different from that in T-cell precursor ALL (T-ALL). On the other hand, the TCR β gene rearrangements in AML show the same pattern as those in T-ALL, and occur more frequently in immature AML or in lymphoid antigen–(CD2, CD4, or CD7) positive (Ly+) AML. Because myeloid/NK cell precursor acute leukemia can be recognized as immature AML or Ly+ AML, the existence of the D62-J61 pattern of TCR β gene rearrangement in myeloid/NK cell precursor acute leukemia is consistent with reports in the literature.

We therefore maintain our conclusion that myeloid/NK cell precursor acute leukemia constitutes a distinct hematolymphoid disease entity. However, the NK cell precursor is, in a way, a T-cell precursor, because both T cells and NK cells have been shown to be derived from the same myeloid antigen–positive progenitor. Therefore, TCR β chain gene rearrangement in myeloid/NK cell precursor acute leukemia might reflect some characteristics of T-cell precursor origin. It might thus be possible for a differentiation pathway of T/NK cell and myeloid lineage to be identified as a result of investigation of the biological significance and underlying mechanism of the TCR β gene rearrangements in immature AML.

Table 1. Serological Reactivity of Selected Rh Phenotypes and WinRho SDF

<table>
<thead>
<tr>
<th>RBC Phenotype</th>
<th>Most Common Genotype</th>
<th>Antihuman Globulin Titer</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>D+ C+c+E+e+ (R1r)</td>
<td>Dc/ce</td>
<td>10,240</td>
<td>118</td>
</tr>
<tr>
<td>D+ C+c+E+e+ (R2r)</td>
<td>Dc/ce</td>
<td>10,240</td>
<td>110</td>
</tr>
<tr>
<td>D+ C+c+E+e+ (R1R)</td>
<td>Dc/ce</td>
<td>10,240</td>
<td>120</td>
</tr>
<tr>
<td>D+ C+c+E+e+ (R2R)</td>
<td>Dc/ce</td>
<td>20,480</td>
<td>123</td>
</tr>
<tr>
<td>D+ C+c+E+e+ (R1R)</td>
<td>Dc/ce</td>
<td>10,240</td>
<td>116</td>
</tr>
<tr>
<td>D+ C+c+E+e+ (R2R)</td>
<td>Dc/ce</td>
<td>10,240</td>
<td>120</td>
</tr>
<tr>
<td>Weak D</td>
<td>Dc/ce (Du 3+)</td>
<td>1,280</td>
<td>78</td>
</tr>
<tr>
<td>D+ C+c+E+e+ (R)</td>
<td>Dc/ce</td>
<td>80</td>
<td>35</td>
</tr>
<tr>
<td>D+ C+c+E+e+ (rr)</td>
<td>ce/ce</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Mean titers (reciprocal of highest dilution) and scores (graded 0 to 12), testing with two lots of WinRho SDF, each with two RBC examples.

Intravenous Anti-D Treatment for Immune Thrombocytopenic Purpura

To the Editor:

In a recent issue of BLOOD, Scaradavou et al1 reported that 72% of 261 D-positive persons with immune thrombocytopenic purpura (ITP) had positive clinical responses manifested by a mean platelet count increase of 76,000/μL after treatment with intravenous anti-D (WinRho SDF; Calgene Corp, Winnipeg/Nabi, Boca Raton, FL). Clinical responders were not distinguished from nonresponders by their gender, duration of ITP, or pretreatment platelet count. Also, approximately 62% of persons treated had a decreased hemoglobin concentration by day 7. This mild treatment-related hemolytic anemia is not unexpected, because intravenous anti-D is proposed to increase platelet counts in ITP. However, 62% of persons treated had a decreased hemoglobin concentration by day 7. This mild treatment-related hemolytic anemia is not unexpected, because intravenous anti-D is proposed to increase platelet counts in ITP.

In the absence of a clear explanation for the unpredictable variation in clinical responses and hemolysis, we postulated that WinRho may have a variable avidity for RBC Rh phenotypes, reflecting the different number of D antigen sites expressed on the RBC membrane (serological “dosage effect”). Specifically, we considered the possibility that WinRho’s formulation resulted in an anti-D product with greater avidity for RBCs whose Rh phenotypes were encoded by two D genes (eg, Dc/De/De) compared with phenotypes encoded by one D gene (eg, DC/ce/ce). To investigate this hypothesis, we performed hemagglutination titers, selecting reagent RBCs that expressed either single or double doses of the D antigen, and used dilutions of WinRho as the anti-D typing reagent. We also performed monocyte monolayer assays (MMA), sensitizing reagent RBCs with WinRho (IgG anti-D) in concentrations that would be expected to occur in recipients after a standard intravenous dose of 50 μg/kg. The MMA is often useful for predicting the likelihood that IgG-coated RBCs will be sequestered and hemolyzed by mononuclear macrophages.

The results of our direct hemagglutination tests did not show serological “dosage effect” (Table 1), nor did our MMA results reflect increased reactivity of mononuclear macrophages for RBC phenotypes encoded by two D genes (Table 2). RBCs that expressed the uncommon weak-D phenotype had decreased responses in all assays. However,
To the Editor:

In the December 15, 1997 issue of BLOOD, Miraglia et al. reported the sequence of the AC133 antigen, a novel 865 amino acid–residue surface glycoprotein found in human hematopoietic stem and progenitor cells. In the November 11, 1997 issue of Proceedings of the National Academy of Sciences of the United States of America, our group described the novel protein prominin, an 858 amino acid–residue polytopic membrane protein specific to microvilli on the apical surface of various murine embryonic and adult epithelia. We wish to bring to the attention of the readers of BLOOD that the human AC133 antigen and mouse prominin are highly related proteins that share the same 5-transmembrane topology and show an average 60% amino acid–sequence identity (Fig 1) and to discuss implications of this relationship.

First, the AC133 antigen may be the human homologue of mouse prominin. This would imply that (1) there is considerable species variation between human and murine prominin/AC133 antigen, in particular in the extracellular domains and (2) the cellular distribution of prominin/AC133 antigen is broader than assumed from the results of the two initial studies. Evidence consistent with this possibility includes the following points. Northern blot analysis using the mouse kidney prominin cDNA clone from adult mouse kidney recognizes a similar, if not identical, protein in the human NT2 cell line, which originates from the neuroepithelium, and show an average 60% amino acid–sequence identity (Fig 1) and to discuss implications of this relationship.

It will be important to determine whether a key feature of prominin, its selective targeting to plasma membrane protrusions, is also observed for the AC133 antigen in hematopoietic stem cells. If so, and on the assumption that for any given species there will be more than one prominent/AC133 antigen family within a given species includes the following examples. Northern blot analysis using the mouse kidney prominin cDNA as probe reveals the presence of similar RNAs in mouse kidney and gut, whereas immunoreactivity is detected in kidney, but not gut, using either the 13A4 monoclonal antibody or two polyclonal antibodies raised against recombinant mouse kidney prominin (D. Corbeil, unpublished data). Likewise, AC133 transcripts were detected in various human tissues whereas AC133 immunoreactivity was confined to human bone marrow. Interestingly, the Caenorhabditis elegans genome contains, in addition to the predicted protein F08B12.1 that is strikingly similar to mouse prominin and the human hematopoietic stem cell antigen AC133. Evidence consistent with the existence of multiple members of the prominin/AC133 antigen family within a given species includes the following examples. Northern blot analysis using the mouse kidney prominin cDNA as probe reveals the presence of similar RNAs in mouse kidney and gut, whereas immunoreactivity is detected in kidney, but not gut, using either the 13A4 monoclonal antibody or two polyclonal antibodies raised against recombinant mouse kidney prominin (D. Corbeil, unpublished data). Likewise, AC133 transcripts were detected in various human tissues whereas AC133 immunoreactivity was confined to human bone marrow.

Second, prominin and the AC133 antigen may be distinct members of a novel family of membrane proteins. If so, the difference between epithelial and nonepithelial members of this protein family may account for some, if not most, of the sequence variation between mouse kidney prominin and the human hematopoietic stem cell antigen AC133. Evidence consistent with the existence of multiple members of the prominin/AC133 antigen family within a given species includes the following examples. Northern blot analysis using the mouse kidney prominin cDNA as probe reveals the presence of similar RNAs in mouse kidney and gut, whereas immunoreactivity is detected in kidney, but not gut, using either the 13A4 monoclonal antibody or two polyclonal antibodies raised against recombinant mouse kidney prominin (D. Corbeil, unpublished data). Likewise, AC133 transcripts were detected in various human tissues whereas AC133 immunoreactivity was confined to human bone marrow.

REFERENCES

Table 2. Monocyte Monolayer Reactivity of RBCs Coated with Anti-D (WinRho SDF)

<table>
<thead>
<tr>
<th>Red Cell Phenotype</th>
<th>Most Common Genotype</th>
<th>Monocytes With Adherent or Phagocytosed Red Cells (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>D+C+c–E–e+ (R1)</td>
<td>DCe/DCe</td>
<td>67</td>
</tr>
<tr>
<td>D+C+c+E–e+ (R2)</td>
<td>D/c/e</td>
<td>77</td>
</tr>
<tr>
<td>Weak D</td>
<td></td>
<td></td>
</tr>
<tr>
<td>D+C+c+E–e+ (R+)</td>
<td>D/c/e</td>
<td>50</td>
</tr>
<tr>
<td>D–C–c+E–e+ (rr)</td>
<td>c/e/c/e</td>
<td>1</td>
</tr>
<tr>
<td>Normal Range</td>
<td>0-3</td>
<td></td>
</tr>
</tbody>
</table>

Testing performed in parallel using a pool of monocytes. For reactivity greater than 20%, 200 monocytes were counted; less than 20%, 600 monocytes were counted.

Because the weak-D phenotype is found in only 1 in 500 patients in our hospital, these observations do not explain the more frequent variability observed in clinical responses and hemoglobin decreases. We conclude that WinRho does not manifest dosage effect for the D antigen when tested by these conventional serological methods. An ITP patient’s Rh phenotype is unlikely to be a reliable predictor of clinical responses or hemolysis after treatment with WinRho.

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AC133 Hematopoietic Stem Cell Antigen: Human Homologue of Mouse Kidney Prominin or Distinct Member of a Novel Protein Family?

To the Editor:

In the December 15, 1997 issue of BLOOD, Miraglia et al. reported the sequence of the AC133 antigen, a novel 865 amino acid–residue surface glycoprotein found in human hematopoietic stem and progenitor cells. In the November 11, 1997 issue of Proceedings of the National Academy of Sciences of the United States of America, our group described the novel protein prominin, an 858 amino acid–residue polytopic membrane protein specific to microvilli on the apical surface of various murine embryonic and adult epithelia. We wish to bring to the attention of the readers of BLOOD that the human AC133 antigen and mouse prominin are highly related proteins that share the same 5-transmembrane topology and show an average 60% amino acid–sequence identity (Fig 1) and to discuss implications of this relationship.

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It will be important to determine whether a key feature of prominin, its selective targeting to plasma membrane protrusions, is also observed for the AC133 antigen in hematopoietic stem cells. If so, and on the assumption that for any given species there will be more than one prominent/AC133 protein, the prominin of epithelial cells could be referred to as E-prominin and the AC133 antigen perhaps as H-prominin (for hematopoietic stem cell prominin).

Even more importantly, the function of prominin/AC133 proteins...
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S. Gerald Sandler, Delores Mallory, Jeff Trimble and Sandra T. Nance

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