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Interleukin-8 in Acute Myeloid Leukemia

To the Editor:

In their recent report, Terui et al[1] describe the apoptotic activity exerted by endothelial interleukin-8 (IL-8) on a number of leukemic cell lines and in particular on K562 myeloid cells both in vitro and in vivo, in a mouse experimental model. The report by Terui et al[1] provides fascinating insights into the complex field of biological signals involved in cross-communication between leukemic and normal bystander cells. We would like to discuss a number of points emerging from their report, particularly its claim regarding "a new therapy for hematological malignancies."

Terui et al[1] were successful in inducing apoptosis in K562 as well as in other leukemic cell lines only in a minority of the overall cell population in each individual test in vitro (~20% of K562 cells underwent apoptosis). Moreover, they used a mouse model in which subcutaneous K562 tumors were partially suppressed by locally injected endothelial IL-8. Although these effects are biologically of great interest, they appear, in our opinion, either too limited or obtained in a setting too different from the usual pattern of leukemic growth, which only rarely presents as solid tumors, for us to be able to postulate substantial advantages in terms of leukemia treatment in vivo. Actually, the target for investigating the antileukemic effect of IL-8 should be primary leukemic cells. However, it may be of interest to remark that primary leukemia blasts can spontaneously produce IL-8[2,3] and express IL-8 receptors.[2] As far as acute myeloid leukemia (AML) is concerned, relevant amounts of IL-8 are produced by the great majority of AML with monocytic components (French-American-British [FAB] M4 and M5),[3,4] which usually respond poorly to therapy in terms of long-term leukemia control. Interestingly, monocytic blasts often localize in nonhematological tissues.[3,4] This phenomenon implies the ability to cross endothelial layers without undergoing apoptotic death, thus escaping the killing mechanisms described by Terui et al.[1] Theoretically, leukemic blasts may not only produce monocytic IL-8 in vivo, but even endothelial IL-8, as HL-60 cells do,[5] or even other N-terminus variants. Blast-derived IL-8 may be at least as important as exogenous IL-8 in terms of leukemia biology. If blast-derived IL-8 were simply a competitor for exogenous endothelial IL-8, this might suggest a limited role, if any, for a therapeutic approach based on the use of endothelial IL-8 in vivo. This point needs to be better clarified.

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Association of CD10/Neutral Endopeptidase 24.11 With Membrane Microdomains Rich in Glycosylphosphatidylinositol-Anchored Proteins and Lyn Kinase

To the Editor:

Ganju et al[1] reported in *BLOOD* that the ectoenzyme CD10 (neutral endopeptidase 24.11, CALLA) expressed on the surface of lymphoid progenitors, mature granulocytes, and several nonhematopoietic cell types is associated with the protein tyrosine kinase (PTK) Lyn and with at least two other unidentified 40-kD and 75/80-kD phosphoproteins. These CD10-associated proteins (Lyn, p40, and