The range of day-1 increments varied widely, both with R-Tx (range: 10-217 × 10^9/L) and AC-Tx (range: 62-216 × 10^9/L). Unexpectedly large increments may occur with R-Tx when a proportion of the platelets is coincidentally HPA-1a/5b negative (estimated likelihood, 1 in 13 where the platelet pool is from 4 "random" donors); unexpectedly low increments may be seen with AC-Tx due to the presence in the fetal circulation of maternal HLA class I antibodies or when platelet transfusions are inappropriately administered. Babies with NAIT should therefore have their platelet counts monitored regularly whenever treatment is used and appropriate changes to treatment instigated when necessary.

In conclusion, we agree with Kiefel et al that R-Tx is an acceptable initial treatment for NAIT where HPA-1a/5b-negative platelets are not immediately available. However, our data show that HPA-1a/5b-negative platelets give larger increments, have a longer half-life, and only occasionally fail to provide therapeutically significant platelet increments. We therefore encourage blood services in other countries to establish panels of HPA-1a/5b-negative donors to provide HPA-1a/5b–negative platelets for immediate use in cases of suspected NAIT and for intrauterine or neonatal therapy of cases of known NAIT.

To the editor:

A recurrent in-frame insertion in a CEBPA transactivation domain is a polymorphism rather than a mutation that does not affect gene expression profiling–based clustering of AML

Mutations in CEBPA, the gene encoding the transcription factor CCAAT/enhancer binding protein alpha (C/EBPalpha), have been reported in multiple studies, and are found in approximately 8% of patients with acute myeloid leukemia (AML). Specific regions of the gene tend to be most commonly mutated: (1) in-frame insertions in the basic/leucine zipper (bZIP) region and (2) truncating out-of-frame insertions or deletions in the N-terminus. Although mutations are most frequently found in these 2 regions, other abnormalities have been described as well. Fröhling et al reported in 6 of 236 AML cases the existence of an in-frame insertion mutation of 6 nucleotides. This insertion is predicted to result in a histidine-proline duplication (HP196-197ins) in a transactivation domain of CEBPA cDNA (see Leroy et al for references). More recently, one other group described the HP duplication in 20 (20%) of 100 AML

References


David Allen, Salim Verjee, Sarah Rees, Michael F. Murphy, and David J. Roberts

Conflict-of-interest disclosure: The authors declare no competing financial interests.

Correspondence: David J. Roberts, National Blood Service—Oxford, Level 2 John Radcliffe Hospital, Headley Way, Headington, Oxford OX3 9BQ, United Kingdom; david.roberts@nclsls.ox.ac.uk.
samples. In this study, the insertion was reported in 7 (39%) of 19 healthy volunteers as well, questioning its role in AML. In a cohort of 285 AML cases, we previously selectively screened for the 2 major mutation types and identified 17 patients with mutations. Here, we asked whether this cohort also included cases with HP196-197ins. By means of a denaturing high-performance liquid chromatography (dHPLC) approach and subsequent nucleotide sequencing, we identified the heterozygous HP196-197ins in 9 patients (3.2% of 282 available samples). We also screened an independent second cohort of 305 AML cases, and again found 12 cases (3.9%) to present with this duplication. Finally, we analyzed a series of 274 nonleukemic blood samples and found 22 individuals (8.0%) to carry the same insertion. Cases with CEBPA mutations were found predominantly in 2 distinct gene expression clusters (Figure 1). We asked whether cases with HP196-197ins associated with specific gene expression clusters as well. The 9 specimens carrying HP196-197ins in the first cohort of 285 AML cases did not cluster with CEBPA mutant cases. Moreover, they did not belong to one single previously defined cluster of AML, but were spread out over several subgroups instead (Figure 1).

We conclude that HP196-197ins represents a common CEBPA polymorphism, rather than a mutation, that does not influence gene expression profiling–based clustering of AML specimens. Whether the higher percentage of HP196-197ins observed in nonleukemic samples compared with AML cases is due to chance, or represents an important difference, remains to be elucidated in larger series.

Bas J. Wouters, Irene Louwers, Peter J. M. Valk, Bob Löwenberg, and Ruud Delwel

This work was supported by a grant from the Dutch Cancer Society “Koningin Wilhelmina Fonds” (EMCR 2006-3322).

Conflict-of-interest disclosure: The authors declare no competing financial interests.

Correspondence: Ruud Delwel, Erasmus Medical Center, Department of Hematology, Room Ee1342, Dr. Molewaterplein 50, 3015 GE Rotterdam, The Netherlands; e-mail: h.delwel@erasmusmc.nl.

References
A recurrent in-frame insertion in a *CEBPA* transactivation domain is a polymorphism rather than a mutation that does not affect gene expression profiling–based clustering of AML

Bas J. Wouters, Irene Louwers, Peter J. M. Valk, Bob Löwenberg and Ruud Delwel