

The Need for Ethnically Diverse Stem Cell Donors

Warren Fingrut^{a,°}, BSc MD

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[°]Corresponding author: wffingrut@alumni.ubc.ca

^a Internal Medicine PGY1, Faculty of Medicine, University of Toronto, Toronto, ON

abstract

A majority of patients who are in need of a stem cell transplant cannot find a suitable genetic match in their families and rely on unrelated donors, individuals who have registered with a stem cell donor database. Many unrelated stem cell donor registries currently direct their donor recruitment teams to target and recruit ethnically–diverse individuals as stem cell donors. However, despite a large body of evidence in the literature highlighting the need for ethnically–diverse stem cell donors, no resource exists that explains why building an ethnically–diverse stem cell donor database is important or needed. The purpose of this review article is to summarize evidence in the literature that highlights the extent of ethnic and racial disparity in match rates in registries in North America and worldwide. Further, the author explains the multifactorial nature of this disparity, with contributing factors including ethnic differences in representation, genetic diversity, and attrition rates. This review aims to 1) equip donor recruitment staff and volunteers with a resource to inform their recruitment efforts; and 2) to support the donor recruitment team to target recruitment of ethnically–diverse stem cell donors.

introduction

Over 70% of patients who need a stem cell or bone marrow transplant cannot find a match in their family and require an unrelated donor to proceed with treatment.¹ These donors are recruited at stem cell drives where individuals are invited to swab their cheeks and to sign a consent form to register as potential stem cell donors.² A growing body of literature highlights the need for ethnically–diverse stem cell donors.^{3–9} Patients in need of a stem cell transplant are more likely to find a genetically–matched donor from their own ethnic group. This is due to the association between individuals' genetic heritage and their Human Leukocyte Antigen (HLA) alleles, which are used to match patients to donors. Minority status is often associated with less–common HLA types, underscoring the importance of building ethnic diversity into the world's stem cell and marrow donor registries.¹⁰ Some registries, including the U.S. National Marrow Donor Program (NMDP)'s "Be The Match" registry, have already adapted their recruitment approach to specifically target ethnic and racial minorities.⁴

The Stem Cell Club was founded in 2011 at the University of British Columbia to improve both the quality and the

quantity of membership on Canada's Stem Cell Donor Database.¹¹ A majority of the males we recruit at our stem cell drives are non–Caucasian (53%), and we also hold ethnically–targeted stem cell drives to recruit Aboriginal Peoples and members of other ethnic minorities.^{11–12} The primary aim of this review article is to provide an overview of the evidence behind the need for ethnically–diverse stem cell donors. This paper will be used to equip our team with an evidence–based resource to inform our stem cell drive campaigns, which currently feature targeted recruitment of ethnically–diverse Canadians as stem cell donors. This review seeks to inform donor registry strategic planning and to offer guidance to any group or individuals who coordinate or volunteer at stem cell drives.

many ethnic and racial minority groups experience lower match rates

In Canada, over 50% of patients do not have a suitable donor on the Canadian unrelated donor registry, and patient ethnicity has been shown to influence the likelihood of finding a donor.¹³ In a study

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by Allan et al., Canadian patients who self–identified as East Indian or Caucasian were most likely to find a donor; with respective success rates of 59.6% of 47 requests and 50% of 2058 requests.¹³ However, patients who self–identified as Black (24.5% of 53 requests) or Chinese (14.3% of 14 requests) had much lower match rates.¹³ In a 2012 study, Gragert et al. used HLA haplotype frequencies to project HLA match rates for the different populations served by the Canadian OneMatch registry of the Canadian Blood Services. They calculated that match rates for Canadian patients searching for adult unrelated stem cell donors ranged from 2% for the Black

group to 46% for the Caucasian group.¹⁴ Similarly, in the United States, multiple studies looking at the U.S. NMDP's "Be the Match" registry have confirmed that patients from U.S. racial- and ethnic-minority groups are consistently less likely to find an HLA-matched donor.^{5-9,14-17} Unrelated donor genetic match rates for Caucasian, Hispanic, Asian/Pacific Islander, and African-American ethnic groups, estimated a number of different ways, have been shown to range from 68-75% for Caucasian people, 34-44% for Hispanic people, 27-68% for Asian/Pacific Islanders, and 19-35% for African-American people.^{5-9,14-17}

This trend holds true outside of North America, as well. A study by Heemskerk et al. analysed unrelated donor searches performed for patients at Dutch transplantation centres, searching the Bone Marrow Donors Worldwide network of donor registries.¹⁸ The authors demonstrated that a patient's country of origin influenced match rates; between 1996 and 2000, only 11% of the patients of Northwest European origin (n=211) lacked a compatible donor somewhere in the world, compared to 50% of patients of non-Northwest European origin (n=56).¹⁸ A 2013 study found that patients of Israel's Arab minority had a significantly lower chance than patients of Jewish origin of finding a match on Israel's local donor registries (25% versus 64%, respectively).¹⁹ Another study in India modelled differences in donor match rates among 14 regional subgroups—each with different ethnic/racial demographics—and showed differences in match rates between these regional groups.²⁰

disproportionate representation of ethnic and racial minorities on stem cell donor databases

Today, many non-Caucasian ethnic groups are not properly represented on the world's registries. This is certainly true within individual countries. For example, on Canada's OneMatch Stem Cell and

Marrow Network, as of May 2015, 71% of registrants are Caucasian.²¹ Canadian Black donors, Aboriginal donors, and Southeast Asian donors each make up less than 1% of Canada's registry, despite making up 2.9%, 4.3%, and 2.8% of the Canadian population, respectively.²¹⁻²² Similarly, in 2009, on the U.S. NMDP's "Be The Match" registry, African-American donors and Hispanic donors made up 7.9% and 9.9% of the registry, despite making up 13.1% and 16.9% of the American population.²³⁻²⁴ Non-Caucasian groups are also underrepresented on worldwide network of potential stem cell donors. The vast majority of the world's registered stem cell donors are from registries based in Western Europe and the United States, with most countries in Africa, Asia, and Eastern Europe—and their ethnic/racial populations—being dramatically underrepresented.²⁵ This disproportionate representation of specific ethnic groups, both within individual registries and worldwide, contributes to observed differences in match rates between ethnic groups.

ethnic/racial differences in genetic diversity

The above studies highlight both smaller donor pools and disproportionate representation of ethnic and racial groups as contributors to decreased match rates. However, studies have also shown that some ethnic/racial groups have more diverse HLA alleles and would be less likely to find a match even if they had an equal proportion of potential donors as Caucasians. A 1995 study by Beatty et al. demonstrated that African-Americans are more polymorphic with respect to HLA and are therefore less likely to find donors at any given registry size.¹⁶ The authors demonstrated this in two ways. First, they modelled new HLA phenotype acquisition, which is the chance that a newly recruited stem cell donor has a novel combination of HLA alleles. They showed that 90% of newly recruited African-American donors had new HLA phenotypes, compared to 72% or 74% respectively for Asian-American or Caucasian donors. Second, the authors modelled match rates in

hypothetical registries composed of donors solely of the same ethnic group. They found that Hispanic and African-American people in these hypothetical ethnically-homogenous registries were still less likely to find a match than were Caucasian, Asian-American, or Native American people. Another study by Mori et al. examined HLA allele phenotypes of the NMDP donors. These authors found that African-American and Asian-American people had a large number of HLA alleles unique to their ethnic groups, whereas Caucasian, Latin American, and Native American people shared a large number of common HLA alleles.²⁶

ethnic/racial differences in attrition from stem cell donor databases

The aforementioned studies demonstrate both decreased donor pools and decreased representation of specific ethnic/racial groups (within registries and on the world's combined registries), as well as increased genetic diversity of specific ethnic groups. However, ethnic/racial differences in donor availability also contribute to observed differences in match rates between ethnic groups.

Some ethnic groups are more likely to be unavailable at the time of donation, due to higher rates of donor ambivalence and attrition. In general, a significant proportion of individuals listed in a stem cell donor registry are not available to donate when called upon. Some registrants have changed addresses and cannot be reached, some

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have health conditions that prevent them from donating, some are temporarily unavailable due to travel or work commitments, and some are no longer willing to contribute.²⁷ The U.S. NMDP statistics show that 20% more Caucasian registrants move forward with the donation process when contacted, compared to non-Caucasians (the authors reported a 60% attrition rate for minority groups vs. 40% attrition rate for Caucasians).²⁷ A study by Confer found that, on the U.S. NMDP, rates of donor unavailability were higher among donors who identified as Black, Asian/Pacific Islander, or American Indian/Alaska Native.²⁸ Racial and ethnic minority populations were shown to be significantly more likely than Caucasian populations to be unable to be contacted, to be contacted but not interested when asked to donate, or to be potentially interested to donate but temporarily unavailable. In contrast, the rates for donor deferral for medical reasons were similar across racial and ethnic groups.²⁸ A similar study looking at The U.K. Anthony Nolan registry found that African, African-Caribbean, Asian, Jewish, and Mediterranean donors were significantly more likely to be unavailable for later stages of the donation process, compared to Caucasian donors.²⁹

The increased attrition rates among members of ethnic and racial minority groups disproportionately disadvantage minority patients searching for a donor. This increased attrition is not necessarily due to differences in general willingness to donate, and it might be secondary to specific barriers to proceeding with the donation process. A study conducted by Switzer et al. identified multiple cultural,

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psychosocial, and donation-related factors associated with race/ethnic group attrition from the registry.²⁷ Compared with Caucasians, potential donors from African-American, Hispanic, and American Indian groups reported more religious objections to donation; African-American people and Asian/Pacific Islanders reported less trust that stem cells would be allocated equitably; Asian/Pacific Islanders and Hispanic people reported more concerns about donation; and Asian/Pacific Islanders reported a greater likelihood of having been discouraged from donating.²⁷ The authors suggest that these findings could be used to inform media campaigns and key messaging at the time of recruitment for stem cell drives targeting these ethnic and racial minority groups in the United States.

Switzer et al.'s study also demonstrated that, across all ethnic and racial groups, ambivalence played a critical role in donation-related decisions.²⁷ The authors propose that at stem cell drives, ambivalent potential donors from all racial and ethnic groups could be identified, and any concerns that may be producing ambivalence could be directly addressed (including medical concerns about the donation process, religious objections, or mistrust of the medical system).²⁷ The authors suggest that registrants be offered a cooling-off period if residual concerns remain, similar to what is recommended in the context of living solid-organ donation.³⁰ They further suggest that, for all groups, self- and social-identification as a potential donor could be emphasized as a potential buffer against attrition.²⁷

Overall, addressing the barriers that limit participation of minority groups will be paramount to boosting registration and lowering attrition rates of ethnically-diverse stem cell donors. To achieve this, further research is needed to explore the barriers experienced by specific ethnic and racial groups and to identify strategies to mitigate those barriers.

conclusion

Despite the continued expansion of the global stem cell and marrow network, people of all ethnicities are needed to register as potential donors. In a 2009 paper by Bergstrom et al., the authors estimated

optimal U.S. NMDP registry size for each race and concluded that there is not an optimal amount of donors registered yet for any ethnicity.⁵ Furthermore, the authors completed a benefit-cost analysis and expanded their analysis in a 2011 paper to include individuals of mixed race.⁷ They found that the benefits of recruiting additional donors exceeded costs for all races/ethnicities. African-American people were shown to have the highest benefit-cost ratio for being recruited as potential stem cell donors, with benefits being ten times the costs. Mixed-race African-American/Hispanic individuals and African-American/Caucasian individuals had the next highest benefit-cost ratios of 9.1 and 8.4, respectively. Recruitment of Caucasian individuals was lowest, at a 4:1 benefit-cost ratio.⁷

Altogether, the above studies demonstrate ethnic differences in HLA match rates. These differences result from a combination of smaller donor pools and disproportionate representation of ethnic/racial groups on the world's stem cell donor registries, and ethnic/racial differences in both HLA diversity and donor attrition rates. Targeted recruitment of ethnically-diverse individuals to become potential stem cell donors is warranted to capture a range of HLA phenotypes and to improve equity in match rates between Caucasians and other ethnic groups.

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disclosures

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