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MORPHOLOGICAL CHANGES OF LYMPHOCYTES ACTIVATED WITH INTERLEUKIN-2

Rosanna Nano, Sergio Barni, Enrica Capelli*

*Dipartimento di Biologia Animale , Università di Pavia e Centro di Studio per l'Istochimica del CNR, Pavia; *Dipartimento di Genetica e Microbiologia, Università di Pavia, Italy*

Peripheral blood mononucleated cells (PBMC) obtained from a healthy subject were cultured as previously described[1] in the presence of recombinant IL-2 (rIL-2) (Proleukin, Eurocetus, Amsterdam), at low doses (1 IU/mL) and high doses (1000 IU/mL) for 6 days (LAK cells). Cocultures of LAK and transformed cells (Chang human cell line ATCC CL 13) were also obtained, and the samples were processed for electron microscopy and analyzed with a Zeiss TEM at 50 KV.

Lymphocytes treated with low doses of rIL-2 showed a low nuclear-cytoplasm ratio, without membrane blebs and with regular nuclear morphology. The scarce cytoplasm was characterized by the absence of lysosomes and a medium concentration of ribosomes (Figure 1a). Lymphocytes cultured in the presence of rIL-2

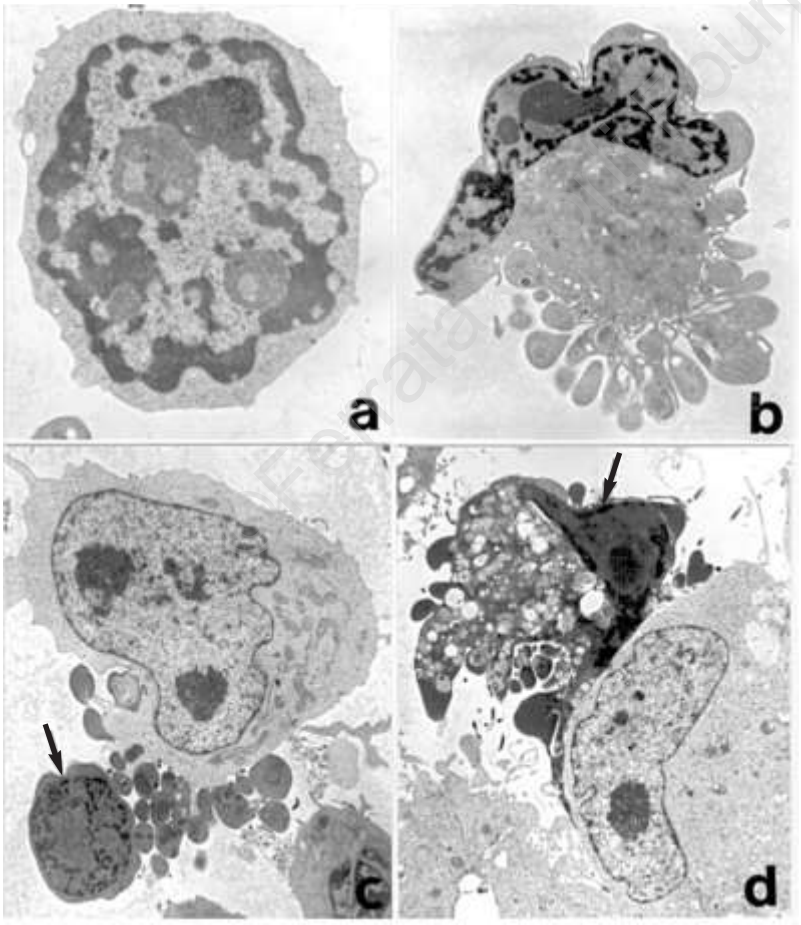

Figure 1. Ultrastructural morphological alterations observed in LAK-Chang cocultures maintained at low doses of rIL-2 (a =x7500; c= x4000) and high doses of rIL-2 (b=x6000; d= x4000).

Correspondence: Prof. Rosanna Nano, Dipartimento di Biologia Animale, Università di Pavia e Centro di Studio per l'Istochimica del CNR, Pavia, Piazza Botta 10, 27100 Pavia, Italy.

at concentrations ranging from 500 to 1000 IU/mL (high doses) showed many morphological alterations, such as membrane extroflexions (raffles and blebs) and clumping of nuclear chromatin (Figure 1b). In general LAK cells appeared hypertrophied when not interacting with transformed cells. At low doses of rIL-2, after the interaction, small round elements separate from the membrane-bound cytoplasmic fragments were observed (Figure 1c).

Analyzing LAK-Chang cocultures revealed atypical features: the nucleus was asymmetrically located at the periphery of the cell, the cytoplasm showed a high concentration of ribosomes, the absence of lysosomes and a characteristic cleavage of the cytoplasm with formation of many blebs when LAK cells were obtained with high doses of rIL-2. This phenomenon was accompanied by a dramatic vacuolization of the cytoplasm and strong degeneration of the lymphocytes (Figure 1d).

These results documented deep morphological alterations in lymphocytes cultured with high doses of the immunomodulator. The cells appear to undergo degeneration. On the contrary, a possible functional recycling of the cells after low doses of rIL-2 stimulation was hypothesized.[2] In conclusion, our findings show that high-dose interleukin-2 plays a crucial role in the morphological features of lymphocytes.

References

1. Capelli E, Nano R, Salvucci O, Bobbio Pallavicini E, Cuccia M. In: Aiuti F, Danieli G, eds. Immunologia '94, Bologna:Monduzzi, 1993; I:745-50.
2. Nano R, Barni S, Capelli E, Prosperi E, Lavezzi L, Salvucci O. DNA-protein cell content of lymphokine activated killer (LAK) and target cells in coculture. Anticancer Res 1995; 15.751-4.