Letter to the Editor

Bone marrow transplant donor recruitment strategies to maximize, optimize, and equalize recipient chances of an acceptable match

Dear Editor,

The number of named alleles of the human leukocyte antigen (HLA) genes, HLA-A, HLA-B and DRB1 are 3399, 4242 and 1883, respectively. Owing to analyses of the frequencies and distributions of these alleles worldwide, 246 HLA-A alleles, 367 HLA-B alleles and 226 HLA-DRB1 alleles are now common or well documented. As the first step in finding a bone marrow match for a new patient, an algorithm scans the entire registry every day and displays possible donors that match the recipient’s genotype. Then, new and complementary HLA typings are requested for loci DQB1 and C and allelic level for Class II, and if the donor is in good health, a confirmatory high-resolution HLA test is performed.

When no compatible donor can be found, the family and friends of the patient engage themselves in campaigns to recruit possible donors, hoping that a match will be found among the new volunteers. These recruitment efforts have sensitized many to the need for bone marrow donation, and approximately 25% of the entries (n = 956,330) in the Brazilian Bone Marrow Donor Registry (REDOME) were obtained from 1431 campaigns to recruit bone marrow donors in 593 Brazilian cities. In 2010, more than 270 such campaigns accounted for 30.1% of new donors. The Health Ministry has limited the annual reimbursement for HLA typings to 300,000 new entrants in the REDOME since 2012 and increased, proportionally, financial resources to improve hematopoietic cell transplantation (HCT). Although REDOME entries cover 97.4% of Brazilian Municipalities, the proportion of entries per city according to population varies greatly, ranging from 0.002% to 23.543% (median: 0.584%).

Two main factors must guide recruitment: (1) the probability of finding a match based on the frequency distribution of the alleles in the population, and (2) the HLA allele frequency in diseases that could benefit from HCT. In a more simplified model, an equal chance to find a donor match should be based on the Brazilian distribution of HLA haplotypes. As haplotypes have a genetic background, cities with well-defined ethnic colonization or a low migration index will have a smaller number of haplotypes with less diversity. The HLA diversity among the volunteers recruited during 18 of these campaigns was compared with the diversity in random samples (consisting of 350, 1250, and 2250 entries) generated from the REDOME. The results showed that the number of haplotypes was directly proportional to the number of new donors (Figure 1). The number of haplotypes also decreases as a function of linked disequilibrium. This loss in diversity due to imbalanced recruitment increases the costs to the Health Ministry in terms of reimbursements for HLA typing to laboratories. It also reduces the chances of finding a bone marrow match for some individuals who share haplotypes that are more common in the REDOME. Moreover, additional costs will also be incurred related to complementary tests to define possible donors among these new entries.

A new recruitment protocol that considers the experiences of other large registries, including the recruitment and maintenance of donors, is proposed. Campaigns should be followed by complementary steps before initial laboratory typing of the samples. A phone call should be made to the potential recruit to confirm the proposal to adhere to the

![Figure 1 – Haplotype quantity and number of recruits in campaigns or randomly selected entries (n = 350, 1250, and 2250). Number of haplotypes calculated with Arlequin.](image)
In AC (Acre), AM (Amazonas), RR (Roraima), MA (Maranhão), and PI (Piauí), >1.5% of the population do not have entries in the REDOME. Every municipality of the states of Amapá, Ceará, Espirito Santo, Paraná, Pernambuco, Rio de Janeiro, Rondônia, São Paulo and the Federal District have volunteers registered in the REDOME.

**Conflicts of interest**

The author declares no conflicts of interest.

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