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Hematopoietic Stem Cell Donor Selection: the Europdonor Experience

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ABSTRACT: International collaboration is essential for the optimal selection of unrelated hematopoietic stem cell donors. This review focuses on the benefit of a joint worldwide donor file called Bone Marrow Donors Worldwide and the experience of the Europdonor Foundation in selecting strategies to identify the best human leukocyte antigen-matched donor in the shortest time. *Human Immunology 67, 405–412 (2006).* © American Society for Histocompatibility and Immunogenetics, 2006. Published by Elsevier Inc.

ABBREVIATIONS

HLA	human leukocyte antigen
BMDW	Bone Marrow Donors Worldwide
EBMT	European Group for Blood and Marrow Transplantation
CTL	cytotoxic T lymphocyte
PBL	peripheral blood lymphocyte
NIMA	noninherited maternal HLA

INTRODUCTION

Allogeneic HLA-identical sibling hematopoietic stem cell transplantation is an accepted form of treatment for a number of hematologic malignancies, syndromes of bone marrow failure, and congenital stem cell disorders. However, the availability of an HLA-matched sibling donor for patients in need of an allogeneic hematopoietic stem cell transplant is only about 30%. Phenotypically matched or partially mismatched family members or unrelated donors can provide suitable stem cell transplants for some of the patients lacking an HLA-identical sibling donor.

In 1970 during a meeting of the Deutsche Gesellschaft für Bluttransfusion Van Rood proposed to start an organization similar to Eurotransplant [1]. While Eurotransplant is an organization for facilitating solid organ transplantations, this new organization will recruit HLA-typed donors from the pool of blood transfusion donors. The idea of a European donor registry did not materialize but it developed into the Dutch unrelated hematopoietic stem cell donor registry called Europdonor, which functioned since the early 1970s but was incorporated only in 1988 when the bylaws of the Europdonor Foundation were officially passed.

In 1974 Shirley Nolan took the initiative to recruit stem cell donors for her son, Anthony [2]. This resulted in the Anthony Nolan Trust, which was the first active bone marrow donor registry. Many countries followed and the development over the past 15 to 20 years of large national registries of HLA-typed unrelated donors has increased the chance of finding a match for a growing number of patients [3–9].

This article focuses on the benefit of a joint worldwide donor file called Bone Marrow Donors Worldwide and the experience of the Europdonor Foundation in selecting strategies to identify the best HLA-matched donor in the shortest time.

THE WORLDWIDE HEMATOPOIETIC STEM CELL DONOR AND CORD BLOOD REGISTRY NETWORK

Searching all registries separately resulted in a large amount of unproductive work (there may be no donor) at a sizeable expense and with considerable time delay. To facilitate the search process for an international donor the Immunobiology Working Party of the European Group

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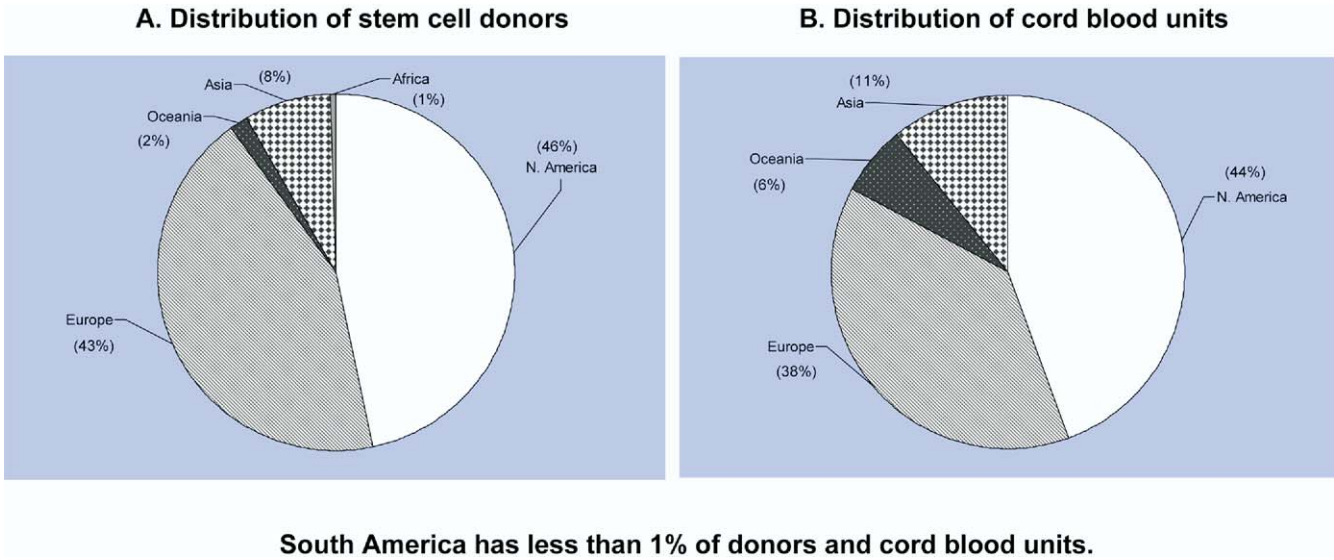

FIGURE 1 Distribution of stem cell donors and cord blood units in the world (August 2005).

for Blood and Marrow Transplantation (EBMT) followed the idea of Jon van Rood in 1988 to collect and compile an easily accessible listing of all donors worldwide in 4-monthly publication: Bone Marrow Donors Worldwide (BMDW) [10]. If no HLA-matched donor is identified in the family, a search in BMDW [11] can determine whether a suitable donor is available in the world without the need to approach all registries individually [12].

The first edition was distributed during the 1989 EBMT meeting and comprised the phenotypes of eight registries with a total of 155,000 donors. Over the past 16 years there has been a steady increase in the number of registries and donors. In 2005, 57 unrelated donor registries from 42 countries participated in BMDW along with 38 cord blood registries from 21 countries (*www.BMDW.org*). The number of donors included in the BMDW database has reached over 10 million. The registries providing donors to BMDW range in size from just under 100 donors to over 4.1 million donors. Completeness of unrelated donor HLA typing varies among the registries but has greatly improved over the years. The proportion of donors fully typed for HLA-A, -B, and -DR has increased from 6% in 1989 to 67% in 2005, resulting in more than 6.7 million HLA-A-, -B-, and -DR-typed donors. This is important as completely typed donors are far more likely to proceed to hematopoietic stem cell donation than those typed for only HLA-A and -B [13–15]. Overall 58% of donors are class II DNA typed and 39% class I DNA typed. The cord blood units are practically all fully typed for HLA-A, -B, and -DR and over 90% of the units are class II DNA typed and 53% class I DNA typed. The stem cell donors and cord blood units are not evenly distributed over the world (Figure 1). The vast majority of donors and cord blood units are of northwest European origin, which has serious implications for patients from other ethnic backgrounds. In Figure 2 the number of stem cell donors and cord blood units typed for HLA-A, -B, and -DR split antigens, the number of different HLA-A, -B, and -DR split phenotypes, and the number of unique phenotypes are given. Unique phenotypes are defined as occurring only once in the BMDW database. In August 2005 there were 4,164,470 HLA-A, -B, and -DR split-typed stem cell donors and cord blood units, representing 764,835 different phenotypes. The latter number is less than 2% of the theoretically possible number of HLA-A, -B, and -DR split phenotypes [16]. Fifty-three percent of these were unique phenotypes (402,586).

There are large differences between countries adding new HLA phenotypes to BMDW, resulting from genetic diversity in their populations and specific recruitment efforts by some registries. Analysis of the HLA phenotype of new donors added to the file has indicated that registries with almost exclusively northwest European donors, such as those in Scandinavia, have a chance of 1 in 16 donors being an HLA-A, -B, or -DR serological split phenotype not already present in the BMDW file. These chances are 1 in 12 for Asian registries, 1 in 8 for registries with some degree of non-Caucasoid donors (such as those in North America), 1 in 7 for registries from the Mediterranean countries, 1 in 6 for Argentina, and 1 in 5 for Mexico.

The fact that some countries have a relatively low contribution adding new HLA phenotypes means that many of the phenotypes occurring in their population are