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# Impact of Haplotype Matching on the Results of Adult Single-Cord Blood Transplantation

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## Abstract

It remains unclear whether the HLA haplotype of unconnected cord blood (UCB) should be matched to that of the case in single UCB transplantation. Therefore, using data from a Japanese registry, we anatomized the effect of haplotype matching on issues. Cases with hematologic conditions aged 16 times or aged who had experienced their first transplant were included (N = 1347). The goods of haplotype matching and high- frequence HLA haplotype on issues were anatomized. Median patient age was 55 times. The accretive frequentness of neutrophil engraftment among groups with 0, 1, and 2 HLA haplotype matches were 79, 82, and 88, independently( P = .008). In a multivariate analysis, the group with 0 haplotype matches was hardly associated with worse neutrophil engraftment (P = .087) and significantly associated with platelet engraftment (P = .044) compared with the group with 1 haplotype match. Two-haplotype matches were associated with a advanced threat of relapse. In the group with 1 haplotype match, the top 3 participated haplotypes were HLA haplotype matching might be considered to ameliorate engraftment. Two- haplotype matches should be avoided if the relapse threat is high. The haplotype itself may have an effect on the threat of acute graft- versus- host complaint and relapse.

**Keywords:** Cord blood transplantation; HLA haplotype; Neutrophil engraftment; Graft- versus- host complaint

## Introduction

Unconnected cord blood (UCB) has been established as an indispensable source of hematopoietic stem cells for adult and pediatric allogeneic hematopoietic cell transplant. One of the advantages of UCB transplantation (UCBT) is the less strict demand for HLA matching compared with that in bone gist or supplemental blood stem cell transplant under standard graft- versus- host complaint (GVHD) prophylaxis, which makes it easier to find seeker UCB units. Another advantage of UCBT is lower frequentness of acute and habitual GVHD despite multiple HLA mismatches and better responses to corticosteroid treatment for acute GVHD compared with supplemental blood stem cell transplant. This compensates for the threat of early transplant mortality and provides a favourable quality of life as well as long- term overall survival after UCBT [1].

On the other hand, the disadvantages of UCBT include pitfalls of graft failure and contagious complications associated with delayed neutrophil engraftment in the early period after UCBT. The median time for neutrophil engraftment was reportedly 21 days and the engraftment rate 80 to 90, which are important slower and lower, independently, than those in supplemental blood stem cell transplant. This is why croakers occasionally vacillate to choose UCB units as stem cell sources. To increase the probability of engraftment, UCB units with advanced total nucleated cell (TNC) count and CD34 cell count and smaller HLA mismatches between the UCB units and cases are generally named. Bettered exertion rules and GVHD prophylaxis and the use of double UCB units in cases for whom it's delicate to find a single UCB unit that contains sufficient TNCs have significantly dropped early transplant mortality. The avoidance of UCB units against which the philanthropist has antidonor HLA antibodies is also pivotal to reduce the threat of graft failure [2].

Although these changes have bettered the prevalence of engraftment after UCBT over the times, the results are still not satisfactory. To achieve better engraftment, a question is whether the HLA haplotypes of UCB units and cases should be matched, which has not yet been examined. Using data from a Japanese registry, we anatomized the goods of haplotype matching and the haplotype itself on issues after singleUCBT.In. In conclusion, the present study revealed that in addition to HLA allele matching and CD34 cell counts, HLA haplotype matching may impact engraftment. Double mismatches at some loci might also impact issues. Further, haplotypes themselves may be associated with better transplant issues. These points should be considered when opting applicable UCB units [3].

## Materials and Method

### Data Collection

Transplant data were attained from the Transplant Registry Unified Management Program. We included 3659 cases progressed 16 times or aged with hematologic conditions who entered a first allogeneic stem cell transplant using a single UCB unit between 2004 and 2015 and for whom philanthropist and patron HLA- A,- B,- C, and- DRB1 allele information was available. We barred cases who demanded data on survival status (n = 3).

The study was approved by the data operation panels of Transplant Registry Unified Management Program and by the institutional review board of Kyoto University, where this study was organized. The study was conducted in agreement with the protestation of Helsinki [4].

### Haplotype Estimation and Categorization

Haplotypes of HLA- A,- B,- C, and- DRB1 loci were estimated using a maximum probability algorithm( Supplementary Figure 1).

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Eight possible haplotype combinations were determined grounded on the results of HLA- A,- B,- C, and- DRB1 genotyping in each case. The chances of the 8 haplotype combinations were calculated using haplotype frequence data from a family study in a Japanese population. The haplotype combination with the loftiest probability among the 8 combinations was used as the prognosticated haplotype of the case. Only haplotypes that were determined to have a liability rate of 80 for both benefactors and donors were included. This estimation was validated in factual patron and philanthropist dyads whose haplotypes were destined grounded on family HLAs and 95 of patron and philanthropist dyads were rightly linked by our haplotype estimation. Haplotypes of 1443 benefactors and philanthropist dyads were determined.

Because further than 4 allele mismatches was associated with grades III to IV acute GVHD, advanced nonrelapse mortality, and lower overall survival and, most importantly, because the presence of further than 4 allele mismatches meant that no haplotype matched in these groups, we barred 96 cases with further than 4 allele mismatches from the analysis. Eventually, 1347 cases were included in the analysis [5].

We divided these cases into 3 groups according to the number of matching haplotypes. In the 2- haplotype match group (n = 82), both haplotypes of benefactors and donors were matched. In the 1-haplotype match group (n = 985), 1 haplotype was participated. The 0- haplotype match group didn't partake any haplotype (n = 280). The 0- haplotype match group was further divided into 2 groups with and without double mismatches at any locus of HLA- A,- B,- C, and-DRB1( 0- haplotype match with double mismatch versus 0- haplotype match without double mismatch) [6].

### Endpoints and Delineations

The primary endpoint of the study was the impact of haplotype matching on neutrophil and platelet engraftment. Other assessed endpoints included the impact on overall survival, relapse, nonrelapse mortality, and acute and habitual GVHD. Neutrophil recovery was defined as an absolute neutrophil count exceeding 500/ μL for 3 successive days after UCBT. Platelet recovery was defined as an absolute platelet count exceeding, 000/ μL without a platelet transfusion. Physicians who performed the transplants at each center diagnosed and graded acute and habitual GVHD grounded on traditional criteria. The intensity of the exertion authority was classified as myeloablative or reduced intensity grounded on criteria outlined by the Center for International Blood and Marrow Transplant Research and information from a questionnaire, as preliminarily described. We defined acute myeloid leukemia and acute lymphocytic leukemia in complete absolution, myelodysplastic pattern with refractory anemia or refractory anemia with ringed sideroblasts, habitual myelogenous leukemia in the habitual and accelerated phase, adult T cell leukemia in complete absolution, other leukemia in complete absolution, carcinoma in complete absolution/ partial absolution, and non-malignant complaint as standard- threat conditions and other conditions as high-threat conditions [7, 8].

## Discussion

In the present study, haplotype matching between benefactors and donors was hardly associated with better neutrophil engraftment and significantly associated with better platelet engraftment. Particularly, 0- haplotype matches with double mismatches at any locus showed the worst neutrophil engraftment. In addition to HLA allele matching and CD34 cell counts; haplotype matching and presence of double mismatches should be considered in UCB selection to achieve better engraftment. To our knowledge, this is the first study to estimate the impact of haplotype matching in single UCBT [9].

HLA allele matching was shown to affect overall mortality and neutrophil engraftment in both the present and former studies. Because further than 4 allele mismatches at HLA- A, - B, - C, and-DRB1 loci avert the possibility of haplotype sharing, these cases were barred from the analysis. Indeed among groups with 1 to 4 allele mismatches, haplotype matching showed better neutrophil and platelet engraftment. There are 2 possible underpinning mechanisms for better engraftment with participated haplotypes avoiding double mismatches at the same locus by matching 1 haplotype and/ or the effect of common haplotypes that render genes single- nucleotide polymorphisms that reduce the threat of graft failure. First, to estimate the impact of double mismatches at the same locus on issues, we divided the group with 0-haplotype matches into 2 groups according to the presence of double mismatches. This bracket revealed that among the 0- haplotype match group, the presence of a double mismatch at any locus may have had a mild impact on neutrophil and platelet engraftment [10].

In conclusion, the present study revealed that in addition to HLA allele matching and CD34 cell counts, HLA haplotype matching may impact engraftment. Double mismatches at some loci might also impact issues. Further, haplotypes themselves may be associated with better transplant issues. These points should be considered when opting applicable UCB units.

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### Conflict of Interest

None

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