



# Unrelated hematopoietic stem cell registry and the role of the Hematopoietic Stem Cell Bank

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## Background

The hematopoietic stem cell bank has been actively recruiting registrants since 1994. This study systematically reviews its operations and outcomes over the last 20 years.

## Methods

Retrospective data on a total of 47,711 registrants were reviewed. Relevant data were processed using PASW Statistics for Windows, version 18.0.

## Results

As of 2013, the Korean Network for Organ Sharing database contained 265,307 registrants. Of these, 49,037 (18%) registrants committed to hematopoietic cell donation from 1994 to 2013. Fifty-seven percent of the registrants were men, and 43% were women. The reasons for opting out of the registry included refusal to donate (70%), family refusal (28%), and others (2%). The donation willingness of registrants was significantly higher than those who refused to receive a mail to confirm their continued enrollment ( $\chi^2=6.103$ ,  $P=0.013$ ). The bank successfully coordinated a total of 512 donors among newly matched donors from 1995 to 2013, of which the bone marrow and peripheral blood stem cell accounted for 40.8% and 59.2% of the total donations, respectively.

## Conclusion

Our recruitment activities focus on promoting voluntary registration and the importance of updating personal contact information. We expect that these data may be useful for diverse studies and demonstrate the positive impacts on the donation program.

**Key Words** Unrelated hematopoietic stem cell register donor organization, Human Leukocyte Antigen (HLA), Peripheral blood stem cell transplantation, Bone marrow transplantation

## INTRODUCTION

Hematopoietic stem cell transplantation (HSCT) is a medical procedure in which diseased bone marrow is replaced by highly specialized stem cells that develop into healthy bone marrow. Since Thomas *et al.* reported the use of allogeneic HSCT in children and adolescents, there has been substantial progress and success of HSCT for treating blood-related disease [1, 2]. Better understanding of transplantation biology and brilliant advances in the HLA related field led to the development of non-myeloablative stem cell, peripheral blood stem cell (PBSC), and umbilical cord blood transplantation [3]. HSCT from HLA-matched siblings or un-

related donors is one of the options for patients requiring a transplant. The National Marrow Donor Program of US reported that only about 30% of patients are likely to have matched sibling donor [4]. As there are relatively fewer registrants in Korea due to the social trend towards low birth rates resulting in the formation of nuclear family, an urgent need for donors to supply stem cells for patients requiring transplants has ensued.

The registrant recruitment and coordination program for unrelated HSCT in Korea was started in 1994, when the Catholic Hematopoietic Stem Cell Bank (CHSCB) and the Korean Marrow Donor Program (KMDP) were founded. A total of 5,824 bone marrow transplants from sibling donors, and 3,173 bone marrow/PBSC transplants from unrelated

donors have been reported since 2010 [5]. Although medical advances in bone marrow transplantation techniques and immunosuppressive medications have dramatically increased the number of unrelated transplants each year [6], more potential donors should be recruited, registered, and coordinated through increased HSCT-related bank activities [7].

Currently, there are five donor centers designated by the Ministry of Health and Welfare in Korea. Each center regularly conducts its own activities to encourage more volunteers to participate in various bone marrow donation campaigns. Government agencies and private organizations have also made concerted efforts to improve awareness of unrelated HSCT and increase the number of volunteers via advertisements in subway screen doors and media. Nevertheless, only about 12.6% of the general public are aware of the importance of the bone marrow, PBSC, or umbilical cord blood donation program [8].

Herein, the study was conducted to analyze current status of the hematopoietic stem cell bank and review the status of the stem cell registry as well as the activities to improve availability of unrelated potential donors by investigating motivations for joining a registry and potential intervention strategies to increase donor availability.

## MATERIALS AND METHODS

### Data collection

As of 2013, the Korean Network for Organ Sharing (KONOS) database contained 265,307 registrants. Of 49,037 (18%) registrants who agreed to donate hematopoietic stem cells from 1994 to 2013, a data of 47,711 registrants who were traceable with contact information was reviewed retrospectively.

**Table 1.** Characteristics of registrants of hematopoietic stem cell registry (1994–2013).

Characteristics		N	%
Age (yr) (N=47,711)	18–20	2,888	6.10
	20–30	39,578	83.00
	30–40	4,982	10.40
	40 <	261	0.50
Gender (N=47,711)	Unrecorded	2	
	Male	26,974	57.00
Nationality (N=47,711)	Female	20,737	43.00
	Korean	47,699	99.97
Employment (N=28,688)	Foreigner	12	0.03
	Student	23,752	82.80
	Employee	2,197	7.70
	Military	878	3.10
	Others	1,861	6.40
Registration methods (N=18,770)	University	16,260	86.6
	Military organization	874	4.7
	Event or campaign	745	4.0
	Individual direct visit	313	1.7
	Others	578	3.0

### Data analysis

Data were processed using PASW Statistics for Windows, version 18.0. Briefly, the status of new registrants, characteristics of the registrants, data for coordination and outcome of stem cell transplants, annual trends in donors, donation methods, and donor characteristics, and data for management of registrants were examined using descriptive statistics. The differences between donation and approval rates, and the transplantation coordination outcomes according to characteristics of the matched donors were analyzed using  $\chi^2$ -tests.

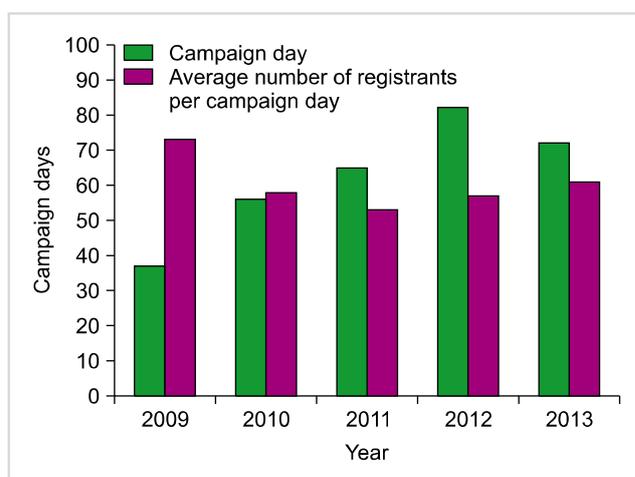
### Ethical considerations

The study protocol was approved by the institutional review board of Catholic University (No. MIRB-00082\_1-002) prior to commencement of the study based on the KONOS database.

## RESULTS

### Registrant enrollment and characteristics

A total of 49,037 registrants were listed in the donor registry for HSC bank from 1994 to 2013, which accounted for 18% of registrants in the KONOS database. Among those registrants, 47,711 registrants whose contact information was available at the time of the study were included in the retrospective review. The characteristics of the registrants in the bank are shown in Table 1. Fifty-seven percent (26,974 people) and 43% (20,737 people) of the registrants were male and female, respectively; whose mean age was  $23.7 \pm 4.51$  years. Among the age groups, most were in their 20s and 30s (39,578 registrants, 83.0%), followed by 30s and 40s (4,982 registrants, 10.4%), 20s or younger (2,888 registrants, 6.1%), and 40s or older (261 registrants, 0.5%). Among 28,688 registrants with occupation information, most registrants were students (23,752, 82.8%), followed by office employees (2,197, 7.7%), soldiers (878, 3.1%), public service personnel (342, 1.2%), professionals (273, 1.0%), religious occupations (186, 0.6%), housewives (132, 0.5%), self-employee (82,



**Fig. 1.** Average campaign day and the number of new registrants per campaign (2009–2013).

0.3%), and unemployed (29, 0.1%). Among 18,770 registrants, 86.6% became registrants via University, 4.7% via military organizations, 4.0% via event or campaigns, 2.4% via religion and enterprise group, and 1.7% via individual recruitment.

The public donor recruitment campaigns were continuously conducted each year, with an average campaign length of 37 days in 2009, 56 days in 2010, 65 days in 2011, 82 days in 2012, and 73 days in 2013 (Fig. 1). The donor recruitment campaign was held primarily in metropolitan areas including Seoul (40.9%) and Gyeonggi Province (28.6%). Other regions outside of Seoul included Gangwon Province (6.8%), Incheon City (5.2%), and Daejeon City (1.0%). On average, 73 people registered during the campaign in 2009, 58 in 2010, 53 in 2011, 57 in 2012, and 61 in 2013. When the late cardinal Kim Sou-hwan inspired the public with his corneal donation in 2009, the number of Koreans who made written pledges to donate their organs after death increased significantly (Fig. 1) that 50–60 people newly registered for organ donation in each campaign on average. Furthermore, variety of donor recruitment campaigns were performed by updating homepage banner and social network service (twitter, Facebook, and Cyworld Club) information, and developing smartphone application through collaboration between the government and private organizations in an effort to build information technology infrastructure for donor recruitment.

### Coordination of HSCT and outcomes

The bank coordinated a total of 2,569 matched HSC donors over a four-year period (2010–2013) among the registrants whose locations were confirmed by the Disease & Health Management Network of the KONOS. Of these, 2,491 matched donors were successfully donated HSCs, because 78 matched donors were also included in the KONOS database.

With regard to the coordination of stem cell transplants, the process of donation increased every year with 524 cases in 2010, 617 cases in 2011, 626 cases in 2012, and 802 cases in 2013. Over the four-year period (2010–2013), 731 recruits (47.8%) agreed to donate stem cells, but 798 recruits (52.2%) refused to donate. The annual agreement rate was 52.4% in 2010, 49.7% in 2011, 44.6% in 2012, and 45.9% in 2013. In contrast, the refusal rate was 47.6% in 2010, 50.3% in

2011, 55.4% in 2012, and 54.1% in 2013. The reasons for registry opt-out included refusal to donate (558 people, 70%), family refusal (225 people, 28%), and others (15 people, 2%). Excluding registrants who made a donation commitment but failed to donate stem cells due to HLA mismatch or physical condition of both patients and matched donors, a total of 190 (26.0%) donations were processed. Of the 2,491 processed donations with matched donors over the four-year period (2010–2013), 760 (30.5%) were permanently deferred from donations and 202 were temporarily suspended for donations (8.10%). The 'deferred from donation' refers to unavailable donation due to physical condition of both patients and matched donors before matched donors' decision to agree or disagree to stem cell transplantation. Among reasons for discontinued donations, patient condition, matched donor condition, and unavailable contact information accounted for 14.2% (108 cases), 19.2% (146 cases), and 66.6% (506 cases).

### Processed donations according to registrant characteristics

Processed donations in terms of matched donor characteristics are shown in Table 2. 481 men (31.8%) agreed to stem cell donation and 528 (34.9%) refused to donate stem cells. In comparison, 246 women (16.2%) agreed to stem cell donation and 259 (17.1%) refused to donate. The difference in the agreement rate between genders was not statistically significant ( $P=0.146$ ). According to route of registration, the agreement and refusal rates were as follows: University, 44.0% and 56.0%; event or campaign, 49.1% and 50.9%; religious organization and enterprise, 48.5% and 51.5%; military organization, 42.5% and 57.5%; and individual direct visit, 93.3% and 6.7%, respectively. The differences in terms of route of registration were statistically significant ( $\chi^2=15.560$ ,  $P=0.004$ ).

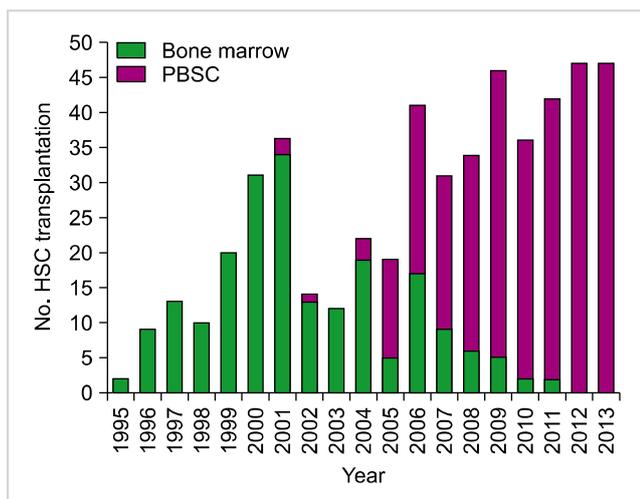
The agreement rate of registrants who agree to receive mail regarding HSCT on the registration form was significantly higher than that of registrants who refused to receive the mail ( $\chi^2=6.103$ ,  $P=0.013$ ).

### Outcomes of stem cell donation

A total of 4,454 stem cell transplants were available in Korea from 1995 to 2013. Of these, the bank successfully coordinated 512 final donors (approximately 11.5%) among

**Table 2.** Processed donations in terms of matched donor characteristics (1995–2013).

Characteristics		Agreement N (%)	Refusal N (%)	$\chi^2$ (P)
Gender (N=1,514)	Male	481 (31.8)	528 (34.9)	0.146 (0.702)
	Female	246 (16.2)	259 (17.1)	
Registration methods (N=1,075)	University	374 (44.0)	476 (56.0)	15.560 (0.004)
	Event or campaign	28 (49.1)	29 (50.9)	
	Religious organization & enterprise	16 (48.5)	17 (51.5)	
	Military organization	51 (42.5)	69 (57.5)	
	Direct visit	14 (93.3)	1 (6.7)	
Agree to receive mail on HSCT (N=717)	Yes	238 (49.7)	241 (50.3)	6.103 (0.013)
	No	95 (39.9)	143 (60.1)	



**Fig. 2.** Unrelated Hematopoietic stem cell (HSC) transplantation and the stem cell source (1995–2013).

newly registered donors. The number of the final donations and source of HSCs from 1995 to 2013 are shown in Fig. 2. The number of final donors gradually increased annually. Unrelated blood marrow transplant (UBMT) showed a declining trend from 2001, while use of PBSC gradually increased from 2004 and became dominant source of transplant from 2012.

Analysis of the characteristics of the 512 final donors revealed a mean age of 24.78 ( $\pm 5.31$ ) years at the time of registration and 30.09 ( $\pm 6.47$ ) years at the time of final donation. The final donors consisted of 392 men (77%) and 120 women (23%). Bone marrow and PBSC accounted for 40.8% and 59.2% of all donations, respectively. University-based donations were most common (49%), followed by event or campaign (21%), individual recruitment (10%), and religious organizations/enterprise (10%). The most common time lap between registration and final donation was five years or less (312 cases, 62%), followed by between 5 and 10 years (125 cases, 24%), 10 years to 15 years (69 cases, 14%), and 15 years or longer (6 cases, 1%).

### Management of new registrants

Korea's data management system using a registrant information-update format has been supported by the government financially from 2009. As a result, 4,150 (8.5%) registrants changed their own information over a five-year period (2009–2013). The most favored method of changing the information was via mail (2,759, 66.5%), followed by telephone (1,030, 24.8%), internet homepage (350, 8.4%), and campaign (11, 0.3%).

In an effort to retain new registrants and maintain the intention of donation, we have regularly sent a web magazine via e-mail twice a year. In addition, calendar is mailed to the registrants with a registrant information-update form once a year. As of the end of 2013, we have sent mails to 29,000 registrants, including information updates, newsletters, and calendars along with an appreciation letter and

souvenirs for the registrants.

## DISCUSSION

This study was conducted to help improve understanding of the program for recruiting and coordinating unrelated HSC donors by analyzing the current status of the HSC bank and its outcomes, with an aim to seek identify ways to establish effective strategies to facilitate registrant enrollment and activate the donation program.

So far, we have made concerted efforts to increase potential donor participation through public campaigns. As a result, a total of 49,037 registrants were listed in the bank from 1994 to 2013, which accounted for 18% of those registered in the KONOS database, and 512 (approximately 11.5%) donors in the bank actually donated their HSCs.

The majority of registrants listed were in their 20s to 30s (83.0%), and were mainly students at the time of registration (82.8%); these observations were consistent with the results of a study conducted by Lee [9], who reported that 49.4% and 31.8% of the total student registrants were students at the time of enrollment and actual donation, respectively. The Match [10] and Laithy [11] also recommended younger donors in order to maximize the odds of success and minimize risks, stressing that the recruitment plan should be focused on younger potential donors or students for all bone marrow coordination centers. University students may be regarded as suitable donors since they typically remain in the database for longer periods of time with a higher possibility to donate.

Analysis of processed or unprocessed donations from 2010 to 2013 revealed agreement and refusal rates for stem cell donation near 50%, which were also consistent with previous reports by Kim *et al.*, who also reported an agreement rate in Korea's unrelated stem cell donors of approximately 50%; however, the agreement rate was lower than that of the advanced countries [12]. Although medical advances in bone marrow transplantation techniques and supportive care have led to improved outcomes and better survival of many long-term HSCT survivors, prejudices and negative responses to HSCT remain unchanged. Among 1,000 Korean people, those willing to donate blood, organ, and bone marrow were 40.6%, 29.2% and 14.3%, respectively. The cited reasons for reluctance to donate bone marrow were 'fear of bone marrow harvest procedures' (52.3%) and 'to avoid body damage' (26.5%) [8].

As far as stem cell donation is concerned, all donors are carefully prescreened to ensure they are healthy and the procedure poses minimal risks to them. However, serious misconceptions about marrow donation remain rampant. Therefore, mitigating doubts and worries about donation will ensure that potential donors are provided with accurate information and knowledge about stem cell donation [8]. All bone marrow coordination centers should make first priority to increase the number of registrants in parallel with intensive training and campaigns to offer donors accu-

rate knowledge and confidence about stem cell donation. In addition, to encourage registrants to maintain their conviction and make donations, the effective follow-up management systems should be established to ensure donation retention and update their contact information.

Analysis of successful donations in terms of registration route showed that higher refusal rates among registrants recruited via University or street campaigns compared to their agreement rates, while 93.0% of recruits who made by direct visits pledged stem cell donation. Another factor that led to successful donation was registrants' positive attitude toward the intended receipt of mails. These results indicated that matched donors' full awareness and firm conviction about stem cell donation at the time of registration could be one of the critical factors for successful donation. Only 29.5% of registrants were aware of stem cell-related donation procedures before initiation of a coordination process [9], reflecting that people made their stem donation pledges with little knowledge on the donation process.

Under circumstances where a mature social atmosphere to actively participate in stem cell donation has yet to be created, there are many restrictions to encouraging people to make a donation pledge via direct visits. In addition, it is also difficult to determine whether matched donors will ultimately commit to donation. These issues may be addressed via expansion of donation culture to a social level; to this end, the government and all registry centers should endeavor to enhance public awareness of stem cell donation and play a pivotal role in developing a social atmosphere to respect the final donor who appreciates the value of their donation.

Systematic management should be required after enrollment to ensure that registrants remain enrolled. It was noteworthy that actual donation in less than one year and between one and two years comprised more than half of the cases of donation within five years after enrollment. With this in mind, special training and education campaigns should be developed for those newly recruited within two years after enrollment to ensure their commitment to become a final donor. Furthermore, each bone marrow coordination center should reaffirm the matched donor's commitment to join the life-sharing campaign at the time of enrollment in order to avoid unnecessary expenditure of financial and human resources.

We have spared no efforts to undertake better ex facto management of registrants via diverse methods. Hershberger *et al.* [13] reported that the critical components of assisting patients in the decision-making process included information about treatment options provided by clinicians, clinicians' attitudes, patients' preferences and values, and in-depth understanding of clinicians about individual circumstances, when patients examined aspects of information processing. Lee [9] also reported that continuous exposure to stem cell-related information is helpful in making final donation decision in registrants after enrollment. These studies indicated that individual attitude of all healthcare providers involved in registration, coordination, and donation procedures may be

an influencing factor in assisting registrants in the decision-making process. In this context, healthcare providers must support the registrant's decision and conviction through a sustained linkage system, coupled with more systematic training programs.

With the full recognition of the registrant's information management system to increase the number of registrants and effective use of stem cells since 2011, the KONOS has endeavored to develop an information system to easily identify HLA-matched volunteers [14]. Nevertheless, the number of registrants is substantially smaller than that of recipients registered in the KONOS's waiting list. Unlike other Western multinational countries, Korean people fortunately have a single genetic makeup. Thus, if approximately 1 million donors, one-tenth level of registrants required in the Western countries, are newly recruited from donation-available unrelated volunteers, Korean patients with diseases treatable by HSCT can find a suitably unrelated HLA-matched donors [15].

Under an effective management system to handle all data related to bone marrow donation, including the number of transplants, and prognosis following transplantation, more accurate evaluation should be performed on the HSCT that made substantial contribution to reducing complications and increasing patient survival rates in a variety of hematologic diseases. Further, additional healthcare resources, such as nurses and coordinators, should be recruited to ensure more efficient management of new registrants and stem cell coordination functions. Financial stability should be secured from the government to undertake the current registration program that is directly linked to the lives of 472 leukemia patients each year.

Critical components to activate the program for marrow donation should include proactive government policies and financing, updated versions of efficient registration procedures and related programs, development of donation-related training programs, systematization of follow-up management programs to retain registrant commitment, formation of a social atmosphere to respect the donors and their families, and active efforts of all healthcare providers. Through increased activation of hematopoietic cell donation, among other activities, we hope that individual life-sharing consciousness may be raised to create a donation culture via social consensus.

Our study had a limitation in that we found some difficulty in performing statistical analysis with limited data, as the majority of data owned by the HSC bank was based on the reports provided by the KONOS and other bone marrow coordination centers. Thus, data collection and management should be made in a more detailed and systematic manner.

#### Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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