Leptin, the ob gene product secreted by adipocyte, decreases food intake while it increases energy expenditure and functions as an important signal for the regulation of body weight.\(^1\)\(^-\)\(^3\) The leptin receptor is an isoform of the B219 gene product, a member of the hematopoietin receptor family, which is expressed in very primitive hematopoietic cells.\(^4\) Recent studies showed that leptin plus erythropoietin acted synergistically to increase erythroid development in vitro.\(^5\)\(^,\)\(^6\) These findings led us to examine the relationship between the serum levels of leptin and hemoglobin.

We surveyed 708 male workers who were not taking any medication. Information regarding smoking habits, alcohol consumption, and physical activity was obtained by questionnaire and/or from medical records. As for the question regarding physical activity, subjects were asked to choose one from the following four answers: no exercise at all, once or twice per week, and three times or more per week. Blood was drawn in the morning after a 12-hour or longer fast. Serum leptin and insulin were determined by radio immunoassay (Linco Research Inc, St. Charles, MO) and enzyme immunoassay (Dinabot, Tokyo, Japan), respectively.

Table 1. Relationship Between Levels of Leptin and Hemoglobin in Male Workers

<table>
<thead>
<tr>
<th>Hemoglobin (g/dL)</th>
<th>n</th>
<th>148</th>
<th>422</th>
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</tr>
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<tbody>
<tr>
<td>Age (yr)</td>
<td></td>
<td>47.7 (0.5)</td>
<td>45.9 (0.3)*</td>
<td>44.6 (0.6)†</td>
</tr>
<tr>
<td>Body-mass index (kg/m²)</td>
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<td>23.2 (0.1)†</td>
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<tr>
<td>Exercise (times/mon)</td>
<td>2.8 (0.3)</td>
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<td>Cigarettes (pieces/d)</td>
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<td>Alcohol (mL/wk)</td>
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<td>Leptin (ng/mL)</td>
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Values are mean (SE). P values are versus the group with hemoglobin levels of <14.5 g/dL. Statistic analysis was performed using the general linear regression model procedures of Statistical Analysis System (SAS Institute, Cary, NC).

*P < .01.
†P < .001.
‡P < .05.

Erythropoiesis is thought to be regulated by erythropoietin, which, in adults, is produced mainly in kidneys, in response to hypoxia.\(^5\) Leptin production occurs mainly in adipocytes, but there has been no report showing that adipocytes have a sensor for hypoxia. It is interesting that bone marrow contains many adipocytes, the role of which is not clear. Although the effect of leptin on hematopoiesis may be modest, the results of our epidemiologic study, together with those of previous studies performed in vitro,\(^5\)\(^,\)\(^6\) suggest that leptin may play some role in hematopoiesis in humans. Further cross-sectional and prospective

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**Relationship Between Levels of Leptin and Hemoglobin in Japanese Men**

To the Editor:

Leptin, the ob gene product secreted by adipocyte, decreases food intake while it increases energy expenditure and functions as an important signal for the regulation of body weight.\(^1\)\(^-\)\(^3\) The leptin receptor is an isoform of the B219 gene product, a member of the hematopoietin receptor family, which is expressed in very primitive hematopoietic cells.\(^4\) Recent studies showed that leptin plus erythropoietin acted synergistically to increase erythroid development in vitro.\(^5\)\(^,\)\(^6\) These findings led us to examine the relationship between the serum levels of leptin and hemoglobin.

We surveyed 708 male workers who were not taking any medication. Information regarding smoking habits, alcohol consumption, and physical activity was obtained by questionnaire and/or from medical records. As for the question regarding physical activity, subjects were asked to choose one from the following four answers: no exercise at all, once or twice per week, and three times or more per week. Blood was drawn in the morning after a 12-hour or longer fast. Serum leptin and insulin were determined by radio immunoassay (Linco Research Inc, St. Charles, MO) and enzyme immunoassay (Dinabot, Tokyo, Japan), respectively.

When the subjects were divided into three groups according to their hemoglobin level (<14.5 g/dL [the lowest quintile], 14.5 to 15.8 g/dL, and ≥15.8 g/dL [the highest quintile]), a negative correlation was observed between the levels of leptin and those of hemoglobin, after being adjusted for age, body-mass index, and physical activity (Table 1). The negative correlation became more apparent after further adjustment for the insulin level. In contrast, when similar analysis was performed to examine the relationship between the levels of leptin and white blood cell counts, no correlation was observed between these two variables after being adjusted for related variables.

This is the first epidemiologic study showing an association between the levels of leptin and those of hemoglobin. Wilson et al\(^7\) failed to show such a correlation between leptin and red blood cell count without adjusting for leptin-related variables. The gender-dependent difference in serum leptin may be due to the difference of hemoglobin levels, adding to fat mass and sex hormones.\(^8\)

Although the effect of leptin on hematopoiesis may be modest, the results of our epidemiologic study, together with those of previous studies performed in vitro,\(^5\)\(^,\)\(^6\) suggest that leptin may play some role in hematopoiesis in humans. Further cross-sectional and prospective

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studies are needed to elucidate the relationship between leptin and hematopoiesis.

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REFERENCES


To the Editor:

In a recent article by Guenechea et al,1 they describe the engraftment of NOD/SCID mice with ex vivo-expanded CD34+ cord blood (CB) cells. In this report, they demonstrate that no changes in the long-term repopulation of NOD/SCID are produced after the transplantation of ex vivo-expanded CB cells. However, the ex vivo-expanded cells result in a delay in the engraftment of the recipients. Although the NOD/SCID model has been evaluated to evaluate long-term repopulating cells and no published data has correlated the early time of engraftment in NOD/SCID mice to the time of engraftment of neutrophils and/or platelets in patients, the investigators propose that this result has direct implications in the design of clinical protocols.

Recent data presented at the ASH meeting in Miami, by our own group2 and Stiff et al,3 demonstrated that ex vivo-expanded CB cells may be useful in transplantation of CB in adults. Compared with previously reported data3 of the use of unexpanded CB in adults, the expanded CB resulted in faster neutrophil engraftment. The culture conditions used by Guenechea et al differ from those used in the clinical studies2,3 and could result in different short-term engraftment. However, it is important to consider the use of the NOD/SCID model in evaluation of short-term engraftment. Firstly, the model was developed as a surrogate assay of human long-term engrafting cells. In clinical settings, patients achieving rapid neutrophil and platelet engraftment can become neutropenic as a result of loss of graft that could be due to the lack of long-term engrafting cells. Also, basic stem cell biology teaches that early engraftment results from committed progenitor cells and the long-term engraftment results from stem cells. This suggests that a stem cell model would not be predictive for early engraftment.

In addition, primate studies by Andrews et al4 demonstrated that rapid neutrophil engraftment with ex vivo-expanded cells was dependent on treatment with recombinant human granulocyte colony-stimulating factor (rhG-CSF) posttransplant. Patients undergoing transplant receive rhG-CSF posttransplant; so, the use of the NOD/SCID model as described is suboptimal if animals are not treated with rhG-CSF.

In summary, the conclusions presented in this manuscript are based on a mouse model that has not been shown to predict early engraftment in patients and is therefore questionable. Investigators should be cautious in using such data in the design of clinical studies until the models are shown in a rigorous manner to be predictive of clinical outcome.

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Bone Marrow Transplant Program
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Denver, CO

REFERENCES

5. Andrews GR, Bridell RA, Gough M, McNiece IK: Expansion of G-CSF mobilized CD34+ peripheral blood cells (PBC) for 10 days in G-CSF, MGDF and SCF prior to transplantation decreased post-transplant neutropenia in baboons. Blood 90:92a, 1997 (abstr, suppl 1)
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