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Human granulocyte colony-stimulating factor receptor expressed on T-cell malignant lymphoma cells [letter; comment]

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HUMAN GRANULOCYTE COLONY-STIMULATING FACTOR RECEPTOR EXPRESSED ON T-CELL MALIGNANT LYMPHOMA CELLS

To the Editor:

Tsuchiya et al¹ recently reported that Ph¹-positive acute lymphoblastic leukemia cells with myeloid surface markers responded to granulocyte colony-stimulating factor (G-CSF) and granulocyte-macrophage CSF. We also experienced a case of leukemic malignant lymphomatosis, in which the tumor cells in the peripheral blood possessed human G-CSF receptor. A 38-year-old man entered a hospital suffering from cervical and mediastinal lymphadenopathy with some bone marrow invasion. Histologic examinations showed malignant lymphoma of the diffuse T-lymphoblastic cell type. Despite combination chemotherapy, marked leukocytosis of 90,600/ μ L appeared thereafter. The characteristics of tumor cells that occupied 98% of the peripheral blood leukocytes were peroxidase-negative and the surface marker profile of the tumor cells was CD2, CD5, and CD7 positive and CD3, CD4, CD8, CD10, CD13, CD19, CD20, CD25, CD33, T-cell receptor (TCR) α/β , HLA-DR, and surface Ig negative, indicating immature T lymphoblasts. Unexpectedly, G-CSF receptor was detected on the surface of the tumor cells, which were more than 98% purified (Fig 1). The dissociation constant was 83 pmol/L and the number of G-CSF receptors per cell was 71. The affinity was as high as that of granulocytes and leukemic myeloblasts, but the number of G-CSF receptors was smaller than that of such cells.^{2,3} Human G-CSF receptors have previously only been shown on the surface of cells in the granulocyte lineage among haematologic malignancies.^{2,3} However, it has been reported that human G-CSF receptor transcripts were detected not only on myeloid cell lines but also on B-lymphoblastoid cell lines.³ Because we have detected G-CSF receptors on lymphoma cells, attention must now be paid when using G-CSF in the course of treatment for malignant lymphoma.

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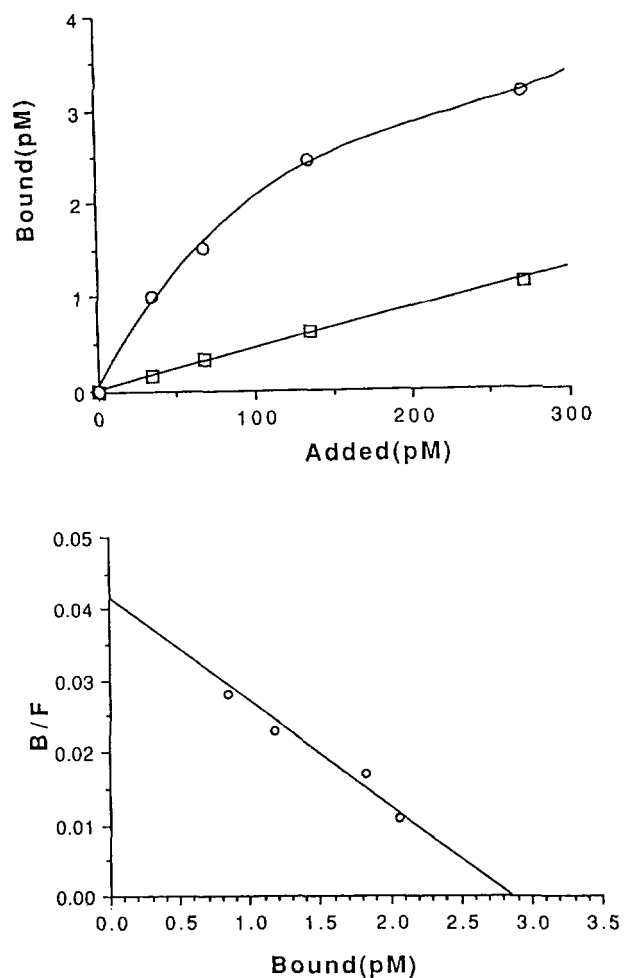


Fig 1. Binding of radiolabeled G-CSF to T-cell malignant lymphoma cells in the upper figure. Lymphoma cells (3×10^6) were incubated with ¹²⁵I-labeled G-CSF for 2 hours at 24°C.² Nonspecific binding was determined in the presence of excess unlabeled G-CSF. Total (○) and nonspecific (□) binding. Scatchard analysis of specific binding appears in the lower figure.

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RESPONSE

The case report by Kondo et al that T-cell malignant lymphoma cells expressed granulocyte colony-stimulating factor (G-CSF) receptors is another example showing that mixed-lineage leukemia/lymphoma (MLL) may have not only mixed-lineage surface markers but also mixed-lineage functions.¹ Several interesting aspects can be pointed out. First, the original diagnosis of the patient was T-cell malignant lymphoma. Kantarjian et al² described T-cell acute lymphoblastic leukemia (ALL) cases with myeloid characteristics such as CD13, CD33, and/or myeloperoxidase stain with electron microscopy. Thus, it is possible that G-CSF receptors are expressed on the blast cell surface in such patients. Second, similar to our case,¹ the dissociation constant of G-CSF receptors of blast cells of their patient was as high as that of granulocytes and leukemic myeloblasts, but the number of G-CSF receptors was smaller than that of such cells. However, we also found G-CSF receptors with a similar value of dissociation constant as that of granulocytes, leukemic myeloblasts, and MLL blasts in malignant lymphoma (morphologically diagnosed) cells from a newly diagnosed patient and the number of receptors was as high as that of normal granulocytes (manuscript in preparation). Accordingly, it

appears that the dissociation constant of G-CSF receptors of MLL blasts is similar to that of granulocytes and leukemic myeloblasts, and that blast cells from some MLL patients potentially have a smaller number of G-CSF receptors than those of granulocytes and leukemic myeloblasts, but there are exception(s). If we can extrapolate the results of Ohno et al,³ who noted the effect of G-CSF after intensive induction therapy in relapsed or refractory acute leukemia, including both lymphoid and myeloid, administration of G-CSF to patients with MLL having a smaller number of G-CSF receptors may carry little risk because, according to their report, the rate of regrowth of leukemic blasts was somewhat slower in the patients treated with G-CSF, albeit without a statistical significance.

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