To the Editor:

Chen and coworkers recently reported finding insulin receptors on tumor cells from the peripheral blood of patients with acute lymphocytic leukemia, acute myelocytic leukemia, acute promyelocytic leukemia, chronic myelocytic leukemia (CML), and acute monocytic leukemia, but not on cells from patients with chronic lymphocytic leukemia. Cells obtained from lymph nodes or lymphomas did not bind insulin. The authors reported dissociation constants (Kd) of about 2 nM and 900–23,000 receptors per cell, as determined by Scatchard analysis of equilibrium binding studies.1

We have recently evaluated insulin and insulin-like growth factor I (IGF-I) binding to cells obtained from the peripheral blood of a patient who had CML with large numbers of circulating megakaryoblasts.2 The cells obtained from Hypaque-Ficoll gradients were greater than 95% blasts, as determined by morphological evaluation of Wright-Giemsa-stained cytospin slides. Cell binding studies were performed as previously described,3 using an adaptation4 of Scatchard analysis to quantitate high affinity receptor parameters. The results of our studies of insulin binding to megakaryoblasts (Table 1) are similar to the data of Chen and coworkers for other types of leukemic cells.5 Our studies with IGF-I revealed greater than 15-fold more IGF-I receptors than insulin receptors on the megakaryoblast. Insulin and IGF-I binding to normal platelets were evaluated using fresh platelet concentrates prepared by differential sedimentation in our blood bank. IGF-I binding could not be demonstrated in normal platelets. Our data on normal circulating mononuclear cells obtained by Hypaque-Ficoll separation are also included in Table 1 for comparison. We related binding of IGF-I to the total mononuclear cell count, as Thorsson and Hintz have demonstrated somatomedin-C/IGF-I binds to lymphocytes as well as monocytes.6

Previous studies have demonstrated little or no insulin binding to mature human erythrocytes7 and granulocytes,8 but insulin receptors are present at higher concentrations on immature red cells9 and immature granulocytes.10 Resting lymphocytes have very few insulin receptors, but after stimulation by mitogens, insulin receptors appear on the surface of activated lymphocytes.11 These data may be extrapolated to suggest that mature or quiescent hematologic cells have low numbers of cell surface insulin receptors, but immature or stimulated cells possess considerably higher levels of insulin receptors.

Insulin receptors have been demonstrated on platelets by electron microscopic identification of colloidal gold-insulin conjugates on their surface,12 but insulin binding to megakaryocytes has not been directly evaluated. This report demonstrates the presence of these receptors on both platelets and malignant megakaryoblasts.

Our studies with this patient add another condition to the list provided by Chen and coworkers of hematologic malignancies whose circulating cells possess insulin receptors. What significance the presence of IGF-I receptors on these cells has is unclear and awaits further studies.

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REFERENCES

3. Boyum A: A one-stage procedure for isolation of granulocytes and lymphocytes from human blood. General sedimentation proper-

Table 1. High Affinity Insulin and IGF-I Binding*

<table>
<thead>
<tr>
<th></th>
<th>CML Megakaryoblasts</th>
<th>Normal Platelets</th>
<th>Normal Mononuclear Cells</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Kd</strong></td>
<td><strong>R0</strong></td>
<td><strong>Kd</strong></td>
<td><strong>R0</strong></td>
</tr>
<tr>
<td>Insulin</td>
<td>3.6 nM</td>
<td>650/cell</td>
<td>1.3 nM</td>
</tr>
<tr>
<td>IGF-I</td>
<td>7.8 nM</td>
<td>11,000/cell</td>
<td>No binding</td>
</tr>
</tbody>
</table>

*\(K_d\) equilibrium dissociation constant; \(R_0\) receptor concentration.


To the Editor:

In a recent article, Newburger et al. describe Auer bodies of fetal leukocytes as a normal phenomenon in fetal hematopoiesis. This finding seems to be in accordance with our observations on the azurophil leukocytes of some primitive vertebrates (osseous fishes). In these animals (Perciformes, i.e., Anguilla anguilla, river eel), the azurophil granules of leukocytes appear under the electron microscope as elongated bodies containing fibrillary or fine tubular structures, which are very similar to some types of Auer bodies seen in human acute myeloid or myelomonocytic leukemias. These findings, together with the observations of Newburger et al., suggest that, in the course of ontogenesis, some phases of phylogeny are recapitulated and that, in disease states, some of these developmental phenomena may reappear (“depression” of genetic information; faulty rearrangement of genes?).

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REFERENCES


ANNOUNCEMENTS

FOURTH ANNUAL LEUKEMIA-LYMPHOMA-MYELOMA CONFERENCE

Longboat Key, FL
June 1–2, 1984

The aim of this conference, organized by the American Cancer Society, Florida Division, is to provide physicians interested in hemopoietic neoplasms the opportunity of acquiring new information in this area, and of interacting with faculty members from the three Florida medical schools, as well as guest speakers from other medical centers. This year’s conference will focus on multiple myeloma and other monoclonal gammopathies, hybridomas and biomedical applications of monoclonal antibodies. Category I credit is offered. For further information, contact Henry A. Azar, M.D., Laboratory Service (113), J. A. Haley Veterans Hospital, Tampa, FL 33612. Telephone: (813) 972-2000, extension 504.

TUTORIAL ON NEOPLASTIC HEMATOPATHOLOGY

A tutorial on Neoplastic Hematopathology will be held at the Huntington Sheraton Hotel in Pasadena, CA on September 17–21, 1984. The Tutorial will be under the direction of Henry Rappaport, M.D. The registration fee (not including meals or housing) is $800.00.

Further information may be obtained by writing Mr. Claude M. Weil, Tutorial Coordinator, c/o International House, University of Chicago, 1414 E. 59th Street, Chicago, IL 60637. Telephone: (312) 753-2277.
Insulin and IGF-I binding to megakaryoblasts [letter]

CA Stuart and GB Weiss