

# National Marrow Donor Program HLA-Matching Guidelines for Unrelated Marrow Transplants

Carolyn Katovich Hurley,<sup>1</sup> Lee Ann Baxter Lowe,<sup>2</sup> Brent Logan,<sup>3</sup> Chatchada Karanes,<sup>4</sup> Claudio Anasetti,<sup>5</sup> Daniel Weisdorf,<sup>4,6</sup> Dennis L. Confer<sup>4</sup>

<sup>1</sup>Department of Oncology, Georgetown University, Washington, DC; <sup>2</sup>Department of Surgery, University of California, San Francisco, California; <sup>3</sup>IBMTR/ABMTR Statistical Center, Medical College of Wisconsin, Milwaukee, Wisconsin; <sup>4</sup>National Marrow Donor Program, Minneapolis, Minnesota; <sup>5</sup>Fred Hutchinson Cancer Research Center, Seattle, Washington; <sup>6</sup>Blood and Marrow Transplant Program, University of Minnesota, Minneapolis, Minnesota

Correspondence and reprint requests: Dennis Confer, MD, National Marrow Donor Program, 3001 Broadway St. N.E., Minneapolis, MN 55413 (e-mail: dconfer@nmdp.org).

Received August 21, 2003; accepted August 25, 2003

## INTRODUCTION

This commentary, sponsored by the National Marrow Donor Program (NMDP), provides guidelines for unrelated hematopoietic cell donor selection in the format of frequently asked questions. The purpose of this document is to review the current relevant data and provide guidelines that we believe represent optimal donor-recipient matching.

## QUESTION AND ANSWER

### What Is the Purpose of the NMDP Donor-Recipient Matching Criteria?

Since its inception in 1987, the NMDP has required evaluation of donor-recipient matching at HLA-A, -B, and -DR. The minimum acceptable match was originally defined by serologic splits at these 6 loci and required at least 5 matches, ie, a 5 of 6 match. Although the required level of resolution has evolved over the years and HLA-DR is now evaluated at the DRB1 allele level, the basic minimum requirement for a 5 of 6 match has not changed. This is because there are abundant data to show that HLA matching at this minimum level can lead to successful transplantation outcomes. However, it is also clear that transplantation outcomes can be improved by matching strategies that increase the degree of HLA compatibility above the minimum (eg, matching for HLA-C).

### What Literature Discusses the Effect of HLA on Marrow Transplantation Outcome?

There are many studies that evaluate the role of HLA matching in outcome. We have chosen to focus

on large, contemporary studies from 3 groups that have evaluated most of the HLA loci by using DNA testing to resolve alleles.

1. Japanese Marrow Donor Program [1]: the study by Morishima et al. is a follow-up to an earlier study by Sasazuki et al. [2] in 1998.
2. Fred Hutchinson Cancer Research Center: this includes a series of studies by Petersdorf et al. [3-5].
3. NMDP: an abstract on this study by Flomenberg et al. was presented in 2001 [6], and a manuscript is in preparation.

### Of the Several Outcome Measures, Which Is the Most Important to Consider?

This commentary is focused primarily on the effect of HLA matching on survival. The effect of specific HLA mismatches on specific outcomes such as graft failure and the incidence of acute and chronic graft-versus-host disease (GVHD) should not be the primary determinant of donor selection but, instead, should be used to assign a specific risk-adapted treatment strategy to the recipient.

### What Do the 3 Studies Suggest Regarding the Association between HLA Matching and Patient Survival?

Associations between HLA disparity and survival differ in the studies as shown in Table 1.

### Why Do Studies Give Different Results?

Potential differences in the 3 studies are numerous and are summarized in Table 2. Sample sizes limited how the mismatches were classified across the multi-

**Table 1.** HLA Locus: Effect of Mismatching on Survival

Study	A	B	C	DRB1
JMDP	Decrease*	Decrease	No effect	No effect (merged DR + DQ)
FHCRC	Decrease (merged class I)			Decrease (merged DR + DQ)
NMDP	Decrease	Decrease	Decrease	Decrease

JMDP indicates Japanese Marrow Donor Program; FHCRC, Fred Hutchinson Cancer Research Center.

\*Decrease in survival caused by an HLA locus mismatch; “no effect” means no effect of a mismatch.

ple loci, and different studies collapsed the loci differently. Morishima et al. [1] collapsed mismatches on A and B together and on DR and DQ together to get a larger sample size for detecting differences among groups. Petersdorf et al. [3] collapsed mismatches on the basis of class I versus class II loci. Flomenberg et al. [6] looked at each locus separately. Neither Flomenberg et al. nor Petersdorf et al. [3] detected significant locus-specific differences in survival, whereas Morishima et al. identified the combined A/B group as having a stronger effect on survival than the other loci. However, because this combined A/B group included single allelic mismatches for A or B, as well as mismatches for both A and B, the observed effect may have been magnified by these multiple mismatches. Both Petersdorf et al. and Flomenberg et al. found trends indicating that survival worsened with increasing numbers of allelic mismatches. Another concern is the generalizability of the Japanese study to other races and ethnicities. The distribution of alleles in the US and Japanese populations was quite differ-

ent, with little overlap in the alleles and mismatches represented in the 2 populations. In addition, the frequencies of GVHD reported in the matched cases in the Japanese study were notably lower than those reported by the Seattle group [7]. There may be other immunologic factors that vary among ethnic or racial groups and influence the relationship between HLA matching and transplantation outcomes.

Only Flomenberg et al. [6] investigated the associations between allele-level and serologic-level mismatches with survival. They found that only serologic-level mismatches at HLA-A, -B, -C, and -DRB1 had a separate statistically significant effect on survival ( $P < .01$ ), although trends ( $.01 < P < .05$ ) were noted for an effect of allele mismatches at HLA-A and -DR on survival. To further assess the effect of allele-level matching, they pooled allele-level mismatches across loci to improve sample size among patients with donors who were matched at the antigen level for HLA-A, -B, and -DRB1 (often called “6-antigen matched”). A single allele level mismatch at HLA-A, -B, -C or -DRB1 was associated with an 8-12% reduction in survival at 5 years.

**What Does the NMDP Suggest as Optimal Match Criteria?**

The reports listed previously suggest that it is advantageous to match at the allele level for HLA-A, -B, -C, and -DRB1. Thus, when possible, donors who are allele level-matched at these 4 HLA loci are recommended. This does not imply that availability of only HLA partially matched donors is a contraindication to transplantation.

**Table 2.** Similarities and Differences in Design of the 3 Studies

Variable	JMDP-Morishima	FHCRC-Petersdorf	NMDP-Flomenberg
Source of transplants	Multicenter	Single center	Multicenter
Stem cell source	Marrow	Marrow	Marrow
Patient diseases	AML, ALL, CML, MDS, SAA, others	CML	CML, AML, ALL, MDS, SAA, others
Median patient age, y (range)	23 (0-51)	36 (1-55) (2001 study)	30 (0-66)
Patient race	Japanese	Predominantly white from the United States	Predominantly white from the United States
No. of pairs evaluated	1298	300 (1998), 548 (2001)	1874
HLA loci characterized (groups of loci that were collapsed for analysis are shown in brackets)	[A, B] [C] [DRB1, DQB1]	[A, B, C] [DRB1, DQB1, DPB1]	[A] [B] [C] [DRB1] [DQA1, DQB1] [DPA1 DPB1]
Match criteria for patients entered into study	Serologic A-, B-, DR-matched only	Serologic matching at A, B, and DR with Dw or DRB1 allele matching; mismatching allowed within guidelines described in 1998 study	Matching at serologic A and B and serologic or allele level at DRB1; 5 of 6 minimum match
Level of match investigated	Allele level	Allele level	Allele level and serologic level for A, B, C, and DRB1; any level for DQ and DP

AML indicates acute myeloid leukemia; ALL, acute lymphocytic leukemia; CML, chronic myeloid leukemia; MDS, myelodysplastic syndrome; SAA, severe aplastic anemia.

**Table 3.** Typing of Patient HLA Loci

HLA Locus	Search Strategy	Matching
<b>A</b>	<b>Yes</b>	<b>Recommended</b>
<b>B</b>	<b>Yes</b>	<b>Recommended</b>
<b>C</b>	<b>Yes</b>	<b>Recommended</b>
<b>DRA</b>	<b>No</b>	<b>No</b>
<b>DRB1</b>	<b>Yes</b>	<b>Recommended</b>
<b>DRB3, DRB4, DRB5</b>	<b>Yes (DRB1 association)*</b>	<b>Unknown†</b>
<b>DQA1</b>	<b>No</b>	<b>No</b>
<b>DQB1</b>	<b>Yes (DRB1 association)*</b>	<b>Uncertain†</b>
<b>DPA1</b>	<b>No</b>	<b>No</b>
<b>DPB1</b>	<b>No</b>	<b>Uncertain</b>

\*Certain alleles at one locus are preferentially associated with some but not other alleles at a second locus. Knowledge of the patient's HLA-DRB3/4/5 or DQB1 assignment can predict which donors also typed for these loci are most likely to carry specific DRB1 alleles. For example, a donor might be typed as DRB1\*1301 or DRB1\*1302. Both of these alleles are common. Each allele has a specific association with DRB3: DRB\*1301 is usually associated with DRB3\*0101 or DRB3\*0202 and rarely with DRB3\*0301. In contrast, DRB\*1302 is usually associated with DRB3\*0301 and rarely with DRB3\*0101 or DRB3\*0202.

†Unknown indicates that the effect of matching has not been evaluated; uncertain indicates that studies disagree as to the importance of these loci in matching.

Other non-HLA factors are often considered when donors are selected, including cytomegalovirus (CMV)-negative serology (for patients with CMV-negative serology), male sex, younger age, ABO compatibility, larger body weight, and matched race. The NMDP found that, besides donor HLA matching, younger donor age was associated with better survival. There was no significant association of donor CMV serology for CMV-negative patients, sex, parity, race, or ABO matching and survival. Female donors with multiple pregnancies were associated with a higher risk of chronic GVHD, but there was no effect on survival [8].

For patients who have multiple highly matched suitable donors, there might be additional benefit from matching HLA-DQB1, -DPB1, and -DRB3/4/5. However, the association between HLA-DQ and -DP mismatching and mortality remains unproven, and the association of HLA-DRB3/4/5 mismatching and survival has not been studied. There are no convincing data to show that deliberate HLA mismatching may be beneficial to achieve graft-versus-leukemia effects.

### How and at What Resolution Should My Patient Be HLA-Typed?

DNA-based testing methods should be used to identify the patient's HLA alleles at the time a search is initiated. Some loci should be characterized because they are important in matching; others assist in designing an efficient search strategy for the patient (Table 3).

HLA typing of members of the patient's immediate family (candidate donor siblings, parents, and children) is necessary to identify a potential related donor, to confirm patient HLA assignments, and to define patient haplotypes—that is, to define which alleles are localized on each chromosome. Haplotype identification is important in developing search strategies because this information is used to predict the probability of finding allele-matched donors. Family typing is particularly helpful if the patient seems to be homozygous at a locus or carries rare alleles.

It is important to initially type the patient as well as possible, because this provides an optimal foundation for the entire search process. Although allele-level typing may require more time than lower-resolution testing, it ultimately speeds better donor selection, allows evaluation of the difficulty of the search, enables better matching leading to fewer transplantation complications, and, in case a complete match is not available, allows the process to proceed more rapidly to the search for a partially matched donor.

### How Do I Search for the Best Donor?

A local or NMDP histocompatibility expert should be contacted for assistance in generating a search strategy and in selecting potential donors from the NMDP search report for higher-resolution HLA testing. This complex subject cannot be covered in detail here. In general, the patient's HLA assignments (including haplotype assignments) are used to predict the probability of finding a matched donor. Knowledge of types that are difficult to accurately assign can be used to identify patient antigens that may be incorrectly typed in the donor pool. Once a search report is generated, knowledge of the associations between HLA alleles (eg, B-C allele associations), frequencies of HLA alleles in each racial or ethnic group, and correlations among the HLA types obtained by different testing methods are used to predict which donors and how many donors must be HLA-typed at higher resolution.

The optimal number of potential donors to select from the search report should be customized for each patient, because many factors influence the likelihood of finding a donor. Factors to be considered include the patient's alleles, haplotypes, and clinical urgency. For patients with highly conserved haplotypes, further typing of a small number (3-5) of donors is usually sufficient. More than 1 donor should be selected because donors may be unavailable, mistyped, or not matched at an allele level. For patients with rare alleles and haplotypes,  $\geq 10$  donors may be required to find the best match. In a clinically urgent search, multiple donors should be simultaneously evaluated.

**Table 4.** Typing of Potential Donor HLA Loci

HLA Locus	Matching	Resolution of Testing
<b>A</b>	<b>Recommended</b>	<b>Allele level</b>
<b>B</b>	<b>Recommended</b>	<b>Allele level</b>
<b>C</b>	<b>Recommended</b>	<b>Allele level</b>
<b>DRA</b>	<b>No</b>	
<b>DRB1</b>	<b>Recommended</b>	<b>Allele level</b>
<b>DRB3, DRB4, DRB5</b>	<b>Unknown*</b>	
<b>DQA1</b>	<b>No</b>	
<b>DQB1</b>	<b>Uncertain*</b>	
<b>DPA1</b>	<b>No</b>	
<b>DPB1</b>	<b>Uncertain</b>	

\**Unknown* indicates that the effect of matching has not been evaluated; *uncertain* indicates that studies disagree as to the importance of these loci in matching.

### How Should Potentially Matched Donors Be HLA-Typed?

Donors selected from the NMDP search report as potential matches should have higher-resolution testing to select the best HLA match. DNA-based testing methods should be used to identify the donor's HLA alleles (Table 4). Some loci should be characterized because they are key to matching; others (labeled unknown or uncertain) should be typed to allow selection of the best match once other donor characteristics have been taken into account. An HLA expert might recommend a strategy that initially targets selected loci for higher-resolution typing to reduce the typing cost; however, this approach should be considered of the recipient's medical condition so as not to unduly delay an urgent transplantation.

### Does the Race or Ethnicity of the Donor Need to Be the Same as the Race or Ethnicity of the Recipient?

HLA alleles and haplotypes are distributed at different frequencies in different racial or ethnic groups. When searching for a donor, for some alleles, an allele-level match is more likely to be found among persons of a particular ethnicity. For alleles and haplotypes found frequently in several races or ethnicities, donors from these populations should be evaluated. Once allele matches are identified, the race or ethnicity of the matched donor should have no effect on the outcome of the transplantation. When donor/recipient pairs serologically matched at HLA-A, -B, and -DRB1 by using DNA-based typing were compared, there was no advantage to being matched by race [8]. It should be recognized that the number of racially mismatched donor/recipient pairs in this study was small, and further studies are needed to confirm these data.

### How Long Do I Search for Donors?

For patients with common haplotypes, a suitably matched donor can usually be identified within 4 to 6 weeks. It may take much longer to identify a donor for less common HLA types. For patients with uncommon types, we recommend that help be requested from a local or NMDP HLA consultant to find the best match.

If an acceptably matched donor cannot be identified within the current NMDP registry, it is very unlikely that newly recruited donors will match the patient in a useful time frame. The NMDP donor file contains 5 million donors (approximately 70% typed for HLA-A, -B, and -DR), and each NMDP search also evaluates an additional 3.5 million donors listed in Bone Marrow Donors Worldwide, so patients who do not find a match in this pool must have infrequent haplotypes. The NMDP adds 20 000 to 25 000 donors to the file monthly. The likelihood that a recipient's type will be represented in those new recruits when it did not appear in the initial file of 5 million is exceedingly low. Therefore, it is recommended that alternative treatment options be re-evaluated for those patients and a decision made as to whether to reduce the matching requirements or select another therapy (eg, unrelated cord blood transplantation, a partially matched related donor transplantation, or nontransplant therapy).

### How Do I Select the Best Partially Matched Unrelated Donor?

If there are no donors who are HLA-A, -B, -C, and -DRB1 matched at the allele level, NMDP data suggest that a single allele-level mismatch (eg, A\*0201 donor and A\*0205 recipient) is preferable to an antigen-level mismatch (eg, A\*0201 donor and A\*1101 recipient). For patients with donors who are matched at the antigen level (ie, a 6-antigen match), Flomenberg et al. [6] reported that a single allele-level mismatch is associated with an 8% to 12% reduction in survival at 5 years. This reduction in survival may be acceptable given the survival rates for alternative treatments.

On the basis of the NMDP data, an allele-level mismatch is preferable to an antigen-level mismatch, but there are as yet no data to distinguish the survival effect of a single-antigen mismatch from that of 2 allele-level mismatches. Data from the Fred Hutchinson Cancer Research Center and NMDP studies suggest that risks accompanying multiple mismatches may be cumulative or even synergistic. If an antigen-mismatched donor is to be used, any antigen mismatch can be selected unless the patient is sensitized to specific HLA antigens, as indicated by a positive crossmatch test [9,10]. In a further analysis of NMDP data, HLA mismatching within a serologic cross-reactive group was not associated with a survival benefit

in comparison to mismatches outside a cross-reactive group. An abstract on this study by Wade et al. [11] has been presented, and a manuscript has been accepted for publication [12].

Beyond these general guidelines, there are not yet convincing data to rank the relative importance for matching for a particular HLA locus (HLA-A, -B, -C, or -DRB1) or for predicting permissible mismatches. It is important to emphasize that within a particular level of mismatch (ie, allele level or antigen level), HLA-DRB1 matching is not more or less important than matching for the HLA-A, -B, and -C loci.

More complex search strategies are required to identify donors with specific mismatches for patients who do not have matched donors. These strategies are needed to limit the number of allele mismatches at other loci. For these searches, we recommend that help be requested from a local or NMDP HLA consultant to find the best mismatch.

Lack of a well-matched donor (HLA matched or a single HLA-A, -B, -C, or -DRB1 mismatch) is not a contraindication to transplantation. In this situation, the physician should consider the success rate associated with the use of a mismatched donor versus the use of other available treatment alternatives (using HLA-mismatched related donors, unrelated umbilical cord blood donors, and nontransplant therapies). In summary, HLA matching at HLA-A, -B, -C, and -DRB1 is best, and allele-level mismatching is preferred to antigen mismatching. More specific details regarding matching remain controversial.

#### **When Should I Launch an International Search for a Donor?**

Every NMDP search will include a general search of Bone Marrow Donors Worldwide as well as an automatic detailed search of certain international registries. Using the Bone Marrow Donors Worldwide report as a guide, searches of other registries may be initiated on filing a specific request to NMDP. Because HLA alleles and haplotypes are distributed at different frequencies in different racial or ethnic groups, the usefulness of international searches will depend on the patient's alleles and haplotypes.

#### **How Should the Clinical Status of My Patient Influence the Selection of the Donor?**

The clinical status of the patient will influence the length of time it is feasible to search for a donor and the degree of mismatch that is considered acceptable. Patients with a relatively stable disease, such as newly diagnosed chronic myelogenous leukemia in a stable phase or low-risk myelodysplasia, are less likely to deteriorate quickly. A search time of 4 months to identify a donor contributes a small clinical risk. In contrast, patients with acute leukemia may have only a

brief remission time in which transplantation is feasible. A prolonged search time exposes patients to additional toxic chemotherapy, an increased risk of infection, and risk of relapse. In these patients, a short search and ongoing consideration of alternatives (autologous transplantation, cord blood transplantation, investigational therapy, and so on) is preferred.

The risk from underlying disease and the availability of therapeutic alternatives also influence the degree of mismatch considered acceptable by the physician and patient. Besides considering differences in life expectancy, the quality of life associated with transplantation from the best available unrelated donor should be compared with the quality of life associated with alternative therapies.

#### **Does the Reduced Intensity of the Conditioning Protocol Influence the Level of HLA Match That I Select?**

There are currently no data to indicate that greater degrees of mismatch are less tolerable in the setting of a reduced-intensity transplantation regimen. The risk of using a mismatched donor must be weighed against the other therapeutic options available to the patient.

#### **What HLA Matching Is Required for Stem Cell Sources Other Than Marrow?**

The data summarized previously involve bone marrow as a stem cell source. At this time, there are no large studies of alternative stem cell sources that have used allele-level HLA typing.

One alternative stem cell source for cases without a suitable donor is the use of umbilical cord blood. Initial reports of umbilical cord blood transplantations have shown that cell dose is the most important determinant of survival. In addition, HLA matching does influence outcome, with better survival in better-matched recipients [13,14]. The precise influence of HLA mismatching on cord blood transplantation results remains to be defined.

The data currently available regarding the role of HLA mismatch in transplantation outcome are generated from series using bone marrow as a stem cell source. Additional analyses of transplantations using peripheral blood stem cells as a stem cell source are needed to determine whether the same principles apply.

#### **If the Patient Has a Mismatched Donor, Should I Use T-Cell Depletion?**

T-cell depletion (TCD) reduces the incidence and severity of acute GVHD, and increasing donor mismatch increases risk of GVHD. Despite this, analysis of the NMDP dataset does not indicate a survival advantage for TCD, whether a graft is matched or mismatched. A prospective randomized trial of TCD

did not show improved survival associated with the use of TCD in either matched or mismatched unrelated donor transplants [15].

### Should We Be Considering Other Loci in Addition to HLA for Donor Selection?

At this point in time, there are insufficient data to advocate matching of loci other than HLA.

### Should Targets of Natural Killer Cell Alloreactivity Be Considered?

There are currently no data to indicate that unrelated donors with mismatches at HLA class I should be preferred in any clinical circumstance. A recent report indicated a strong antileukemic effect and survival advantage with haploidentical related donor transplants with particular HLA class I mismatches that generate donor killer cell reactivity directed toward patient tissues [16]. This association was observed only for recipients with acute myeloid leukemia. Application of a similar mismatching algorithm to 2 small, unrelated donor transplant series has generated conflicting data [17,18]. In one series by Giebel et al. [17], in which pretransplantation antithymocyte globulin was used to achieve TCD in vivo and patients received relatively high cell doses, HLA-B or -C mismatching for a killer cell immunoglobulin-like receptors (KIR) binding epitope was associated with better survival. In contrast, the Davies et al. study [18] showed no advantage for KIR ligand incompatibility (ie, deliberate but selected mismatches of HLA-B and -C) for survival. The negative result of the study by Davies et al. may reflect the fact that only a minority of cases in this study received T cell-depleted stem cells, and, even in the depleted cases, a relatively high number of T cells were included in the graft. A study to assess the role of KIR alloreactivity in the large NMDP unrelated donor transplant population is in progress.

### Where Can I Find Additional Information?

NMDP web sites include <http://www.marrows.org/> and <http://www.nmdpresearch.org/>.

### ACKNOWLEDGMENTS

We thank Dr. Stella Davies for helpful and thought-provoking discussions.

### REFERENCES

- Morishima Y, Sasazuki T, Inoki H, et al. The clinical significance of human leukocyte antigen (HLA) allele compatibility in patients receiving a marrow transplant from serologically HLA-A, HLA-B, and HLA-DR matched unrelated donors. *Blood*. 2002;99:4200-4206.
- Sasazuki T, Juji T, Morishima Y, et al. Effect of matching of class I HLA alleles on clinical outcome after transplantation of hematopoietic stem cells from an unrelated donor. *N Engl J Med*. 1998;339:1177-1185.
- Petersdorf EW, Gooley TA, Anasetti C, et al. Optimizing outcome after unrelated marrow transplantation by comprehensive matching of HLA class I and II alleles in the donor and recipient. *Blood*. 1998;92:3515-3520.
- Petersdorf EW, Gooley T, Malkki M, et al. The biological significance of HLA-DP gene variation in haematopoietic cell transplantation. *Br J Haematol*. 2001;112:988-994.
- Petersdorf EW, Hansen JA, Martin PJ, et al. Major-histocompatibility-complex class I alleles and antigens in hematopoietic-cell transplantation. *N Engl J Med*. 2001;345:1794-1800.
- Flomenberg N, Baxter-Lowe LA, Confer DL, et al. Impact of HLA-class I and class II high resolution matching on outcomes of unrelated donor BMT. *Blood*. 2001;98:813a (abstr.).
- Hansen JA, Yamamoto K, Petersdorf E, Sasazuki T. The role of HLA matching in hematopoietic cell transplantation. *Rev Immunogenet*. 1999;1:359-373.
- Kollman C, Howe CW, Anasetti C, et al. Donor characteristics as risk factors in recipients after transplantation of bone marrow from unrelated donors: the effect of donor age. *Blood*. 2001;98:2043-2051.
- Anasetti C, Amos D, Beatty PG, et al. Effect of HLA compatibility on engraftment of bone marrow transplants in patients with leukemia or lymphoma. *N Engl J Med*. 1989;320:197-204.
- Ottinger HD, Rebmann V, Pfeiffer KA, et al. Positive serum crossmatch as predictor for graft failure in HLA-mismatched allogeneic blood stem cell transplantation. *Transplantation*. 2002;73:1280-1285.
- Wade JA, Takemoto SK, Thompson J, et al. No deleterious effect of HLA-mismatching outside cross reactive groups (CREG) compared to within CREG mismatches following unrelated donor bone marrow transplant. *Biol Blood Marrow Transplant*. 2001;7:96.
- Wade JA, Hurley CK, Takemoto SK, et al. HLA mismatching within or outside of cross reactive groups (CREG) is associated with similar outcomes after unrelated donor bone marrow transplant. *Blood*. In press.
- Wagner JE, Barker JN, DeFor T, et al. Transplantation of unrelated donor umbilical cord blood in 102 patients with malignant and nonmalignant diseases: influence of CD34 cell dose and HLA disparity on treatment-related mortality and survival. *Blood*. 2002;100:1611-1618.
- Rubinstein P, Carrier C, Scaradavou A, et al. Outcomes among 562 recipients of placental-blood transplants from unrelated donors. *N Engl J Med*. 1998;339:1565-1577.
- Wagner JE, Thompson JS, Carter S, Jensen L, Kernan NA. Impact of graft-versus-host disease (GVHD) prophylaxis on 3-year disease-free survival (DFS): results of a multi-center, randomized phase II-III trial comparing T cell depletion/cyclosporine (TCD) and methotrexate/cyclosporine (M/C) in 410 recipients of unrelated donor bone marrow (BM). *Blood*. 2002;100:75a.
- Ruggeri L, Capanni M, Urgan E, et al. Effectiveness of donor natural killer cell alloreactivity in mismatched hematopoietic transplants. *Science*. 2002;295:2097-2100.
- Giebel S, Locatelli FW, Lamparelli T, et al. Survival advantage with KIR ligand incompatibility in hematopoietic stem cell transplantation from unrelated donors. *Blood*. 2003;102:814-819.
- Davies SM, Ruggeri L, DeFor T, et al. Evaluation of KIR ligand incompatibility in mismatched unrelated donor hematopoietic transplants. *Blood*. 2002;100:3825-3827.