PAPER I

Circulating T cells derived from patients with untreated acute myelogenous leukemia are heterogeneous and can be activated through the CD3/TCR complex

CIRCULATING T CELLS IN PATIENTS WITH UNTREATED ACUTE MYELOGENOUS LEUKEMIA ARE HETEROGENEOUS AND CAN BE ACTIVATED THROUGH THE CD3/TCR COMPLEX

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Objectives. T lymphocyte defects may contribute to the immune insufficiency seen in acute myelogenous leukemia (AML). We therefore characterized the T cell system for untreated AML patients.

Methods. T lymphocyte subsets were analyzed by flow cytometry for 45 AML patients. The *in vitro* interferon-γ (IFNγ) release in response to stimulation with anti-CD3 plus anti-CD28 in the presence of autologous AML cells was examined for 31 patients.

Results. The majority of circulating lymphocytes were $CD3^+$ T cells, and $CD19^+$ B cells usually constituted <10% of the lymphocytes. Most T cells expressed the αβ T cell receptor ($TCR\alpha\beta^+$), and only a minority of the cells was $TCR\gamma\delta^+$. Both $CD4^+$ and $CD8^+$ T cells were detected, the CD4:CD8 ratio showed a wide variation but was generally >1.0. The majority of $CD4^+$ and $CD8^+$ T cells were $CD45RA^+$ cells. The T cells could be stimulated to release IFNγ in response to anti-CD3 plus anti-CD28 ligation even in the presence of excess autologous AML blasts, and for a subset of patients (6 of 27) these IFNγ levels could be further increased by the novel protein kinase C (PKC) agonist PEP005.

Conclusions. Circulating T cells in patients with untreated AML are mainly $CD4^+$ or $CD8^+$ $TCR\alpha\beta^+$; both $CD45RA^+$ and $CD45R0^+$ can be detected, and these cells can be activated through the CD3/TCR complex even in the presence of excess AML cells. For a subset of patients T cell responsiveness can be further increased by targeting PKC and these data therefore suggest that T cell function is not inhibited in AML patients.

Key words: cytopenia – T lymphocytes – chemotherapy – cytokines – AML