Targeted recruitment of optimal donors for unrelated hematopoietic cell transplantation: The Stem Cell Club process

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Abstract

Objective/Background: Patients in need of hematopoietic stem cell transplantation often cannot find a suitable HLA-matched donor in their families and rely on unrelated donors. Individuals can register with their country’s donor registry either online or at a stem cell drive by providing consent and a tissue sample for typing.

Methods: Stem Cell Club is a donor recruitment organization in Canada that recruits Canadians as stem cell donors. This article outlines the Stem Cell Club’s protocol for donor recruitment at stem cell drives including five core components: prescreening, informed consent, registration, tissue sample collection, and reconciliation.

Results: At stem cell drives, recruiters approach individuals from the most-needed demographic groups, catch their attention, explain the purpose of the drive, and prescreen them to ensure eligibility. Recruiters then secure informed consent, educating registrants about the stem cell donation process, the risks involved, the right to withdraw, and donor–patient anonymity. Recruiters subsequently ask registrants to register by providing their contact/demographic information, completing a health questionnaire, and signing a consent form. Recruiters also guide registrants to provide a tissue sample (e.g., buccal swab) for typing. Finally,
Introduction

Patients with various blood and immune/metabolic diseases may require a stem cell transplant as part of their treatment. However, approximately 70% of patients do not have a suitable HLA-matched donor in their family and require an alternative donor. Unrelated donors remain the most common alternative donor choice for allogeneic transplantation [1]. Haploidentical and umbilical cord donors both represent emerging sources of stem cells [1]. As of May 2020, there are over 35 million stem cell donors listed on registries in 54 different countries around the world [30]. Transplant physicians can search the global inventory using their national registry. Individuals can become listed on a donor registry by providing informed consent as well as a DNA sample (through a buccal swab, blood sample, or saliva sample). Generally, donor recruitment organizations offer eligible adults the opportunity to register either online or in person at a stem cell drive.

Stem cell drives are an important method to engage individuals to the donor registry, educate them about stem cell donation, and recruit them as potential donors. The World Marrow Donor Association (WMDA) has published a number of guidelines to inform donor recruitment efforts [2,4,5,29]. However, to the best of our knowledge, there are no protocols available in the literature to guide stem cell donor recruitment at drives.

Stem Cell Club is a donor recruitment organization in Canada [6]. To date, the organization has recruited over 12,000 donors at hundreds of drives across Canada. The club maintains a service-level agreement with Canadian Blood Services, enabling chapters to run donor recruitment drives independently on their behalf. In this article, we outline the Stem Cell Club’s protocol for donor recruitment at stem cell drives (Fig. 1 and Table 1). This protocol incorporates relevant WMDA guidelines and draws on Stem Cell Club’s experience spearheading drives in Canada.

Recruiting the most-needed stem cell donors

Stem cell drives should be designed to target recruitment of the most-needed donor demographics: younger individuals, individuals from a diversity of ethnic backgrounds, and males [7,8]. Younger individuals (up to 35 years) should be preferentially recruited as these donors are associated with improved survival in transplant recipients [9,10]. Individuals from diverse ethnic backgrounds should be targeted preferentially as patients are more likely to find an HLA-matched donor in their own ethnic groups [11]. Many ethnic/racial minority groups experience lower match rates, both within [12,13] and outside of North America [14,15]. This is due to the combination of smaller donor pools, disproportionate representation on individual registries and on the worldwide network, and ethnic/racial differences in genetic diversity and in attrition from registries [8]. Finally, males should be preferentially recruited as donors as transplant physicians mostly prefer to select male donors for their patients when multiple donor options exist [7,16]. Male donors are associated with decreased risk of chronic graft-versus-host disease in transplant recipients, especially compared with parous female donors [9,10]. Male donors also yield higher cell counts in peripheral blood progenitor cell collections and are more likely to meet target CD34+ cell dose [7]. At individual drives, recruiters should be guided to balance targeted recruitment of male registrants with recruitment of registrants from a diversity of ethnic backgrounds, including females.

Before the drive

Ahead of a drive, it is important to train the recruiters. A WMDA guideline outlines the recommended topics to be included in a recruiter training program [17]. The Stem Cell Club has published an online recruiter training program, guiding recruiters on how to volunteer at, lead, and organize stem cell drives [6]. The training program employs a spiral curriculum where learners revisit core topics several times throughout the program, and the complexity of the material increases with each revisit [18]. This training is supplemented with a video series which demonstrates the role of the recruiter at each station of the stem cell drive. Finally, recruiters attend a mock stem cell drive practical workshop to practice and allow for validation of skills (Stem Cell Club training resources are available at www.stemcell-
Recruiters are initially tasked with catching the attention of potential registrants. Recruiters explain the purpose of the stem cell drive and proposed tissue sample collection. They outline the role of blood stem cells in the production of red blood cells, white blood cells, and platelets (Fig. 2), and explain the indications for stem cell transplantation. Recruiters discuss the steps that would follow should the registrant match to a patient, and introduce the registrant to the two possible stem cell collection methods: bone marrow (BM) and peripheral blood stem cell (PBSC) donation. The recruiter clarifies that the registrant could match to a patient anywhere in the world and emphasizes that the program is voluntary, with no remuneration for donation [3,4,19].

Finally, the recruiter performs a donor eligibility assessment. Age eligibility requirements vary according to registry. Minimum age of consent depends on jurisdiction, with age 18 years set as the minimum age of consent in

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areas where no regulations exist [4]. WMDA guidelines stipulate that registrants older than 60 years should no longer be listed as donors [4]. Some registries restrict recruitment to include only younger individuals as a strategy to improve the quality of their donor lists. WMDA guidelines outline the donor medical suitability at the time of recruitment as having two objectives: 1) protecting the recipient from harm and 2) protecting the safety of the donor by minimizing avoidable risk [5]. Registrants uncertain about their suitability can be referred to the WMDA donor medical suitability guidelines (available at https://wmda.info/professionals/promoting-donor-care/donor-suitability/) for diseasespecific guidance. Finally, donors need appropriate healthcare coverage, which can either be provided by the registry or supplied by the individual, and this should be discussed if applicable. Ineligible individuals should be professionally and sensitively redirected to help in other ways, including through donating blood if eligible.

Informed consent

Informed consent is a moral, ethical, and legal requirement to become a stem cell donor. In addition, Switzer et al. [20] showed that registrants were more likely to be ambivalent towards donating if they felt less informed or had unanswered questions at the time of recruitment. Ambivalence has been shown in subsequent studies to be associated with attrition at multiple stages in the donation process [21,31]. Recruiters show the registrants diagrams detailing both the stem cell collection processes (PBSC and BM; example informed consent diagrams are available at www.stemcellclub.ca/supplies.html). PBSC collection is the predominant graft source used for adult unrelated donors. Recruiters highlight that this procedure is preceded by a series of injections of a growth factor (granulocyte colony-stimulating factor [G-CSF]) which mobilizes the stem cells in advance of collection. During collection, blood is run in a circuit through the apheresis machine, centrifuged, and separated out into red blood cells (which are returned to the donor) and stem cells collected for donation. The donor sits in the circuit for several hours until the collection is completed. This process can require up to two separate collection periods. BM donation is performed much less commonly than PBSC donation; BM donation is conducted under general anesthesia. A hollow needle is used to withdraw stem cells from the BM of the pelvic bone.

Following discussion of the donation methods, recruiters educate registrants about common and serious risks of each, including pain, common toxicities, and recovery time. A prospective study by Pulsipher et al. [22] assessed toxicity and recovery in 2,726 BM donors and 6,768 PBSC donors who underwent collection from 2004 to 2009. Pain was a common side effect for both the collection procedures; BM and PBSC donors experienced similar levels of pericollection pain and toxicity on their peak days of discomfort (Day +5 of G-CSF for PBSC donors, and within 48 hours of collection for BM donors). A majority of BM donors experienced skeletal pain, generally localized to the site of collection. Pain associated with PBSC donation involved musculoskeletal locations throughout the body and higher rates of headache [22]. Fatigue, insomnia, anorexia, and dizziness were common toxicities for both procedures [22]. Recovery occurred more quickly in PBSC donors, with more than half completely recovered by 1 week after collection. Only 18% of BM donors reported complete recovery at 1 week, with 67% reporting recovery at 1 month [22]. An earlier prospective study by Pulsipher et al. [23] assessed 2408 unrelated PBSC donors between 1999 and 2004, and found that nearly all donors will experience bone pain, 25% will have significant headache, nausea, or citrate toxi-
Fig. 4 Demonstration of barcode labelling. A barcode sticker is affixed to all swab kit components to (A) individual swabs, (B) the swab kit envelope, and (C) the registrant’s consent form.
city, and a small percentage will experience serious short-
term adverse events (though recovery from these events
was universal).

Regarding long-term risks of donation, recruiters advise
registrants that a small percentage of BM donors report
long-term, persistent discomfort. In the 2013 study by Pul-
sipher et al. [23], 3% of BM donors did not report full recov-
ery at 6 months compared with 0% of PBSC donors. Recruiters also discuss the risks associated with G-CSF. A
review by Shaw et al. [24] discusses the reassuring lack of
evidence for the development of hematological malignan-
cies in healthy donors who receive GCSF for mobilization
of stem cells ahead of PBSC collection. The authors con-
clude that, to date, long-term outcome studies and genetic
analyses have provided reassuring evidence that the use
of G-CSF to mobilize PBSCs for transplantation is a safe and
acceptable donation method.

Recruiters then educate registrants on the anonymity
of both the patient and donor. Registrants must be willing to
accept that they cannot direct their donation to a patient
of their choice [4]. Finally, recruiters outline the regist-
trant’s right to withdraw at any time.

WMDA-standards for securing informed consent stipulate
that all registrants must also be given a pamphlet detailing
the above information [30].

Registration

At the registration station, individuals provide demographic
information, medical history, and signed consent to join the
registry. The accurate capture of registrant information is
essential if they are to be selected as donors. Errors in
paperwork can lead to delays in registering or requirement
to re-register, outcomes which can be expensive for reg-
istries and frustrating for donors. Recruiters are tasked with
ensuring that paperwork is completed correctly, following
good documentation practices [25]. The privacy and confi-
dentiality of registrants and their paperwork is paramount.
Breaches must be documented and reported to the registry.
Recruiters also inform registrants about data collection,
storage, usage, and confidentiality. Registrants are told that
their personal data will be kept strictly confidential, with
each profile assigned a unique donor number as the only
identifier to be used in registry communication. Anonymized
health and demographic information is shared with the
unique donor number with other registries.

Tissue sample collection

The tissue sample collection station begins with an informed
consent checkpoint. Recruiters ask the following questions
to the registrants: (a) What happens if you are a match?
(b) What are the risks involved in donating? and (c) What
happens if you say no? Through discussion around these
questions, recruiters identify and address any gaps in the
registrant’s understanding of the program.

There are three modalities to collect tissue for DNA typ-
ing: buccal swab, saliva sample, and blood sample. This pro-
tocol focuses on buccal swab. This method of tissue
collection is preferred over blood collection in particular
as it is less invasive, logistically simpler, and registrants
can collect their own tissue samples. Recruiters assign a
set of unique barcode labels to each registrant and affix a
label onto each cotton swab as well as the registration form
and envelope (Figs. 3 and 4). Recruiters guide the regis-
trants to brush their cheek with an appropriately labelled
buccal swab for 30 seconds (Fig. 5). This process is repeated
times, with the registrant swabbing a different cheek area each time. The registrant places each swab into a plas-
tic holder following sample collection (Fig. 3). After the
four swabs are collected, the holder is placed into the
envelope, which is then sealed.

The reconciliation station is the final opportunity for a
recruiter to interact with the registrant and error check
the registration process together. Recruiters review the reg-
istration paperwork and sealed envelope to ensure that
each has a barcode label affixed and that they match both
each other and the remaining unused labels. Recruiters also
review registrants’ paperwork to identify errors that may
have been missed. Recruiters ask registrants if they have any remaining questions. This is particularly important as unanswered questions at the time of recruitment are significantly associated with registrant ambivalence [20].

Recruiters deliver final information to the registrant: they will remain on the registry until the age of 60 years or time of withdrawal from the registry [4]; the registry may contact them to verify their information; and they have the responsibility to notify the registry of changes in their contact information, commitment to be a donor, or medical status, including pregnancy or other conditions that may preclude donation temporarily or permanently [30]. Recruiters should also clarify procedures the registry will take to trace the registrant, should they not be reachable. Finally, the recruiter thanks the registrant for their registration. Recruiters may also promote cord blood donation to women where applicable and invite registrants to consider donating blood if eligible.

To complete processing the registrant at the drive, the recruiter completes several forms: the tracking log, registrant data sheet, and outcomes tally (Fig. 6A–C). Tracking logs (Fig. 6A) allow the registry to determine what barcode labels to expect inside the set of registration kits received following a stem cell drive. Recruiters affix one barcode label from each registrant onto the tracking log. This form is subsequently delivered to the registry together with the kits. Registrant data sheets (Fig. 6B) log each registrant’s first name and contact information. In the unfortunate event that registration kits do not make it to the registry, these forms allow the registry to contact registrants to notify them of the security breach and make them aware that they will not be listed. Accordingly, these forms are kept with the recruiter until the registration kits are delivered safely to the registry, at which time they are shredded. The outcomes tally (Fig. 6C) guides recruiters to record the demographics of the registrants recruited.

### A Tracking log: Collected buccal swab kits

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Apply non-barcode label in numbered box below. *Please indicate N/A in any unused boxes*

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Fig. 6 (A–C) Reconciliation and (D) shipping paperwork. (A) Tracking log: to catalogue the barcode labels of each, a barcode label for each completed registration kit is affixed onto one of these forms and delivered with the kits to the registry. (B) Registrant data sheet: to record each registrant’s first name and a contact number, so that new registrants can be contacted and notified in the event that their registration kits are damaged or lost. (C) Outcome tally: to determine success in recruitment of the most-needed donor demographics and support quality improvement. (D) Event reconciliation log: to summarize all completed tracking logs.
Finally, the recruiter bundles registration kits into groups of five, wrapped with an elastic band, and places them into a clear plastic bag for delivery or shipment to the registry.

**Post-drive**

Following the drive, the recruiter completes an event reconciliation log (Fig. 6D), summarizing the completed tracking logs. The recruiter then identifies any tracking logs, registrant data sheet, and event reconciliation logs containing unused boxes and writes in "end-of-record" in pen following the last entry of these forms as well as for the reconciliation log, as per good documentation practices [25]. The clear plastic bag filled with bundled registration kits is placed into a box which is then sealed and affixed with confidentiality labels. Recruiters then complete a post-event report, detailing drive outcomes, shipping waybill if applicable, the stem cell drive strengths and weaknesses, and suggestions for future events. These data guides the quality improvement of stem cell drives. Finally, supplies are inventoried and returned to storage, and volunteer recruiters involved are thanked for their contributions.

**Evaluation of protocol impact**

**Recruiting the most-needed stem cell donors**

To determine the impact of the use of this protocol with respect to recruitment of the most-needed donor demographics, we examined the demographics of the donors recruited by Stem Cell Club from January 2017 to December 2017. These data were extracted from post-event reports.
logged by recruiters after each drive. During this time period, 4,096 donors were recruited at drives run by Stem Cell Club which employed this protocol. At the drives at which sex outcomes were recorded, 48% of 3,506 registrants recruited were males. Furthermore, at the drives at which registrant age and self-reported ethnicity outcomes were recorded, 82% of 1,550 males self-reported as non-Caucasian, and 59% of males were aged 17–25 years.

**Metrics of quality stem cell donor recruitment**

To evaluate the quality of stem cell drives using this protocol, newly registered stem cell donors at three stem cell drives run by Stem Cell Clubs at university campuses in Ontario and British Columbia were invited immediately after recruitment to participate in a survey. This survey assessed registrants on their knowledge, commitment, and experience at the stem cell drive as these factors have been shown to be associated with ambivalence and/or attrition from the registry [20,21]. Of the 374 stem cell donors who registered during the study stem cell drives, 241 completed the post-drive survey and consented to be included in this analysis, reflecting a 64% participation rate. To assess ambivalence, we employed the Simmons Ambivalence Scale. This 7-item scale has been used to assess ambivalence in previous studies of marrow donors [20]. We dichotomized the responses for each item to reflect whether participants expressed any ambivalence (score = 1) or no ambivalence (score = 0). Mean scores were 1.8 ± 0.15 out of 7 on the scale, with 34% of participants scoring 0, 19% scoring 1 of 7, 12.5% scoring 2 of 7, and 34.5% scoring 3 or more of 7 (Figure Supplementary figure 1).

To assess knowledge, registrants were asked to complete a 14-question, true or false, informed consent quiz to assess their knowledge according to WMDA-suggested procedures for informed consent at the time of registration [3]. The mean score on this quiz was 83 ± 12% (Supplementary Table 1). Over 80% of participants understood all of the following: donation non-remuneration; BM and peripheral blood collection methods; ineligibility to donate with blood-borne or transmissible diseases; donor right to withdraw; donor responsibility to update the registry if contact information changes; and data storage, privacy, and confidentiality. However, 37% of participants did not know that there are restrictions to registering as a donor, 32% did not know that donor and patient remain anonymous prior to donation, 28% did not know that they would receive a growth factor before peripheral blood collection, 27% did not know that not all registrants go on to donate stem cells, and 25% were not familiar with the common side effects.

Registrant perception of their knowledge about stem cell donation significantly improved after the stem cell drives: 80% of survey participants reported feeling at least moderately informed after the drive compared with 29% before the drive ($p < .0001$; Wilcoxon rank-sum test; Figure Supplementary figure 3). Moreover, 85% agreed or strongly agreed that recruiters were very knowledgeable (Figure Supplementary figure 4), and 86% reported no unanswered questions after the drive.

**Conclusion**

As outlined above, Stem Cell Club has demonstrated a capacity to recruit the most-needed donors at drives...
employing this protocol. Donor recruitment organizations continue to struggle with recruitment processes that are not selective enough or that may not target the right audience. Worldwide, targeted recruitment of male donors remains a challenge: of the 2.65 million new donors recruited to the 100 unrelated donor registries of the WMDA in 2015, 59% were females [7]. Recruitment of donors online presents similar challenges: a report on the Anthony Nolan Registry of the United Kingdom detailed that from October 2012 to December 2013, 70% of online registrants were females [27]. Donors from ethnic/racial minority groups also continue to be underrepresented worldwide [8]. Stem Cell Club has successfully applied this protocol to recruit thousands of donors across a variety of settings across Canada, including both large and small drives at university campuses, high schools, community settings, and rural venues [6,28]. The launch of donor recruitment organizations similar to Stem Cell Club in other jurisdictions, supported by this protocol, could improve the ability of registries and transplant centers to target specific donor groups and recruit the most-needed donors.

The protocol also serves to standardize stem cell drives run by different teams of recruiters across settings, helping to ensure that the donors recruited have the same high qual-
ity donation experience, regardless of where and when they register. The data presented above support that Stem Cell Club has shown strong performance on key indicators of stem cell drive quality at stem cell drives which have employed this protocol. Deployment of this protocol could help donor recruitment organizations achieve similar quality outcomes with their drives, thereby helping to improve the quality of the donors they recruit.

Declaration of Competing Interest

D.A. is a paid medical consultant with Canadian Blood Services (CBS). W.F. receives grant funding from CBS. H. M. declares no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.hemonc.2020.04.001.

References

The Stem Cell Drive


