptotic-cell clearance has been supported by various experiments. In contrast accelerated apoptosis of lymphocytes *in vitro* has been described but was not specific to systemic lupus erythematosus (SLE) patients. However, these experiments were performed with lymphocytes from "healthy" SLE patients, and lupus disease activity frequently increases during the course of an infection. To test the implications of infection on apoptosis dysregulation, these authors investigated apoptosis of activated lymphocytes of SLE patients suffering from an acute infection.

Significant findings

When cultured, an increased number of peripheral blood mononuclear cells (PBMC) from patients suffering from an infection were apoptotic, in comparison to PBMCs from healthy controls or from patients with other autoimmune diseases. Apoptosis levels returned to baseline at the end of infection. In comparison to activated lymphocytes from healthy controls, *in vitro* activated lymphocytes from SLE patients showed hyporesponsiveness to IL-2 and IL-7, but not to IL-4 and IL-15; however, this response is not specific for SLE patients. In contrast, apoptosis of resting lymphoblasts from SLE patients was not inhibited by addition of gammac-chain cytokines (IL-2, IL-4, IL-7 and IL-15), whereas all these cytokines inhibited apoptosis of healthy control lymphoblasts. IL-2 and IL-15 inhibited apoptosis of lymphoblasts from patients with other autoimmune diseases. This hyporesponsivness to gammac-chain

cytokines is more important if cells are derived from patients during a phase of high serological activity, or from patients with Th1 dominant cytokine profiles in their serum (e.g., high IL-12, detectable IFN-gamma).

Comments

These data demonstrate an increase in lymphoblast apoptosis in SLE patients, which suggests a correlation between two unexplained observations in SLE patients: (i) an excess of apoptotic cells, and (ii) the association of infections and SLE. Infection leads to the death of lymphoblasts, which undergo apoptosis and produce apoptotic bodies, and could be responsible for the development of autoreactive B and T cells. However, the differences observed betwen SLE patients and patients with other autoimmune diseases is not very significant, and the molecular basis of this hyporesponsiveness must be investigated to understand the defect present in SLE patients.

Methods

cell culture, measurement of apoptosis

References

1. Lorenz HM, Grunke M, Hieronymus T, Winkler S, Blank N, Rascu A, Wendler J, Geiler T, Kalden JR: Hyporesponsiveness to gammac-chain cytokines in activated lymphocytes from patients with systemic lupus erythematosus leads to accelerated apoptosis. Eur J Immunol. 2002, 32: 1253-1263.