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Contribution: J.D.B. designed research and performed research, collected, analyzed, and interpreted data, and wrote the manuscript; J.T. and A.M. performed research, collected, analyzed, and interpreted data, and wrote the manuscript; B.C. analyzed and interpreted data and wrote the manuscript; D.G.B. participated in the design of the research protocol; and B.S. wrote the manuscript.

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To the editor:

Successful mobilization and engraftment of PBSCs derived from donor cord blood cells after a previous allogeneic RIC single unrelated cord blood transplantation

We describe a successful salvage treatment with intensive chemotherapy and stem cell transplantation for a relapse of Hodgkin lymphoma (HL) after single umbilical cord blood transplantation with a reduced intensity-conditioning regimen (RIC).[1,2] The originality of this observation is the source of cells for the second transplantation; the grafted cells were obtained by the mobilization in the blood of stem cells (PBSCs) originating from the cord blood unit (CBU) used for the previous transplantation.

A 24-year-old patient was diagnosed with a nodular sclerosis classic HL (stage II Bb according to the Ann Arbor classification) in May 2007. A primary refractory disease was observed after 4 courses of adriamycin, bleomycin, vinblastine, and decarbazine (ABVD); 2 courses of mitoguazone, ifosfamide, vinorelbine, and etoposide plus rituximab (MINE-R); 2 courses of high-dose cytarabine (Ara-C), cisplatin, and dexamethasone (DHAP); and cervical irradiation (supplemental Table 1, available on the *Blood* Web site; see the Supplemental Materials link at the top of the online article). In August 2008, despite the availability of autologous stem cells and because of the chemotherapy refractoriness, we performed an allogeneic transplantation with RIC and a single unrelated CBU (6/6 HLA compatibility, 2.1×10^7 nucleated cells [NC]/kg, and 0.5×10^5 $CD34^+$ cells/kg). RIC consisted of fludarabine (40 mg/m^2/d on day −6 to day −2), cyclophosphamide (50 mg/kg/d on day −6), and a total body irradiation (2 Gy on day −1). Graft-versus-host disease (GVHD) prophylaxis associating oral mycophenolate mofetil (MMF; 1 g 3 times a day) and cyclosporine A (CsA; 4.5 mg/kg twice a day) was started on day −3. After thawing and washing, the viability of cells was 55%, the patient received 0.9×10^7 NC/kg and 0.3×10^5 CD34/kg. No grade > 2 conditioning-related toxicity was observed; the patient received G-CSF from day +22 to day +25 and was discharged at day +25 after the graft. Neutrophils were > 1000/L at day +40 and platelets > 50 000/L at day +52 after transplantation. Grade IIa acute (day +29) and chronic GVHD (eyes and mouth) were treated with appropriate doses of corticosteroids. MMF was stopped at day +30 and CsA at day +240. Complete remission (CR) was confirmed at 3 and 9 months after CBU transplantation. Full donor chimerism was documented by quantitative PCR[3] on day +40 and sustained until relapse at 16 months. A relapse occurred in January 2010; the patient received 3 cycles of salvage chemotherapy (GVD) between April and July 2010 (supplemental Table 1).

Table 1. PBSC $CD34^+$ cells collection

	1st apheresis (July 2010)	2nd apheresis (August 2010)
Separator	Cobe Spectra	Cobe Spectra
Time collection, min	182	183
Volume treated, mL	9011	8001
Volume collected, mL	161	166
Circulating $CD34^+$ cells, /mm^3	44.1	28.8
Total collection, $\times 10^6$/kg	2.46 (2 bags)	1.65 (2 bags)

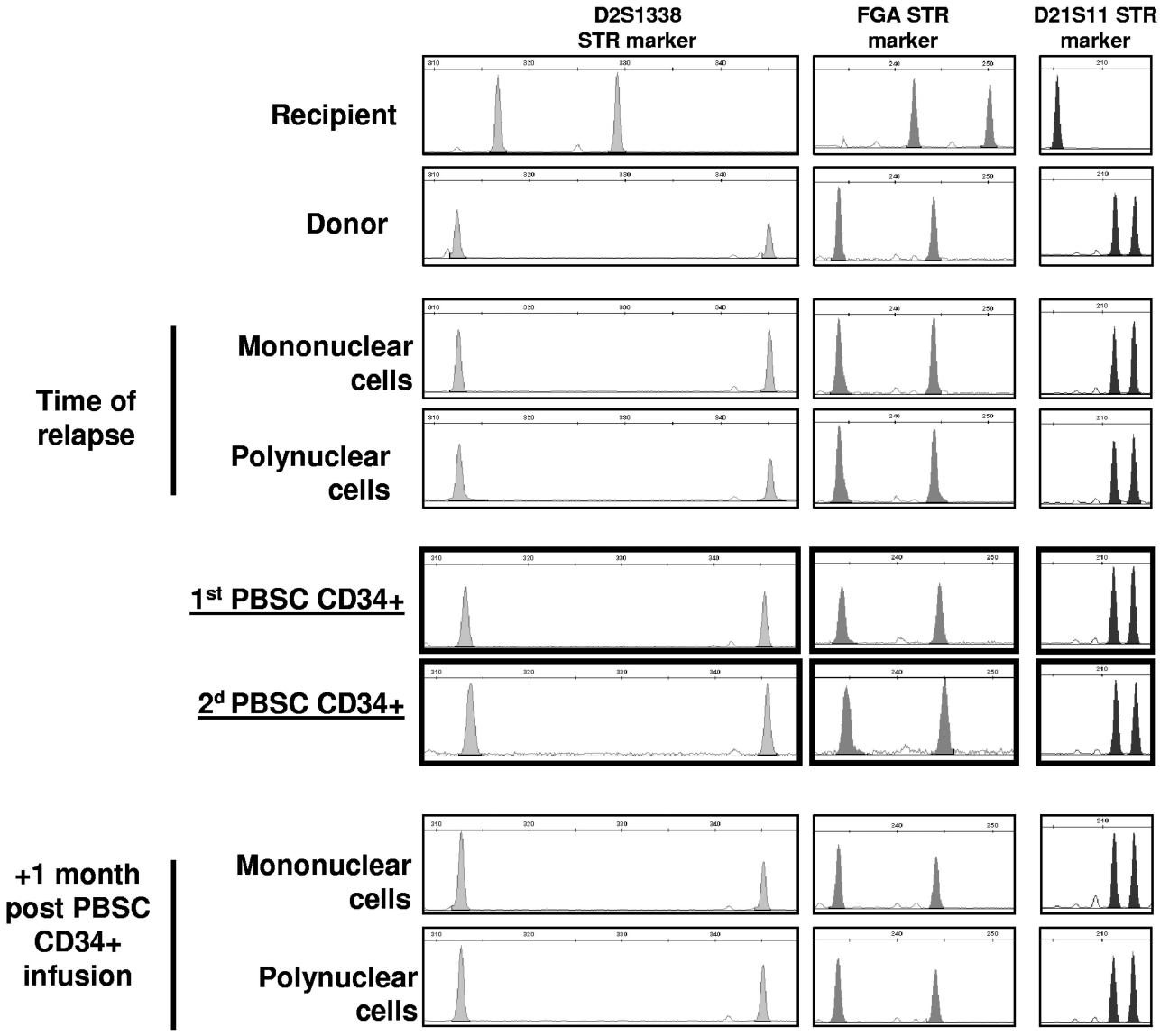

Figure 1. Chimerim analysis using STR (short tandem repeat) multiplex polymerase chain reaction. Genomic DNA, extracted from mononuclear, polynuclear, or PBSC CD34$^+$ cells, was used as a template for amplification of 16 polymorphic STR markers (AmpFlSTR Profiler Plus Kit; Applied Biosystems). Full donor chimerism was detected in all informative STR markers (9 of 16) at time of relapse (January 2010), after salvage chemothery in both PBSC CD34$^+$ collections (July and August 2010) and 1 month after PBSC infusion (October 2010). Three representative STR markers (D2S1338, FGA, and D21S11) were depicted.

PBSC CD34$^+$ cells were stimulated with G-CSF (10 μg/kg/d for 5 days) after the second and third salvage cycles in July and August 2010 (Table 1). Apheresis collected 4.11×10^6 CD34$^+$ cells/kg; these cells originated from the previous transplanted CBU as shown by PCR analyses in blood and on the collected product (Figure 1). A second SCT, conditioned with carmustine, cytarabine, etoposide, and melphalan (BEAM), was performed in September 2010 with the injection of 2.79×10^6 CD34$^+$/kg (viability of 92%). The patient experienced transient grade 4 mucositis without any documented infection and rapidly recovered from aplasia with G-CSF support started on day +7; neutrophils were > 1G/L at day +11 and platelets > 50 G/L at day + 42 after the second transplantation. A sustained second CR has been maintained up to now and chimerism evaluations showed 100% derived-CBU cells at 1, 3, and 7 months.

This is the first report showing that, although CBUs contain 10 times fewer progenitor cells than bone marrow, CD34$^+$ cell mobilization is feasible after CBU transplantation, allowing short- and long-term hematologic repopulation to occur by mobilized PBSCs issued from the original transplanted CBU.[4]

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To the editor:

Selection of unrelated cord blood grafts

We are concerned about statements in the article by Barker et al,[1] who describe a factor of 0.75 × TNC (total nucleated cell) to "correct" the TNC content of RBC-replete cord blood units. No data are provided to justify such an opinion, and the authors cite only "personal communication with multiple US investigators, 2004-2009."(p2334) Implementation of this policy, if incorrect, would underestimate the progenitor cell content of RBC-replete units resulting in the inappropriate rejection of some such units by transplant physicians in favor of RBC-reduced units with an apparently higher TNC dose after application of the "correction factor" for RBC-replete units. This would jeopardize the success of hematopoietic cord blood transplants because it is well known that their success is highly dependent on cell dose.[2,3] The authors attempt to justify their opinion by pointing out that RBC-replete units have a 25% higher TNC than RBC-reduced units, and they imply that the number of hematopoietic progenitor cells is erroneously elevated by that percentage. It is true that the TNC of RBC-replete units is elevated, in part because of the lack of neutrophil depletion. However, the authors ignore the fact that essentially no progenitor cells are lost in plasma depletion-reduction processing (plasma depletion/reduction or PDR) because during processing only a portion of the plasma is removed. In contrast, all processing methods that produce RBC-reduced units lose significant numbers of progenitor cells.[4-7]

To study this issue, we divided 10 cord blood units in half and processed one-half by RBC reduction using the most commonly used hetastarch method and the other half by plasma reduction. As indicated in Table 1, the average TNC of plasma-reduced units after processing was 124% of that in RBC-reduced units (81.56×10^7 vs 65.77×10^7, respectively [$P = .002$; 2-sample t test]). Of major importance is that plasma reduction caused virtually no loss of $CD34^+$ cells, whereas there was a 16% loss of $CD34^+$ cells in the RBC-reduced units, so that the postprocessing $CD34^+$ cell count in plasma-reduced units was 121% of that in RBC-reduced units (1.415×10^6 vs 1.165×10^6, respectively, [$P = .003$]). The recoveries of colony-forming units (CFU) were also higher for plasma-reduced products: 225% for CFU-GM ($P = .05$) and 186% for total CFU ($P = .01$). This indicates that the higher TNC value of RBC-replete units does not exaggerate the number of progenitor cells available and that a "correction factor" is inappropriate. The cell dose that is ultimately infused can be affected by washing cord blood units[1,6,7] and this may be of significance for the subset of transplant centers that wash plasma-reduced products but do not wash RBC-depleted products.

Because there are no data to support the use of the authors' proposed 0.75 "correction factor," and our data indicate that the authors' assertion that such correction should be applied to the TNC of RBC-replete units is incorrect, we submit that the authors' important and potentially detrimental statement should not be accepted by the transplantation community at this time.

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