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ABSTRACTS
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Efficient and Safe Non-Medical Cord Blood Donor Authorisation in a Public Cord Blood Bank

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Aims:
The NHS Cord Blood Bank (CBB) banks an average of 2000 cord blood units (CBUs) per year. FACT-NetCord standards mandate that a medical review of CBUs is completed prior to listing for search. Historically all such reviews were undertaken by medical staff. Facing high workload & limited medical staff resources we implemented a novel way of managing this review process.

Methods:
NHS-CBB employs healthcare scientists (HCS) experienced in managing CB collection operations but not medically qualified. HCS were systematically trained in the application of UK CB donor selection guidelines & completed a period of supervised donor file authorisation. Operating procedures were developed describing scope & limits of donor authorisation by HCS. Donor medical histories out of scope mandate referral to clinical staff. Several months after initial implementation (phase 1), the internal process was further refined to enhance scope for HCS donor authorisation (phase 2). After full implementation, 200 random donor files were audited to analyse safety & efficiency of the new process & compare phases 1 & 2. All CBUs selected for release continue to have a full review of medical, processing & quality data undertaken by a physician.

Results:
All measurements (adherence to procedures by all staff, donor authorisation rates by HCS, turn-around times) improved from phase 1 to phase 2. HCS compliance with all aspects of the donor authorisation process increased from 96 to 99%. HCS authorisation rates increased from 32 to 48% of CBUs. Clinical team compliance with their respective procedures was 82-84%. Percentage of files authorised for listing within 90 days of CBU collection improved from 10% to 56% (historically single figure rates).

Conclusions:
Non-medical donor authorisation is safe & can help turn-around in a resource-limited environment. Authorisation rates by HCS improve with personal experience & can be safely increased to a point by adjusting processes. However, there is ongoing need for clinically qualified staff to manage referred files. The complexity of managing referred files had been underestimated, & need for regular refresher training of all staff has been identified. NHS-CBB has been successfully re-accredited by FACT-NetCord since introducing this system. The bank enjoyed a record issue rate in 2017 & the enhanced searchable inventory may have contributed.
The NHS Cord Blood Bank Activity and Patient Outcomes: Trends in the Last 15 Years

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Background and aims:
Umbilical cord blood (UCB) is a frequently utilised source of stem cells for patients undergoing haematopoietic stem cell transplantation. The NHS Cord Blood Bank (CBB) is one of two public UCB banks operating in the UK, and has been FACT-Netcord accredited since 2004. The present work aims to summarise the activity of NHS CBB over 15 years.

Methods:
Patient, transplant and donation data were obtained from the Eurocord Registry and NHSBT databases for the period April 2002 to March 2017. Characteristics were compared across 5-year time periods (A: 2002-06, B: 2007-11, C: 2012-17) using Fisher’s exact test (categorical variables), log-rank test (Kaplan-Meier estimates of overall survival [OS]) and Gray’s test (cumulative incidence).

Results:
The number of banked and transplanted cords increased over the 15-year period, from A: 986 banked and 22 transplanted per year to C: 2,278 banked and 53 transplanted per year on average. There are currently 23,321 units available in the NHS CBB (October 2017), of which c.17,000 have a TNC above 90x10⁷. Transplant outcome data were available for 452 first UCB transplants using 478 NHS CBB units during 2002-2017. Of the 272 adult transplants (patients≥16 years), across the study period the majority were for male patients to treat acute leukaemia with reduced intensity conditioning. An increasing number were double cord transplants (A: 58%, B: 81%, C: 90%, p<0.0001). OS at one year post-transplant, myeloid engraftment at 60 days and one-year post-transplant relapse rates were similar across the study period (OS, A: 55%, B: 53%, C: 58%, p=0.78; engraftment, A: 79%, B: 87%, C: 90%, p=0.36; relapse, A: 18%, B: 18%, C: 22%, p=0.70). Of the 180 paediatric transplants, across the study period the majority were for male patients to treat acute leukaemia or non-malignant blood disorders with myeloablative conditioning. Most were single cord transplants. One-year OS and 60-day myeloid engraftment were similar across the study period, although one-year relapse rates fell and then rose again (OS, A: 63%, B: 76%, C: 65%, p=0.36; engraftment, A: 89%, B: 91%, C: 85%, p=0.33; relapse: A: 18%, B: 7%, C: 23%, p=0.05).

Conclusions:
The NHS CBB has increased in size and in provision of UCB transplants for patients requiring haematopoietic stem cell transplant over the time period analysed. Outcomes after UCB transplant using units from our bank are favourable and compare well with outcomes reported in the literature.
Comparison of Ex Utero and in Utero Cord Blood Collection Methods, Canadian Blood Services Cord Blood Bank

Karen Mostert¹, Mike Halpenny¹, Daniel Bartlett¹, Todd Campbell¹, Nicholas Dibdin¹, Tanya Petraszko¹, David Allan¹, Heidi Elmoazzen¹

¹Canadian Blood Services, Cord Blood Bank, Ottawa

Aim:
Cord blood stem cells can be collected using two common techniques: ex utero or in utero cord blood collections. Canadian Blood Services Cord Blood Bank (CBS CBB) has operated using both models since September 2013 at The Ottawa Hospital, Civic and General Campuses in Ottawa, Canada. This study compares both models to evaluate the optimal collection model for the cord blood bank. There are multiple factors that influence a successful collection and both models pose different challenges. Ultimately cord blood (CB) collections must have sufficient volume and a high total nucleated cell count (TNC) to qualify for storage [1.3 x 10⁹ Non-Caucasian/1.5 x 10⁹ Caucasian] into the public bank. Our previous data (Transfusion. 2016 Mar; 56(3)) confirms that delayed cord clamping has a significant negative impact on the volume of cord blood and TNC count for both collection techniques.

Methods:
A retrospective analysis comparing ex utero and in utero collections with respect to volume, TNC, bankability, quality events reported and contamination rates, was performed for CB units collected between September 30, 2013 and December 08, 2017. Further analysis was conducted with respect to the influencing factors for both collection models such as hospital engagement and training.

Results:
A total of 8705 CB units were collected over a five-year period: 4776 (55%) and 3929 (45%) CB units were collected using ex utero and in utero collection methods, respectively. The ex utero model produced 4464 (93%) units that met acceptable volume; 1113 units for production (23.3% eligible unit rate), a TNC median of 1.76 X 10⁹, with a bankable rate of collections of 17%, and a reported quality event rate of 23%. The in utero model produced 3305 (84%) units that met acceptable volume; 647 units for production (16.5% eligible unit rate), a TNC median of 1.77 X 10⁹, with a bankable rate of collections of 12% and a reported quality event rate of 53%. Contamination rates were 0.15% and 0.41% for ex utero and in utero respectively.

Conclusions:
Our results indicate that the ex utero collection model using dedicated CBS CBB staff performed better than the in utero model. The ex utero collection method has resulted in more qualifying units stored, lower contamination rates and less quality events compared to the in utero model. Effective December 2017, CBS CBB no longer operates the in utero collection site and maintains an ex utero model at all collection hospitals.
P-04-17-1: Selection of Donor and Stem Cell Source

Friday June 29, 2018 | 10:30 – 11:00

A New Registry Lead Initiative Supporting UK Transplant Centres in Selection, Acquisition and Provision of Cord Blood Units for Haematopoietic Stem Cell Transplantation

Laila Roberts¹, Daniel Gibson², Charlotte Green¹, Roger Horton², Sharon Vivers¹, Irina Evseeva¹

¹Anthony Nolan, Operations, London
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Introduction and Aims:
Selection and provision of Cord Blood Units (CBU) for patients in need of Umbilical Cord Blood Transplantation (UCBT) is a complex process. A range of quality parameters, the practices of Cord Blood Banks (CBB) worldwide and an overall lower usage of UCBT by Transplant Centres (TCs) mean TCs often seek additional support when requesting CBUs. Anthony Nolan piloted two new services: “CBU Shortlisting Service” and “CBU report quality checklist service” to find out if a proactive approach can improve TC experience of requesting CBUs by optimising the process.

Methods:
Two UK TCs received the pilot services over a 10 month period during 2016-2017. Services were provided to all patients for whom formal CBU searches were requested. For each patient we produced a comparison table with suitability and quality parameters of ten shortlisted CBUs based on national guidelines (Hough, 2016), quality checklists for all CBU Reports based on NetCord-FACT international standards (6th edition, 2016) and suitability/quality check at work-up request stage. Patients undergoing formal CBU search process in the 10 month period prior to the pilot were used as the control group – 20 patients from TC1 and 40 patients from TC2. Factors compared included number of CBU searches, provisions, cancellation rate and user feedback.

Results:
CBU searches were run for 30 adult and paediatric patients from TC1. 37% of cases resulted in CBU provision compared to 10% in control group. CBU work-up cancellation rate fell from 62.5% to 25%. The Clinical Team found the pilot helpful in optimising the process of cord selection, giving additional confidence in requesting CBUs.
19 paediatric patients from TC2 were included in the pilot. No significant differences in the factors measured were identified, however TC reported that the pilot was of benefit in optimising their process of requesting CBUs and provided reassurance at all stages of CBU acquisition.

Conclusions:
Registries can improve TC experience of CBU requests by enhancing search reports with a shortlist of suitable CBUs, flagging product quality issues and CBB operational specifics. Increasing communication and support helps to optimise all stages of CBU request, and to decrease shipment cancellations. Anthony Nolan and NHSBT have now launched the Cord Support programme in the UK including a range of free educational and advisory services covering all areas of CBU selection and provision.
Expedited Search Process: Selection, Typing and Transplant (STaT)

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¹Be the Match/National Marrow Donor Program, Case Management and Operations Services, Minneapolis

Aims:
Patients transplanted earlier in their disease have better outcomes. Haploidentical transplants continue to increase in part due to the time and cost associated with unrelated donor transplant. We aimed to determine if NMDP could consistently deliver an available and screened donor ready to be requested for workup in 14 calendar days for patients in need of an urgent transplant and meet the transplant centers (TC) targeted collection date.

Methods:
Three USA TCs enrolled patients in need of an urgent transplant, defined as <6 weeks from start of search to transplant, into the STaT process. TCs communicated their ranked donor list, product preference (PBSC and/or marrow) and target transplant date to NMDP. The donor center/registry received a message with product preference and timeline to transplant. The additional information provided by the TC was used to educate the donor and confirm availability and willingness to meet the desired timeline and product preference. All donors were confirmatory typed using an NMDP contract laboratory with 3-day HLA turnaround time. Success was defined as having health history and availability screening, infectious disease and HLA testing for a workup ready donor to the TC by day 14. TCs requested donors for workup according to standard process.

Results:
To date, 54 patients enrolled in the STaT process. For patients with donors requested for testing, 37/42 (88%) were delivered a workup ready donor within 14 calendar days. Nineteen patients proceeded to transplant with a median time of 70 days (range 22-162; 2 directly to work up). Of those transplanted, 3 (16%) met the targeted timeline to transplant, 14 (74%) had patient related delays, and 2 (10%) had a delay in finding a suitable donor. Twenty-one (39%) of the patients did not proceed to transplant and no longer have an active search for reasons including: patient was no longer a transplant candidate, an alternate source was selected (cord blood, haplo), or patient treatment plan changed. Of the remaining patients, 6 have scheduled transplant dates and 8 have transplant dates pending.

Conclusions:
In a majority of cases NMDP can deliver a workup ready donor for an urgent patient. However, even with a donor ready to proceed to workup many delays occur, with most being patient related. Rapid time to transplant can be successful, however, additional process improvements by registries and TCs are needed to optimize the process.
British Bone Marrow Registry Activity and Patient Outcomes: Trends in the Last 15 Years

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Background and aims:
The success of unrelated donor searches relies on the existence of large international donor registries. The British Bone Marrow Registry (BBMR) is the UK’s second largest volunteer stem cell donor registry, with 347,757 active donors as of 1st April 2017. In the present work authors provide an overview of donation activity of BBMR over 15 years including patient outcome data.

Methods:
Data on donation characteristics were extracted from BBMR databases and on patient outcome from the EBMT database (where available). Comparisons for categorical variables were performed by χ² or Fisher’s exact tests and for continuous variables by Mann-Whitney test across three, 5-year long time periods (period A: 2002-2006, period B: 2007-2011, period C: 2012-2016). Kaplan-Meier estimates of overall survival were compared using the log-rank test.

Results:
Over the last 15 years 2378 haematopoietic stem cell donations were performed from BBMR donors (53% within the UK). The number of donations gradually increased over time (A: 567, B: 691, C: 1120). Use of bone marrow (rather than peripheral blood - PB) as the source of stem cells declined (A: 46%, B: 27%, C: 15%, p<0.001). Male donors were increasingly preferred to female donors (A: 57%, B: 65%, C: 70%, p<0.001). Median donor age fell slightly recently (A: 37, B: 37, C: 34 years, p=0.022).Clinical outcome data were available for 1536 transplants. Patient median age significantly increased by period (A: 34, B: 44, C: 53 years, p<0.001). The main transplant indication remained acute leukaemias in all time periods (A: 51%, B: 47%, C: 50%), but the relative proportion of the other diagnoses changed by time (p<0.001). Over time reduced intensity (RIC)/non-myeloablative conditioning regimens became more commonly applied than myeloablative regimens (A: 45%, B: 57%, C: 64%, p<0.001). The incidence of grades II-IV acute GVHD reduced (A: 30%, B: 32%, C: 25%, p<0.025). Overall survival did not change significantly by time (at 5 years, A: 49%, B: 48%, C: 50%, p=0.96).

Conclusions:
BBMR provides an increasing number of stem cell donations within the UK and internationally. Our survey confirms recent trends observed in the allogeneic HSCT field such as preference for young male donors and PB stem cell source instead of bone marrow, increasing patient age and use of RIC, and some shift in diagnostic indications. Outcomes after HSCT using BBMR donors are favourable and compare well with outcomes in the literature.
Hematopoietic stem cell (HPC) transplant has become a clinical option, and in some cases the standard of care, for the treatment of numerous diseases including hematological malignancies and hereditary immune system and metabolic disorders. Due to improvement in post-transplant outcomes and increased indications for transplantation, combined with an aging population and reduction in family size, use of unrelated donors and cord blood units (CBUs) in allogeneic HPC transplant continues to rise. OneMatch surveillance of trends in product choice allows registry adaptation to changes in the field of transplantation medicine and enables allocation of resources to best meet patient need. In 2017, OneMatch provided search services to 1,122 Canadian patients residing outside of Quebec, representing a 28% increase in Canadian search activity from 2016 and a 44% increase over 2015. Of these patient searches, 92% (n=1,034) were newly-created, whereas the remaining searches had been re-initiated following a period of search dormancy (n=88). OneMatch facilitated collection and/or procurement of 417 products on behalf of Canadian patients compared with 328 and 365 in 2016 and 2015, respectively. Of adult donor grafts procured (n=383), peripheral blood stem cells (PBSC) comprised 90.6% of product compared with of 83.4% in 2016 (n=309). Donor lymphocyte infusion (DLI) accounted for only 3% of total product requested. Despite advances in haploidentical transplantation, use of CBUs and mismatched adult donors have remained constant; CBU has comprised 5% of grafts selected in both 2017 and 2016, and use of mismatched donors accounted for 76.8% and 77.7% of donor products, excluding DLI, respectively. Use of domestic donors has similarly remained consistent with OneMatch donors comprising 12.5% of donors collected for Canadian patients during 2017 with a modest increase in use from 2016 (10.4%). Despite historic aversion to HLA-DRB1 mismatch, an increase in disparity at this locus among mismatched donors selected for transplant has been observed; frequency of DRB1 disparity has increased from 3% to 6% to 9% over the past three consecutive years, although HLA-A remains the predominant disparate locus among mismatched transplants. Together, these data demonstrate a steady increase in allogeneic transplant in Canada and support our ongoing commitment to recruitment and retention of altruistic donors and provision of allogeneic search services.
O-08-45-1: Selection of Donor and Stem Cell Source

Friday June 29, 2018 | 10:30 – 11:00

Keeping Unrelated Donors in the Race: Determining How Time to Transplant for Urgent Patients Impacts Therapy Selection and What Registries Can Do to Remain Competitive with Alternate Therapies

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¹National Marrow Donor Program / Be The Match, Case Management, Minneapolis

Aim:
Time to transplant is an important factor for better patient outcomes. The search for a suitable donor is typically the longest step for a patient receiving an unrelated allogeneic transplant. We sought to understand if the length of time involved in the search for an unrelated allogeneic donor (URD) impacts therapy selection for urgent patients and potential targets which, if achieved, would allow TCs to consider an URD even for urgent patients.

Method:
73 coordinators from 61 U.S. transplant centers (TCs) participated in a survey aimed at understanding TC needs surrounding time to transplant. There were six questions as part of the survey including asking whether the TC would like to participate in a follow-up call with NMDP on this topic. 17 TC coordinators participated in focus group calls where six additional questions were discussed regarding the donor search phase, donor clearance, and meeting requested collection dates.

Results:
78% of survey respondents felt that up to 50% of their patient population were in need of transplant within 4 weeks of initiating an URD search. 66% of respondents cited the URD search as a common barrier when managing an urgent timeline. 64% of respondents indicated that they are likely or highly likely to select an alternate donor source (haplo or cord) due to urgency and a lack of confidence that an URD could meet their timeframe. 85% of respondents would be encouraged to use an URD for patients in need of an urgent transplant if donor clearance could reliably be obtained within 4 weeks of initiating the URD search.

Additional feedback from focus group calls confirmed that TCs would like to receive donor clearance quickly to ensure they have a suitable donor early in the transplant window. Comments included "We would like to receive clearance as soon as possible; the closer it gets to transplant the more stressful it is for everyone" and "knowing we can get the (collection) dates we request would be most beneficial".

Conclusion:
There is a significant need for unrelated allogeneic transplant within four weeks from the time of search initiation. If a fully matched URD could be reliably cleared within four weeks TCs would be encouraged to consider a fully matched URD as the patient’s best transplant option over an alternate cell source. In order to accommodate TC needs for urgent patients we need to identify and clear donors as quickly as possible and consistently meet requested collection dates.
Finding the Optimal Time to Request a Work-Up: An Analysis of the Unrelated Search Process in the Netherlands

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\textsuperscript{1}Matchis Foundation, Transplant Center Services, LEIDEN

**Aim:**
Analyse the unrelated donor search to identify delaying factors, allowing for process optimization.

**Methods:**
We analyzed search cases of all Dutch patients submitted to our registry in 2017 (n=610). Efficiency of the search process was evaluated by calculating the time between start search and donor found or collection. A donor was found if they matched the HLA criteria of the transplant center after confirmatory typing.

We analyzed all work-up (WU) cases (PBSC and BM) for which a request was submitted to our registry in 2017 (n = 511). Cases were included in the efficiency analyses when a collection actually took place (n= 327). These were further divided into 5 groups by time span from submission date to requested collection date to determine the optimal time span, as follows 1-20 days (N=35), 21-27 days (N=67), 28-34 days (N=77), 35-41 days (N=66) and >41 days (N=82).

**Results:**
Time between start of the search and BM/PBSC collection is on average 3 months. It takes on average 24.5 days with a median of 21 days to identify a suitable donor. In 60 cases no suitable donor or CBU was found.

The WU process for BM/PBSC takes on average 44 days with a median of 39 days from start WU until collection. On average, for each patient reaching a collection, 1.4 WUs were requested.

When looking at the specific groups, the average WU request to collection date was, 29.5, 31.9, 37.4, 41.7 and 67.1 days respectively. The percentage of collections being performed on the requested collection dates were 23%, 30%, 43%, 55% and 50%. If the requested date was not provided (and no postponements occurred) the average deviation was 8.7, 6.1, 7.0, 5.2 and 4.8 days. The amount of WU requests needed to reach collection were 1.7, 1.6, 1.2, 1.3 and 1.3. The percentage of postponements which occurred were: 17 %, 18%, 21%, 8% and 26% respectively.

**Conclusion:**
To optimize patient care, a WU should get the desired collection date in most cases and have a short delay if the desired date is not available. Also, a WU should have fewer postponements to reduce costs. The best combination of these two factors is found in the group 35-41 days. Furthermore, only 1.3 WU requests were needed to reach a collection. Remarkably, this group has a very low percentage of postponements, not fitting the trend of an increase in postponements with earlier request dates. We think this could be because a specific group of stable patients is filtered out by selecting this group.
Unrelated Argentine Donors in Hematopoietic Stem Cell (HSC) Transplant from 2008 to 2017. Results from the Argentine Registry

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¹Incuai, Argentine HSC Registry, Buenos Aires

Introduction:
 Argentine HSC Donors Registry has been created in 2003 to offer an option for patients (pts) that need an Hematopoietic stem cell transplant with unrelated donor since they have malignant or non malignant diseases without a related histoidentical family donor. Our second objective was the incorporation of Argentine USC donors to the international database Bone Marrow Donor Worldwide. In 2014 the Argentine Registry started HLA typing in high resolution and significantly increased the recruitment of donors impacting in a positive way in the amount of HSC collection as from 2015. On 2017 we doubled the number of donors and we hope that the greatest impact will be reflected as of 2018.

Materials and methods:
one hundred and five HSC transplants for one hundred and one patients have been included in this study that required blood stem cell transplantation with unrelated argentine donor during 2008-2017, four of them required two transplants, of which 75 were transplanted in Argentine Transplant Centers (TC) and 30 in 13 different international Registries (Germany, Australia, Belgium, Canada, USA, Spain, France, Hungary, Italy, Norway, Portugal, United Kingdom, Uruguay). For the evaluation we included, the source of HSC collection, age, diagnosis, time of search, and overall survival. The median age of the argentine pts was 14 years old and 41 years old for international pts. The HSC source was bone marrow in 34 pts (32%) and peripheral blood in 71 pts (68%). The diagnosis was: Acute Lymphoblastic Leukemia 27 (26%), Acute Myeloblastic Leukemia 21 (20%), Severe Aplastic Anemia 12 (11%), Myelodisplastic Syndrome 11 (10%), Non Hodgkin lymphoma 4 (4%), Fanconi Anemia 3 (3%), DHIS 3 (3%), other diagnosis 15 (14). Considering the patient / donor high resolution HLA compatibility in HLA-A, B, C, DRB1 and DQB1, 53 (54 %) where 10/10, 39 (39 %) were 9/10 and 7 (7%) was 8/10.

Results:
The median time of response for donor search request and shipping the HLA sample was 11 days. The median time from a search request to the transplant with an unrelated argentine donor for argentine and foregein pts was of 3 months and 27 days. At one year the overall survival was 74 %. The overall survival at one year for pts according to the HLA compatibility patient/donor was 74% for 10/10 and 69% for 9/10.

Conclusion:
This shows the importance of having an Unrelated Donors Registry in our country. In 2008only 2,4 % or argentine patients has a local donor, and 19 % in 2017
Genebandhu: An Emerging Hematopoietic Stem Cell Registry from India

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\textsuperscript{2}Amity Institute of Biotechnology, Amity University, Noida

Background:
Genebandhu stem cell registry has been actively recruiting matched unrelated hematopoietic stem cell donors since May 2012. Matched Unrelated Donor (MUD) Hematopoietic stem cell transplantation (HSCT) is one of the options for about 70% of patients who do not have a Matched Related Donor (MRD).

Aims:
Reviewing systematically operations/working protocol and outcomes of Genebandhu since May 2012 to understand the importance of an emerging registry like Genebandhu in Indian population.

Material and Methods:
Retrospective analysis of the recruited donors was done in term of Genebandhu working protocol/operations and outcomes. Recruitment of Matched unrelated hematopoietic stem cell donor were planned and organized to spread awareness among the people and motivate them to register themselves as donor in the database. Till date 9862 donors were being recruited in Genebandhu database since May 2012

Results:
Genebandhu have organized over 135 donor recruitment camp in these last five years and able to recruit 9682 donors. All these donors have consented to donate Hematopoietic Stem Cells (HSC) if matched with a patient. HLA typing of 6629 donors is completed. Genebandhu has facilitated lifesaving of 11 HSCT from this small number of typed donors. Out of these 11, 2 were overseas transplant patients.

Conclusions:
To conclude, present study elaborate the ways to establish effective strategies to facilitate more donor recruitment; the need of this hour for country like India, where in every 6 minutes, somebody is diagnosed with hematological disorders. This data also implicate that amplified efforts are needed to increase donor recruitment to create a larger data pool of matched unrelated hematopoietic stem cell donor, so that chances of saving many vital lives are increased by multiple folds in India.
A Two-Year Evaluation of the Hematopoietic Stem Cell Transplantation (HSCT) Scenario from the Brazilian Bone Marrow Donor Registry (REDOME)

Juliana Cardoso¹, Rafael Furukawa¹, Natiele Tavares¹, Alexandre Almada¹, Danielli Oliveira¹

¹Brazilian Bone Marrow Donor Registry (REDOME), Rio de Janeiro

Aims:
Our purpose was to show how is the Brazilian HSCT reality in terms of HLA match, mismatches setted up, clinical indications, stem cell source and donors’ country origin.

Methods:
We evaluated 773 non-related HSCTs performed between January 2016 and December 2017.

Results:
The main stem cell source was bone marrow (BM) (60.6% - 2016, 61.7% - 2017) while peripheral blood stem cells (PBSC) was the second most selected (38.3% - 2016, 36.9% - 2017) and cord blood unit (CB), the third one (2.9% - 2016 and 2017). Regards to the donor’s origin, of all BM collected the majority was from Brazilian donors registered at REDOME (79% -2016, 74% - 2017 Considering PBSC donors, REDOME was also the main provider (66%). Finally, CBU reflected a different scenario where the main origin was international (73% - 2016, 64% - 2017 x 27% - 2016 and 36% - 2017 of the REDOME origin). The HLA match analysis considered only BM and PBSC and revealed that 71.4% of BM donors, presented 10x10 HLA match, and this result was 76.6% among PBSC donors,9x10 HLA match showed us that BM was the main stem cell source (27.7%) compared to PBSC (23.4%). We also had 8x10 HLA match and it represented 0.9% of total BM transplants. When we investigated the HLA loci mismatches, we found that the main locus enrolled was A locus (50.5%), followed by B (25%), DQB1 (13.8%), C (11.2%) and DRB1 loci (3.1%). Lastly, we aimed to look up if there was a relation between the clinical indication and the donor HLA match. According to the disease classification, there was no difference between the two HLA match groups - 10x10 and 9x10- as follows Acute Leukemias (57% x 60%), Aplastic Anemias (15% x 10%), Myelodysplastic Syndrome (9% x 10%), Chronic Leukemias (6% x 7%), Immunodeficiencies (5% x 4%) and Non-Hodgkin lymphoma (3% x 5%).

Discussion and Conclusion:
We confirmed previous observations that, in Brazil, the main cell source chosen for HSCT is the BM and we noticed a slight decrease (4%) in PBSC usage. Following international recommendations, the HSC source is a decision made by the donor and the physician and it involves many aspects, the other factors evaluated were quite similar what has been seen worldwide. This study was the first that brought together the two-year Brazilian experience of HSC transplantation, in terms of source chosen and HLA mismatches setted up and may guide other studies helping us to better understand this Brazilian pattern.
Extended Typing and Confirmatory Typing from Brazilian Donors to International Patients in 2017

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Aims:
The aim of this study was to demonstrate how long it takes between the request date and result date for HLA extended typing and confirmatory typing from Brazilian REDOME donors to international patients in 2017.

Methods:
For this analysis, we selected all 88 donors that had their Hematopoietic Stem Cells (HSCs) exported in 2017 and all HLA extended typing and confirmatory typing requested in the same year, comparing the median between these two scenarios.

Results:
Considering the 88 donors only 32% were required to perform HLA extended typing and 68% were straight to confirmatory typing. The median time, from the date request arrive at register until result date, for HLA extended typing results was 21 days while the median time including all HLA extended typing requests in 2017 (n=2825) was 26 days, thus a disparity of 5 days. In the confirmatory testing phase, again considering request date until result date, requests were dealt on a median time of 12 days and 2% of these requests included confirmatory typing along with the workup phase due to the urgent nature of patient. Comparing these data with the 1156 CT requests in 2017, the median time was 13 days, so a difference of only 1 day was found between the first and the second scenario.

Conclusions:
To sum up, this survey has demonstrated that the study of each phase of the process of HSC donation highlightes the major challenges and opportunities to improvement. In this context, we can quote the delay of HLA extended typing result, compared to World Marrow Donor Association (WMDA) recommendation of 15 days which can justify the fact that majority of donor requests included CT tests directly. In addition, our great challenge is to understand the reason for such lag (21 and 26 days) always considering the main objective of REDOME, offer high quality services to our network in Brazil and abroad, as well as to patients waiting for HSC transplantation.
Family and Social Pressure as a Main Factor in Donor Back-out and How to Address It

Raghu Rajagopal

1Datri Blood Stem Cell Donors Registry, CEO, Chennai

Background:
DATRI currently has over 300,000 donors. A significant number of back-out by donors (more than 40%) is due to influencers in donors life (nearly 30%). DATRI’s objective is to achieve high retention rate and recruit large number of donors. Thus a new strategy was conceived to counsel influencers in a donors life to ensure successful donations.

Methods:
After retrospective analysis for the reasons of back-outs for the period 2015-2016, new guidelines for recruitment & counselling were implemented:

At the recruitment stage - a) Donors were asked if they would be able to take independent decisions or if influencers would be involved in the decision making process. They also had to indicate who these influencers were. b) In smaller city colleges, parental consent was obtained especially for female donors. c) Local spiritual and religious leaders were involved in communities with dominant belief systems.

At the counseling stage - a) Heads of educational institutions and volunteers were asked for assistance during counselling. b) Dedicated volunteers, from corporate organizations and institutions were asked to assist during counselling. c) Donors from similar backgrounds were requested to assist while counselling new donors.

Matched donors were mapped back to a KPI metric related to donor recruiters. Donor back-out adversely impacts the donor recruiters KPI; hence only good quality donors are recruited

Results:
After implementation of the above strategies, a decrease in back-out ratio from 48 % (in period 2009-2016) to 27% in 2017 was accomplished. Back-out due to influencers reduced from 23% (in 2009-2016) to 6% (in 2017).

This decrease in back-out was despite an increase in donor recruitments. 176,217 donors were recruited from 2009-2016; whereas 126,278 were recruited in 2017. With an increase in the registered donor base, we also saw an increase in counselling allocation from 946 in 2009-2016 to 699 in 2017.

By effective counselling of the influencers, we were able to increase the number of CT fulfilled to 416 in 2017 as compared to 201 CT for the period 2009-2016.

Discussion:
Our study highlights the characteristics of influencers in India. Counselling the influential family members, community and religious leaders is often as important as counselling the donor. By adopting the above methods and efficiently seeking the assistance of veteran donors, we were able decrease the back-out by matched donors.
Given the fact that there was no structure in Greece to facilitate populating and managing a national bone marrow donors pool, CBMDP -Save a Life was established in 2010 by doctors and members of the local academic community. It operates within the framework of the University of Patras and under the legal umbrella of the Hellenic Transplant Organization (HTO). The registry's goal is to reach 120,000 HR- A,B,C, DRB1 typed donors by 2020, based on a research in which we analyzed HLA haplotype frequencies of the Hellenic ethnicity. We found that a Hellenic registry of ~250,000 donors is sufficient to meet the needs of about 50% of transplants performed for Greek patients. Until 2014, all grafts for Greek patients were imported (~120 grafts/year). Nearly half of the unrelated transplants were performed with mismatched donors, since it was impossible to identify a fully matched donor. When CBMDP began operating, it faced several challenges. First, we outsourced processes to partners, allowing for the centre to focus on network supervision, fundraising, donor management and QA policies. We signed collaboration agreements with >85 Recruitment Hubs across Greece with the task of raising awareness and recruiting donors on behalf of the Centre. These hubs operate under the supervision of CBMDP, which trains members of the hubs and supplies them with material. Moreover, we established collaborations with Support Medical Hubs that operate within hospital blood banks or other medical departments and support all medical processes when a matching donor is found in their area. Graft collection is performed at collection centres that operate within fully accredited Transplant Units licensed by the public health system and are EBMT and FDA registered. Each of the above collaborators of the Centre has a well-defined role in the process from the donor recruitment to the confirmatory typing and the donor work up. Graft collection is done after written information and consent of the HTO. The Centre's financial resources and sustainability stem from provisions from the University of Patras, donations, sponsorships and revenue from services. In 2018, CBMDP counts >50,000 HR typed donors, enlisting an average of >2,000 new donors/month. It has provided >70 grafts to patients worldwide since 2013, with a sharp increase of provided grafts/year. It is connected via EMDIS to other registries and is a qualified member of WMDA while in the process of submitting for WMDA accreditation.
P-16-54-2: Emerging Registries

Friday June 29, 2018 | 15:30 – 16:00

Enriching Stem Cell Donor Ethnic Diversity by the Establishment of a National HSCT Donor Registry in Qatar

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Verification of HLA-compatible donor availability is a major determinant of clinical outcome in allogeneic hematopoietic stem cell transplantation (HSCT). This process is generally supported by prompt accessibility to family members and marrow donor registries allowing for identification of suitable unrelated donors. In Qatar, the significant ethnic heterogeneity of the country poses a unique challenge for donor recruitment. The population includes immigrants from Arab, Asian and African countries, whose immunogenetic profile is expected to result in low probability donor searches. Moreover, the proximity of immediate family members is unavailable for most such immigrants. In this context, setting up a national stem cells donor registry is critical to improving the likelihood of identifying unrelated donors displaying at least some degree of HLA compatibility with our population cohort.

We established a number of strategies facilitating setting up of a national donor registry representing ethnicities common in Qatar but rare in Western registries.

Educational pamphlets and multimedia campaign materials were designed to enhance public awareness. The German Marrow Donor Program (DKMS) supported these activities by providing reference printed materials. To further promote donor enrolment, we partnered with existing organ donation platforms and directly approached secondary educational institutions, universities and local charities. The process to meet international standards required to include HLA typing results into international registries is ongoing.

Our experience indicates that implementation of a stem cells donor registry requires the deployment of unanticipated resources and operational policies when applied to contexts characterized by ethnic and geographical diversity. Our solutions may be of interest to healthcare providers and administrators operating in a similar context and working towards building an HSC donor registry.
Repeat Donors Require Extended Disclosure Principles for the Release of Personal Information—Case Report

Daniela Griffiths\textsuperscript{1}, Frank Stötzer\textsuperscript{1}, Harald Klüter\textsuperscript{1}

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Background:
Post-transplant communication policies vary in different countries. While some refuse contact between donor and recipient others allow an anonymous contact and release of personal information after a certain time. Repeat donors may come into situations where the release of personal information overlaps with subsequent requests for donations or post-transplant clinical protocols and thus may feel pushed into donation.

Case:
In 2013 we received a request for a CT plus various additional blood samples for a young patient suffering from FEL. The donor was then promptly activated for BM only donation. In 2014 the donor was again activated to donate HPC. The enrolment of the recipient in a study required consent of the donor who thus became aware that the recipient was a child. Conform to NMDP policies the recipients family requested the release of personal information one year after the second donation. Since then, donor and recipient have been in contact. In 2017 the donor was requested for a research support activity requiring a blood donation plus donors explicit consent. By the time of the request, the donor was already informed and familiarized in detail by the donors family.

Results:
The case report shows two possible hazards. One is the German standard allowing personal contact two years after the first donation which here is not sufficient to avoid a collision between the release of personal information and the request for subsequent donations. The second is the unintentional release of information on recipients in connection with fixed study protocols. The patients family had informed the donor before donor assessment. The donor, being a father, had not refused a donation once he became aware that the recipient was a child.

Conclusion:
The disclosure period, especially when patients are enrolled in studies that require post-transplant follow-up donations, should be renewed after each donation. Large amounts of patient related information in connection with study protocols require a conscious approach; the need for a correct ethical conduct of scientific research is essential but must not collide, even unintentionally, with the altruistic motive of the donor and the concept of donation. A non-disclosure agreement for study participants towards their donor is thus necessary. The decision to donate must remain unbiased to ensure the safety of donor and donation.
Survival Rate of an Unrelated Hematopoietic Stem Cell Transplantation Provided by Thai National Stem Cell Donor Registry

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¹Thai National Stem Cell Donor Registry (TSCDR), National Blood Centre, Thai Red Cross Society, Bangkok

Introduction:
National Blood Centre, Thai Red Cross Society has established an unrelated stem cell donor registry since 2002. At the end of fiscal year 2016, 215 patients were transplanted with unrelated hematopoietic stem cell using donors obtained from Thai National Stem Cell Donor Registry (TSCDR). This study aims to analyze the survival of hematopoietic stem cell transplantation in different groups of patients when using unrelated donor from TSCDR.

Materials and methods:
Starting from May 2001 to August 2016, an unrelated hematopoietic stem cell transplantation outcome data of 215 patients were collected from 4 transplant centers in Thailand and other 10 countries using the patient follow-up questionnaire of TSCDR. Forty-seven patients were excluded due to incomplete information. The diseases of patients were categorized in 7 groups, AML, ALL, CML, Thalassemia, MDS, Severe Aplastic Anemia and other diseases. The patient survival was determined in different groups of patients using Kaplan-Meier analysis.

Results:
The transplant outcomes were collected from 168 patients, age between 1-73 years which were 84 pediatric patients (age < 15 years) and 84 adult patients (age ≥ 15 years). There were 113 patients transplanted in Thailand and 55 patients transplanted in other countries. The overall 10-year survival was 70%. The survival rate of patients transplanted in Thailand and other countries were 70.0% and 66.7%, respectively (p=0.550). Altogether, there were 55 Thalassemia patients, 38 AML patients, 24 ALL patients, 12 CML patients, 9 MDS patients, 8 SAA patients and 22 other diseases. Ten-year survivals of Thalassemia, ALL, AML and CML were 84.8%, 31.3%, 71.1% and 75.0% respectively. Five-year survival of MDS and 8-year survival of SAA were 50.0% and 31.3% respectively. There were no different survival rates in 4 variables, age group (p=0.828), sex (p=0.688), product type (p=0.053) and HLA mismatch (p=0.130).

Conclusions:
An unrelated stem cell donor can be used as alternative for allogeneic hematopoietic stem cell transplantation in Thailand. The survival rates are depending on the disease. More detail of variables data should be collected for further study.
DKMS today lists more than 7.8 million donors and provided over 7,000 stem cell products in 2017.

By offering post-donation support and counselling through feedback management and an improved service for grieving donors, DKMS ensures donor satisfaction as well as physical and emotional well-being. A team of especially trained feedback managers makes sure that any feedback/problem donors have during or after donation is taken care of, be it medically, organizationally or emotionally. Feedback regarding organizational issues is followed-up to improve internal and external (e.g. at collection centers) processes. Medical issues are handled in close collaboration with collection centers and DKMS’ medical team. This may involve additional medical examinations, treatment, or insurance procedures. 488 donors that have donated in 2017 (9.1% of donors) were processed by feedback management, which clearly shows the need for specific donor support.

In 2016, DKMS revised the way donors are informed about the passing of recipients to soften the phenomenon of "donor grief" that has been described before (feelings of sadness, disappointment, helplessness). Donors now receive a carefully worded first letter which informs them about the recipient’s death. This letter includes a condolence card and flower seeds which can be sown in memory of the recipient. A second letter includes a link to a DKMS webpage dedicated to grieving donors and offers donors to call if they need further help. A survey evaluating this revised service after 1 year showed that 96.6% of the donors appreciated the wording of the letters and 80.5% the condolence card as well as the flowers. An additional finding showed that 94.9% of donors felt sufficiently informed about the possibility that their recipient could pass away. Donor comments showed that the service was well accepted and appreciated, and the measures offered help them to cope with their recipients’ passing and the feelings referred to as "donor grief".

In summary, both processes guarantee that donors feel appreciated and taken care of even in demanding situations. Thus, donors’ well-being and satisfaction post-donation is ensured. This ultimately contributes to fulfill the ethical responsibility donor centers have for their donors.
An Ethical Challenge: Informing and Counselling Donors About Genetic Findings

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¹DKMS, Cologne

Genetic diagnostics on HSC donors or indirectly on donor cells after transplantation provide distinct ethical, logistic and legal challenges for donor centers. In order to sensitize for the possible implications and necessary efforts, we present different aspects of genetic findings in donors.

- In 2017, DKMS received CT requests for two patients with metachromatic leukodystrophy. Here, we describe how the requirements to obtain donor consent before arylsulfatase A genotyping were met to ensure donors with wild type ARSA alleles for high enzyme activity. Both patients were successfully transplanted.

- Routine cytogenetic and molecular diagnostics in stem cell transplant recipients can reveal acquired or constitutional abnormalities in donor cells. Due to the lack of a formal consent for genetic testing and uncertainty to which extent donors wish to be informed, the donor center has to decide if clinical relevance for the donor outweighs the right not to know. We present an overview of incidental genetic findings in DKMS donors from 2014 – 2017 and discuss the rationale for recommending a genetic counselling or not.

- HLA B*58:01 is associated with a substantially higher risk of severe cutaneous drug reactions to allopurinol, a frequently used drug for the treatment of hyperuricemia and gout. HLA screening before prescription is discussed, and has not been introduced solely due to the costs. For fully typed HSC donors, this information is already available and donor centers might consider to inform affected individuals.

Due to technological advances and stricter regulations, even more findings and subsequent decisions about counselling can be expected in the future. Discussing and aligning strategies to address potential concern for stem cell donors within WMDA could reduce the ethical burden for donor centers and registries.
The Serological Characteristics and Family Genetics of a Novel HLA Allele, HLA-B*13:26

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¹Blood Center of Shandong Province, China, HLA Laboratory, Jinan
²Red Cross Society of China ShanDong Branch, Jinan

Aims:
To investigate the novel sequence and its family genetics and the antigen serological characteristics of the novel HLA allele, B*13:26.

Methods:
The new allele was first detected from a registered donor of Han ethnic from Shandong province of northeast during a routine HLA SBT typing using ROSE-HLA-SBT commercial kit (ROSE Europe GmbH, Germany), analyzed by Conexio Genomics software. As to clarify the unusual HLA-B SBT typing results, the donor and the family were typed again using new DNA isolates by HLAssure™ SE SBT HLA B Typing Kit (Texas BioGene Inc. Texas, U.S.A), sequence analyzed by AccuTypeTM SBT software (Nova BioSoft LLC, Oklahoma, U.S.A.). The serological specificity was typed by Terasaki HLA Class I Typing Tray (One Lambda, U.S.A.).

Results:
The initial SBT results showed that there was no fully matched assignment was obtained at HLA-B locus, which suggested the possible existence of a novel allele. The repeated single allele-specific sequencing results were consistent with the initial SBT results and showed that the subject has a novel nucleotide sequence at HLA-B locus. The new sequence was mostly close to that of HLA-B *13:01:01, but has 4 nucleotides substitutions in exon 3 at: nt 387 G→C (codon105 CCG→CCC), 412 A→G (codon114 AAC→GAC), 419,420 TA→CC (codon116 TTA→TCC); which result in the amino acid exchanges of Asn114→Asp, Leu116→Ser. A nucleotide BLAST search in the IMGT/HLA Database confirmed the existence of this new HLA-B*13 allele. The name HLA-B*13:26 has been officially assigned by the WHO Nomenclature Committee. This follows the agreed policy that subject to the conditions stated in the most recent nomenclature report (Marsh et al. 2010), names will be assigned to new sequences as they are identified. The complete HLA typing of the subject donor and his daughter were A*26:01, B*13:26, DRB1*07:01; A*02:01, B*15:11, DRB1*09:01 and A*02:01, B*15:11, DRB1*09:01; A*02:01, B*48:01, DRB1*15:01 respectively. So the novel allele bearing haplotype should be A*26:01, B*13:26, DRB1*07:01. According to the serological reactivity patterns, the antigen encoded by the novel B*13:26 allele showed most likely the characteristics of B13.

Conclusions:
A novel HLA-B allele, HLA-B*13:26, was identified. The haplotype expressing the new allele is A*26:01, B*13:26, DRB1*07:01. The serological specificity of the novel allele showed most likely the characteristics of B13.
Common and Well-Documented (CWD) Alleles in the Chinese Population

Wu Baohong

1China Marrow Donor Program, Technology Services Dept., Beijing

In order to solve ambiguous results in the human leukocyte antigen (HLA) genotype, one of the effective methods is to build a Common and Well-documented (CWD) Alleles. Now, both The Ad-Hoc Committee of the American Society for Histocompatibility and Immunogenetics (ASHI) and European Federation for Immunogenetics (EFI) had published the CWD table for their respective populations. Given the high genetic polymorphism, it is important to build a CWD alleles table based on Chinese population. This project, referring to ASHI's definition of CWD, intended to construct the CWD table of HLA-A, -B, -C, -DRB1, -DQB1 sites through analyzing more than 1 million unrelated donor high-resolution typing data from the China Marrow Donor Program (CMDP). The results showed that the number of HLA-A, -B, -C, -DRB1, -DQB1 sites for Common alleles were 26, 53, 26, 35, 15, respectively and were 139, 184, 111, 111, 44, respectively for well-document allele in the Chinese population. The CWD allele accounted for 33.78% of the whole founded alleles. The CWD data differs from that of ASHI and EFI. Conclusion: The project establishes the CWD table of the Chinese population, and the date possesses the characteristics of population distribution.
Prevalent HLA Alleles in the Indian Based Registry "Genebandhu"-Powerful Tool for Matched Unrelated Donor (MUD)

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³Amity Institute of Biotechnology, Amity University, Noida

Background:
Voluminous number of patients suffering from blood related diseases need lifesaving stem cell transplant with handful of them is lucky to find suitable related family donors. Most of these individuals need to find voluntary matched unrelated donors. The ultimate purpose of the adult stem cell registry is to evolve a database of matched unrelated donors (MUD) with a large HLA diversity. India is populated with diverse ethnic group of people hence it is essential in terms of histocompatibility to find MUD in India, with registered donors from various ethnic backgrounds.

Objectives:
The aim of this study was to profile the distribution of HLA-A, -B, -C, -DRB1, -DQB1 alleles frequencies of the registered MUD in Indian population.

Materials and Methods:
The HLA typing of all these registered MUD during the period of 5 years were performed using sequence based technology (SBT) and the typing result were analyzed to estimate HLA-A, -B, -C, -DRB, -DQB1 alleles frequencies.

Results:
The Genebandhu has a donor database of 6629 matched unrelated donors. Few out of all customary list of most frequent allelic groups for HLA-A, -B, -DRB1 observed in our study are mentioned in table 1:

Conclusions:
To conclude, considering divert Indian population and crucial need of MUD for stem cell donation, present study throws light on profiling and importance of diverse HLA alleles in Indian subcontinent. Study also highlights on further needs of ongoing enrollment of individuals in such registries to accomplish the upcoming needs for MUD in developing countries like India.

<table>
<thead>
<tr>
<th>HLA Locus</th>
<th>Frequent HLA-Alleles</th>
</tr>
</thead>
<tbody>
<tr>
<td>HLA-A¹</td>
<td>01:01, 02:01, 02:05, 02:06, 02:11, 03:01, 03:02, 11:01, 24:02, 26:01, 68:01</td>
</tr>
<tr>
<td>HLA-B¹</td>
<td>07:02,08:01,13:01,15:01,15:02,18:01,27:05,35:01,35:03,37:01,40:01,40:06,44:03,50:01,51:01,52:01</td>
</tr>
<tr>
<td>HLA-C¹</td>
<td>01:02,02:02,02:03,03:02,03:03,04:01,04:04,03:05,01:06,02:07,01:07,02:08,01:12,02:12,12:03</td>
</tr>
<tr>
<td>HLA-DRB1¹</td>
<td>01:01,03:01,04:03,07:01,10:01,11:01,11:04,03:13,01:13,02:14,04:15,01:15,02</td>
</tr>
<tr>
<td>HLA-DQB1¹</td>
<td>02:01,03:01,04:02,05:01,05:02,05:03,06:02</td>
</tr>
</tbody>
</table>

Table 1: Comprehensive list and distribution frequencies of all the alleles.
The importance of HLA alleles in the process of hematopoietic stem cell transplantation, especially the process of unrelated donor search, is well known. Macedonian Bone Marrow Donor Registry was established in 2010 and lists volunteer donors from different nationalities living in the Republic of Macedonia. The aim of this study was to determine the HLA allele and haplotype frequencies of the volunteer donors from the Macedonian Bone Marrow Donor Registry and to compare these results with the frequencies of Macedonians deducted from a family study. We have analyzed 1541 donors, with different nationalities, Macedonian, Albanian and Macedonian Muslims that were most numerous in MBMDR, and typed them for HLA-A, -B, -C, –DRB1. Donors of Macedonian nationality were additionally typed for HLA-DQA1 and HLA-DQB1 using the SSO method (One Lambda, CA, USA). The most frequent alleles in Macedonians were HLA-A*02, 01, 24; HLA-B*35, 18, 51; HLA-C*07, 04, 12; HLA-DRB1*11, 16, 13; HLA-DQA1*01, 05 and HLA-DQB1*05, 03, 06; in Albanians they were HLA-A*02, 24,01; HLA-B*51, 18, 35; HLA-C*07, 04, 12, HLA-DRB1*11, 13,16; and in Macedonian Muslims they were HLA-A*02, 01, 24; HLA-B*18, 51, 35, HLA-C*07, 04, 02 and HLA-DRB1*11, 16, 14. The most common haplotype in Macedonian was HLA-A*01-B*08-C*07-DRB1*03, while in Albanian and Macedonian Muslims it was HLA-A*02-B*18-C*07-DRB1*11. The comparison of the HLA allele groups between Macedonian from MBMDR and family study showed similar results except for HLA-A*32, HLA-A*37 and HLA-C*04. This study confirms the close relationship between the populations living in the Balkan Peninsula.
The degree of HLA matching between patient and donor is crucial to the outcome of haematopoietic stem cell transplantation. In the absence of a sibling donor, the clinical outcome of a patient is largely dependent on the ability to find a well matched HLA-A, -B, -C and DRB1 unrelated donor in the early phase of disease. However, finding such a donor remains a challenge due to the high degree of HLA polymorphism and in many cases the lack of completely or high resolution typed registered donors. In May 2014, the HLA typing strategy for donors on recruitment changed in Perth from HLA-A, -B and –DRB1 by Sanger sequencing based typing to 9-loci (HLA-A, -B, -C, -DRB1, -DQB1, -DPB1) typing by Next Generation Sequencing (NGS) on the Ion Torrent PGM platform. In addition to changing the typing strategy, retrospective 9-loci high resolution typing of young (<30 years old) male donors was performed. The change in donor typing strategy not only provides higher resolution at more loci but also a cost benefit with a reduced turnaround time of HLA typing in the laboratory. The impact of such a typing strategy on the usage of the Western Australian donor pool has been monitored since the implementation of NGS. To determine the benefit of NGS on donor usage; the number of verification typing (VT) requests, donor work up (WU) requests, the number of days on the registry before request and the location of the transplant centre request were evaluated for the year preceding the implementation of NGS and in the years after NGS implementation. The results of 9-loci super high resolution of only ~8000 volunteer donors shows that VT and donor WU requests have increased, the time a donor is on the registry before request is reduced and the number of WU requests by international registries have increased while local donor requests for local patients have increased.
HLA Allele and Haplotype Frequencies Determined by Family Segregation Using Super High Resolution Typing of 9 HLA Loci by Ion Torrent Next Generation Sequencing

Dianne De Santis¹, Alana Chin¹, Gabriella Tassone¹, Irena Vukovic¹, Sandra Crabtree¹, Rebecca Whidborne¹, Laila Gizzarelli¹, Patricia Martinez¹, Lloyd D'Orsogna¹

¹PathWest, Clinical Immunology, Perth

HLA matching between donor and a patient in haematopoietic stem cell transplantation (HSCT) is crucial to the clinical outcome. The search for a donor usually involves the initiation of a family study which includes the HLA typing of the patients mother and father if available, siblings and in some instances the extended family. Only ~30% of patients have a related donor, and for patients without related donor, the preferred donor is an HLA matched unrelated donor. The HLA gene complex is highly polymorphic and is characterised by high degree of linkage disequilibrium. The high diversity of HLA genes and haplotypes amongst world populations, and the lack of high resolution 6-loci typed donors on the Bone Marrow Donor Registry remains a challenge in the search of a well matched donor. The identification of allele and haplotype frequency within a population can be used as a prediction tool to determine the likelihood of a particular allele being inherited with another. HLA haplotypes have been defined by family segregation studies generally only for A-B-C-DRB1 to 2-field typing resolution. With the development and implementation of Next Generation Sequencing (NGS), we are now able to determine HLA allele and haplotype (A-B-C-DRB1-DQB1-DPB1-DQA1-DPA1) frequencies to 4-field typing resolution. In this study, we have typed by NGS, the parents of approximately 200 family studies performed since 2014 and determined the allele and haplotype frequencies. We hypothesise that super higher resolution typing obtained by NGS of 9 loci will identify novel haplotypes which can be used to better predict the likelihood of a matched donor in the absence of full HLA donor typing.
High Rejection Rate by HLA Matched Donors Identified from the Saudi Stem Cell Donor Registry

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Background:
Stem cell donor registries are worldwide are established to recruit healthy stem cell donors and to facilitate collection and transportation of the stem cell product to transplant centers. Our Saudi Stem Cell Donor Registry (SSCDR) was established in 2011 in Riyadh, Saudi Arabia to provide identify potential stem cells donors from HLA matched unrelated donors to for any patient in need for stem cell transplantation. The aim of this study was to evaluate the rate of acceptance and rejection among potential donors identified through database search registered donors.

Methodology:
This is a retrospective study in which we have reviewed the search files of 2015, 2016 and 2017.

Results:
In 2015 we identified a total of 17 potential donors, found that 6 (36%) N=6 (F=4) have accepted the donation and 11 (64%) N=11 (F=4) have rejected donation. In 2016 we identified a total of 45 potential donors found that 20 (44%) N=20 (F=10) have accepted the donation and 25 (56%) N=25 (F=10) have rejected. In 2017 we identified a total of 68 potential donors found, that 31 (46%) N=31 (F=13) have accepted the donation and 37 (54%) N=37 (F=22) have rejected. The main reason for rejection was family concern (21, 29%) followed by unknown reason (19, 26%), personnel issue (19, 26%), no answer from the donor (8, 11%) and Medical reasons (6, 8%).

Discussion and Conclusion:
We found a high rate of rejection from our registered donors therefore we decided to improve our method of recruitment to decrease this number. Among the changes that we have implemented is to intensify the education about the program, ask potential donors to share their willingness to donate with their family members before signing the consent form in addition to adding several checkpoints to at the recruitment stage to filter out any hesitating potential donors.
Contribution of Frequent HLA-A*B~DRB1 Haplotypes to Donor Search Outcome in Croatia

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Recent studies about HLA polymorphisms in Croatians included HLA haplotype frequency analysis in the Croatian Bone Marrow Registry revealing 50 most common HLA-A*B*DRB1 haplotypes as frequent (>0.1%). The rest of the haplotypes were defined as less frequent (<0.1%) or rare if they included at least one HLA allele observed three times at maximum in our population. This retrospective study included 362 patients transplanted with an unrelated donor from 2012 to 2017 in UHC Zagreb. All patients had family derived haplotypes. The aim was to assess the distribution of HLA haplotypes in order to evaluate the probability of finding a donor in the national or international registry. In the group of 73 patients (20.17%) who received a transplant from national donor (group 1), 92 different haplotypes were found while in the group of 289 patients (79.83%) who found an international donor (group 2), the diversity of haplotypes was much higher, 432 different haplotypes. HLA-A*01:01~B*08:01~DRB1*03:01 haplotype showed the highest frequency in both groups, however its presence was significantly higher in group 1 (18.49% and 2.94%, respectively; P<0.0001). HLA genotypes consisting of two frequent haplotypes, as well as genotypes consisting of one frequent and one less frequent haplotype were significantly more present in group 1 than in group 2 (23.29% vs. 4.84%, P<0.0001 and 60.27% vs. 44.29%, P=0.0179 respectively;). Genotypes with both less frequent haplotypes were significantly more observed in group 2 (47.06% vs. 15.09%, P<0.0001). The same states for the genotypes consisting of one less frequent and one rare haplotype, which we found in 6 patients with international donor and just 1 patient with national donor. The presence of at least one frequent haplotype represents a positive predictive factor for finding a donor in our registry while patients bearing less frequent or rare haplotype will mostly benefit from finding a donor worldwide.
The Croatian Bone Marrow Donors Registry (CBMDR) has been founded and joined the BMDW in 1994. By the end of 2017, CBMDR enlisted almost 50,000 HCS donors, with the number of new donors yearly added ranging from 2,981 to 8,889 donors. The aim of this abstract is to present the work done by the Tissue Typing Centre in the period 2007-2017, regarding the HLA typing of the donors in CBMDR. The need for a method that can offer a sufficient level of resolution with ability to process large number of samples led to the introduction of a PCR-SSO method based on the Luminex technology into our routine work. The majority of CBMDR donors (99.3%) are typed for the HLA-A, -B and -DRB1 loci using this method (low-intermediate resolution). In addition, 25.1% of CBMDR donors are typed for the HLA-C locus, and 0.6% for the HLA-DQB1 locus. The PCR-SSP method and SBT method are used for the high resolution typing which is done only per request for a national/foreign patient. The number of donors with high resolution HLA typing is therefore small (HLA-A (n=172), -B (n=286), -C (n=422), -DRB1 (n=598), -DQB1 (n=214)). Total number of HLA typing performed per request (2010-2017) was 138 and 1,275 (low and high resolution, respectively). The benefits our Centre has gained from being the laboratory providing services to CBMDR, in terms of HLA typing and expertise in HLA field necessary for donor search, are multiple: from the introduction of new methodologies which are accompanied with obtaining required equipment and valuable education, to obtaining experience in handling large numbers of samples, demanding data management as well as education in specific areas such as participation in WMDA training programmes for search coordinators.
NOTIFY Library: Sharing the Lessons Learned from Living Donor Reactions

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The importance of reporting serious adverse events and reactions (SAE/Rs) associated with the donation of cells or organs from living donors is well recognized. Centralized reporting is important as many SAE/Rs are rare and can only be appreciated if collated over time. In addition, trends can be appreciated when large databases are available.

The NOTIFY project was begun in 2010, bringing together experts in multiple areas of vigilance and surveillance monitoring with the goal to support the sharing of published vigilance information for teaching purposes and for greater transparency on the use of Medical Products of Human Origin (MPHO).

One of the key outputs of the project is a publically available online Library of SAE/Rs collected and analyzed by dedicated editorial groups of international experts (www.notifylibrary.org). The Living Donor group of NOTIFY gathers validated or published reports of SAE/Rs in all donors to the Library. There are currently 283 records in the areas of cell, organ, blood, tissue and reproductive cell donation (143, 85, 32, 18, and 5 records, respectively). Of the 142 records of hematopoietic progenitor cells (HPC) donation complications that have caused harm to the donor, 94 are related to peripheral blood stem cells and 48 to bone marrow. SAEs that resulted in unsuitable HPC release, loss or mix up are described in 23 records. The HPC related records of the Library are linked to a total of 137 references, mostly published articles in scientific journals or case reports from regulatory and vigilance programmes.

The WMDA S(P)EAR committee plays an integral role in updating the NOTIFY Library. A representative from S(P)EAR is a member of the NOTIFY Living Donor editorial group and is responsible for adding to the Library all SAE/Rs which have been reported to the committee and deemed by the committee to be important to report to NOTIFY. This includes reports that describe new or rare events, that include new detail about causality or symptoms, or that are reported with a donor group or donation method that is not previously documented. Annual reports and other relevant documents are posted on the Background Documents section of the NOTIFY website.
Notes on Efficient Donor Recruitment: Estimation from Haplotype Frequency in the Japanese Population

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Aims:
The availability of HLA-allele-matched donors is important issue to consider an optimal donor registry size. In fact, HLA-A, -B, -C and -DRB1 allele-matched unrelated donor is the primary alternative donor for allogeneic hematopoietic cell transplantation in Japan. However, it is inefficient to design donor registry size in order to find an HLA-matched donor for all patients, due to infrequent HLA types. Here, we analyzed the probability of finding at least one HLA-matched donor according to donor pool size to discuss efficient donor recruitment in Japan.

Methods:
Data on frequency of 3,361 HLA-A-B-C-DRB1 four loci haplotypes from 18,604 Japanese members with frequencies equal to 0.005% or more in the Japanese population were used from the Allele Frequency Net Database. The availability of finding an HLA-A, -B, -C and -DRB1 allele-matched donor was estimated using two different methods based on the haplotype frequencies: an actual measurement method (AMM) and a formula method (FM).

For AMM, HLA genotype frequencies were added up in the genotypes which could find at least one donor, which was calculated according to the genotype frequencies in a certain number of donor pools. For FM, the probability p(n) in a registry including n individuals is given by 

$$p(n) = \sum_{i} f_i [1 - (1 - f_i)^n]$$

with fi being the frequencies of the i-th genotype in the donor population.

Results:
According to AMM, the probabilities of finding an HLA-matched donor were 40.5% in 100,000 donors, 54.4% in 300,000, 60.0% in 500,000 and 63.4% in 700,000. On the other hand, according to FM, the probabilities were 47.8% in 100,000 donors, 59.9% in 300,000, 65.3% in 500,000 and 68.8% in 700,000. The probabilities calculated by FM were slightly higher than those by AMM. The probabilities increased by 8.6% or 7.7%, 3.2% or 3.1%, 2.1% or 1.9% and 1.6% or 1.3% in AMM or FM, respectively, as the registry size increased by 100,000.

Conclusions:
The rate of increase in the probability of finding an HLA-matched donor will become smaller as the registry size increases due to the diversity and frequency of haplotypes. Therefore, it is important to set a target donor registry size for efficient donor recruitment by considering the haplotype frequencies in the population.
Stem Cell Donation at School

Bert Elbertse

1Stichting Matchis, Donor recruitment , Leiden

The Matchis foundation started in 2017 with lessons and information about stem cell donation at schools in the Netherlands for different age groups.

**Young people in the age of 14-18 years:**
For young people, students aged 14-18, a special education curriculum was developed with the following objectives:

- Familiarize the subject stem cell donation: what is it, why is it an important topic, why do we try to find more stem cell donors? What is your own opinion about stem cell donation?
- Would you like to become a stem cell donor yourself? And if you become a stem cell donor, what is the procedure?

Besides the subject stem cell donation also blood donation is part of the lesson. The lesson takes about 50 minutes. In the lessons we use special presentations, video material and interactive means. At the end of the lessons there is a test to see how much the students have learned.

Teachers are specially trained in the subject

A total of 500 lessons will be distributed across the Netherlands, after which an evaluation will take place.

**Children 8-12 years:**
A paper package is developed for the group of young people up to about 12 years old. Young people can learn about the subject stem cell donation in a playful way. With the made package they can tell short stories about Stem Cell donation to their classmates or make a piece of work about this subject. The material consists of many pictures, cutouts, background information, stories and a comic. The material can be digitally transmitted or send as hard-copy.

**We want to present the following:**
- Our objectives with this project
- The developed materials
- The first results
Donor Attrition: How Low Can We Go? The British Bone Marrow Registry Experience

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\textbf{Background and aims:}
International donor registries devote significant resources to recruitment, but the success of searches also relies on the availability and reliability of the donors recruited. Deferral of donors adversely affects patient outcomes. The aim of the present work is to assess donor attrition and associated factors at post-VT (verification typing) stage within British Bone Marrow Registry (BBMR) to help refine recruitment and retention strategies.

\textbf{Methods:}
Requests for final donor work-ups from April 2002 to December 2016 were analysed retrospectively. Reasons for cancellation were categorised: cancellation by transplant centres (TCs), mixed reasons or donor reason. We examined associations between the latter and various factors including the blood donor reliability score (BDRS) by multivariable logistic regression analysis.

\textbf{Results:}
A BBMR final/backup donor was selected for 2942 stem cell donations. 20.2\% of requests were cancelled, 53\% of which were cancelled by TCs. Donor reasons accounted for 38.9\% of deferrals (7.8\% of all requests), of which 68.8\% happened for medical reasons, 26.6\% for pull-out on personal grounds and 4.8\% for uncontactable donors. In 8.1\% mixed reasons contributed to deferral. The most frequent medical reasons for withdrawal were obesity and hypertension/cardiovascular disease. Medical ineligibility was associated with increasing age (OR=1.45 per 10-year increase, p=0.005), stem cell source (OR=0.34, p=0.001, BM vs PB) and poor BDRS (OR=1.57, score 5 [worst] vs 1-4). Donor pull-out showed association with donor age (OR=2.07, p=0.013, 30-40 vs other ages), non-white ethnicity (OR=3.87, p=0.007), stem cell source (OR=0.35, p=0.027, BM vs PB), poor BDRS (OR=2.35, p=0.009, score 5 [worst] vs 1-4) and higher number of total blood donations (OR=1.02 per additional donation, p=0.004).

\textbf{Conclusions:}
Cancellations for donor reasons were unusual (7.8\% of requested donations), comparing favourably with international data (12.4\% requested donors, WMDA Annual Report 2015). Information on most frequent health issues prompted a review of safety of high BMI donors and change in acceptance policy to allow wider recruitment and lower deferral of donors. Blood pressure review is now requested at time of VT and BBMR are exploring the possibility of checks at recruitment. A questionnaire is being developed to explore personal reasons which cause donors to withdraw which will guide targeted recruitment and retention strategies.
The Registry of Unmet Needs (RUN) is a new initiative which aims to address the needs of patients that our collective donor pool of Bone Marrow Donors Worldwide (BMDW) is currently not able to serve. We have developed data collection templates and have invited all registries to submit data about patients from the past three years who do not have an HLA match. Our goal is to analyze this pooled data for trends and to inform global recruitment strategies to address this unmet need. In an effort to normalize the data we have arranged to run BMDW searches at a fixed point in time for all patients allowing a variety of definitions of match to be applied uniformly. For example: "if the patient does not have at least one donor with a probability of 8/8 high resolution match > 75% for A, B, C, DRB1".

The analysis plan includes the following aspects:
1. Search prognosis: determination of expected genotype frequency and expected number of matches given population-specific registry sizes
2. Multi-population imputation to assign high resolution haplotypes and population identifiers to each haplotype based on haplotype frequency reference data
3. Rare allele analysis based on the "common and well documented allele list
4. Region analysis on the alleles using allele frequency reference data
5. Geospatial analysis of haplotypes

In addition to patient HLA, our template includes other available patient attributes (year of birth, race/ethnicity, ancestry, specific geographical origin and language). We plan to collect family HLA data, where available, for the purpose of phasing haplotypes by segregation. While the project is in the data collection phase, it already has representation from six continents. We anticipate that this analysis will produce specific messages that will be relevant to all registries in WMDA and can inform the messaging around "World Marrow Donor Day".
For a more sustainable registry, better planning in the recruitment of volunteered adult unrelated donors is needed due to the challenges faced by Singapore's Bone Marrow Donor Programme's (BMDP) search and selection service when finding a suitable matched unrelated donor for Singaporean patients seeking treatment locally. This study on match level and donor source was conducted first in 2016 with 90 donor genotype that were used to search within the worldwide database for matching donors. In 2017, the sample size was expanded, focusing on the 3 main ethnic groups; with total sample size of 150 donor genotypes from BMDP's donor database, Chinese (N=50), Malay (N=50) and Indians (N=50), representing patients needing a matched unrelated donor. All 150 donors selected to represent patients had high resolution, 6 loci typing (HLA-A, B, C, DRB1, DQB1 and DPB1).

As usual practice, BMDP's search and selection service utilises the in-house knowledge of national, international haplotype frequencies and linkage disequilibrium, to develop a recommendation list of up to 6 suitable donors for each genotype. Suitable donors are identified as those being typed at various levels of resolution from low to high, with a minimum of at least 3 Human Leukocyte Antigen (HLA) loci, A, B and DRB1 listed. HLA compatibility was based on 10/10 HLA matching level. Mismatched donors with up to 2 mismatches were considered as well. The source of donors is listed on Bone Marrow Donor Worldwide (BMDW) website, which includes BMDP registered donors.

42% of Chinese 'patients', 24% of Malay 'patients' and 4% of Malay 'patients' had at least 1 potential 10/10 matched donor, in Singapore.

Indians in Singapore are poorly represented on the BMDP register. BMDP ranked 11 out of 20 countries for donor source for the Indian group. Malays have almost equal numbers of donors on the register as the Indians, but much better likelihood of finding a matching donor. BMDP ranked 3 out of 12 countries to locate matching donors for the Malay group. Chinese are the significant majority with 79% of the total register, hence BMDP is ranked 1 out of 10 countries to find donor for the Chinese group.

For "patients" with difficult searches, their alleles were noted down to deduce how frequent these alleles exist in our study and their frequency rank in the Asia-Pacific region. Both Indian and Malay groups had alleles that were rare. Diversity from the Indian community is needed in the BMDP register.
Hematopoietic stem cell transplant (HSCT) program was established in Qatar for adult patients older than 14 year old since 2015. Translating a sustainable allogenic HSCT program within existing clinical infrastructure has posed challenges relative to recruitment of sibling donors, identifying unrelated donors and optimization of available resources. We experienced difficulties in obtaining HLA typing data from sibling donors residing in developing countries who are unable to access immunogenetics laboratories due to distance or high cost of testing. Moreover, timely visa issuing for transfer of donors to Qatar and coverage of daily expenses while in the country could not be always ensured. With respect to unrelated donors we faced difficulties in identifying compatible donors in international donor registries. In fact, local residents are mostly Asians and Africans and often possess rare HLA alleles that are underrepresented in existing international registries. In addition, obtaining cellular products in cases where a donor had been identified often failed due to lack of a local registry. Locally, establishing a mechanism facilitating timely referral of transplant candidates by the treating hematology was not immediate. Furthermore, our laboratory faced significant pressure due to increased requests for HLA testing and shorter reporting time.

To address these challenges, we improved our pathways for sibling accessibility by financially supporting HLA testing in underserved areas and the transfer of potential sibling donors to Qatar. At a national level, we are in the process of establishing a country-based registry with the scope of recruiting donors representing the population diversity of the state of Qatar. At the laboratory level, strategies have been revised by the laboratory personnel to improve responsiveness to increase demands.
P-37-50-1: Donor Recruitment and Retention
Friday June 29, 2018 | 10:30 – 11:00

**HLA-A, B, C, DRB1 and DQB1 Allele and Haplotype Frequencies in Volunteer Bone Marrow Donors from Eastern Region of Saudi Arabia**

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**Background:**
Hematopoietic stem cell transplantation is the standard treatment for many hematological and genetic disorders. Finding a matched unrelated donor for a patient can be challenging in large countries with high HLA diversity due to the presence of mixed ethnicities. The aim of this study was to evaluate the HLA allele and haplotypes frequencies from registered donors from Al-Qatif area (a large populated city in the Eastern region of Saudi Arabia) and compare them with registered donors from Riyadh area, Saudi Arabia.

**Methodology:**
A cross-sectional study was performed on 2221 bone marrow donors from Al-Qatif, previously registered with the Saudi Stem Cell Donor Registry (SSCDR) as stem cell donors. Blood samples were collected and HLA-A, B, C, DRB1, DP and DQB1 alleles were identified by sequence-based typing method (SBT).

**Results:**
The most common alleles within HLA-A locus G groups were A*02:01:01G and A*01:01:01G with a frequency of 0.11 and 0.10 respectively. The most common alleles within HLA-B locus G groups were B*52:01:01G and B*18:01:01G with a frequency of 0.09 and 0.08 respectively. The most common alleles within HLA-C locus G groups were C*04:01:01G and C*12:03:01G with a frequency of 0.18 and 0.10 respectively. The most common alleles within HLA-DRB1 locus G groups were DRB1*10:01 and DRB1*03:01:01G with a frequency of 0.15 and 0.14 respectively. And the most common alleles within HLA-DQB1 locus G groups were DQB1*02:01:01G and DQB1*05:01:01G with a frequency of 0.24 and 0.21 respectively. The most frequent HLA-A-C-DRB1 haplotype combinations were A*01:03-C*15:05-DRB1*10:01 and A*01:01-C*15:05-DRB1*15:02 with a frequency of 0.03 and 0.02 respectively. The most frequent HLA-A-C-B haplotype combinations were A*24:02-C*12:03-B*18:01 and A*01:03-C*15:05-B*73:01 with a frequency of 0.03 and 0.03 respectively. The most frequent HLA-DRB-DQB1 haplotype combinations were DRB1*10:01-DQB1*05:01 and DRB1*03:01-DQB1*02:01 with a frequency of 0.15 and 0.14, respectively.

**Discussion and Conclusion:**
When comparing the allele and haplotype frequencies of Al-Qatif population to the database in our registry¹ we found significant differences. To increase the HLA diversity within our Saudi registry more efforts should be taken to include donors from all over the Kingdom to increase chances of finding matching donors for patients of different ethnic or racial background.
Donor Recruitment and Retention
Friday June 29, 2018 | 10:30 – 11:00

Donor Recruitment in ISCDP

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Unrelated donors are volunteers that they don’t have a relationship with recipient and are considered to be able to act and decide freely. Their gift is considered altruistic. Altruism is an act performed voluntarily to help another person, without the expectation to receive any reward. Reasons to register as a donor are diverse. The voluntary choice to become a registered stem cell donor was based on motives that were also found in other types of volunteers. In ISCDP, type of motivation in this case are:

1) Empathy-related motives,
2) Exchange-related motives,
3) Normative motives,
4) Idealized helping motives,
5) Positive feeling motives and
6) Past experience based motives.
High-Resolution HLA-Haplotype Frequencies of 20,767 Potential Hematopoietic Stem Cell Donors from Saudi Arabia

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In the context of hematopoietic stem cell transplantation, HLA haplotype frequencies play a pivotal role for search algorithms designed to identify matching unrelated donors and are essential to estimate the probability to find such a matching donor in a registry of a given size.

We present frequencies for 5-locus HLA haplotypes and HLA alleles based on a data set of n=20,767 individuals enlisted as potential hematopoietic stem cell donors with the King Faisal Specialist Hospital and Research Centre in Riyadh. All DNA samples were typed at high-resolution for HLA-A, -B, -C, -DRB1, and -DQB1 at DKMS Life Science Lab with a high-throughput amplicon-based next generation sequencing approach targeting exons 2 and 3. We used Hapl-o-Mat, our implementation of a maximum likelihood estimation via an EM algorithm, to calculate haplotype and allele frequencies. Haplotypes with frequencies smaller than 1/(2n) = 2.4e-5 were disregarded to account for sample size restrictions.

A*02:01~B*50:01~C*06:02~DRB1*07:02~DQB1*02:01 was observed to be the most frequent haplotype with an estimated frequency of f=1.6%. A cumulative haplotype frequency of f=25% (f=50%) is reached by the most frequent 74 (322) 5-locus haplotypes. The most common alleles per locus were found to be HLA-A*02:01 (f=17.6%), HLA-B*51:01 (f=13.1%), HLA-C*06:02 (f=15.6%), DRB1*07:01 (f=15.7%), and DQB1*03:01 (f=30.4%). Based on these frequencies, the chance to find a matching 10/10 donor from Saudi Arabia for a patient of the same ethnic group is 25% (50%; 75%) in a registry comprising n=114,227 (n=887,100; n=6,686,700) donors.

This study illustrates the diversity of HLA in Saudi Arabia and predicts the required number of donors for an effective registry. Establishing HLA frequencies based on geographical distribution in the country is a consequent next step.
The current selection practice in hematopoietic stem cell transplantation (HSCT) for an unrelated donor includes matching of HLA-A, -B, -C, -DRB1, and -DQB1 at high typing resolution defined by the respective antigen recognition domain (ARD). Several publications suggest additional consideration of HLA-DPB1 in donor selection to improve clinical outcome. In contrast to the first 5 loci, a donor with beneficial HLA-DPB1 genotype is not chosen by matching ARD but by shared T-cell epitopes (TCE) in otherwise mismatched HLA-DPB1 alleles, ie. permissive mismatches.

Here, we investigated to which extent the inclusion of HLA-DPB1 to the donor profile requires stem cell donor registries to recruit additional donors to sustain current matching probabilities when permissive mismatches are applied in the selection practice.

In September 2011, DKMS Germany added HLA-DPB1 to the typing profile of all newly recruited donors. Based on a sample of n=250,000 donors of self-assigned German ethnic background with high resolution typing by NGS, we estimated six-locus haplotype frequencies using HaploMat, our implementation of the EM-algorithm. Using these haplotype frequencies, we calculated matching probabilities under application of TCE group matching for HLA-DPB1. For comparison, we also computed matching probabilities based on 8/8, 10/10 and 12/12 high-resolution matching.

The relative difference in numbers of registered donors to maintain a given matching probability is considerably smaller between a 8/8 matching paradigm and a 10/10 paradigm than between 10/10 and 12/12. Sustaining a matching probability of 80%, adding HLA-DPB1 to a 10/10 selection profile requires about six times as many donors as adding HLA-DQB1 to a 8/8 selection profile. This can be understood in terms of the high linkage disequilibrium between HLA-DRB1 and HLA-DQB1. However, when HLA-DPB1 permissive mismatches are considered, the number of donors to maintain a matching probability of 80% is only about 2.3 times as large as in a 10/10 paradigm.

The addition of HLA-DPB1 to the donor recruitment typing and the application of TCE group matching allows donor registries to maintain a high matching probability with considerably fewer donors as would be required by ARD matching under a 12/12 paradigm.
OptiMaS: Probabilistic and Population Specific HLA Matching Algorithm of the WMDA Search & Match Service

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The OptiMatch® search engine for the probabilistic matching of volunteer unrelated stem cell donors to patients in need of transplant was introduced by the German National Bone Marrow Donor Registry (ZKRD) in 2006. In the subsequent years, the core parts of OptiMatch® were isolated into a deployable stand-alone matching service called OptiMaS (OptiMatch® as a Service). The Canadian OneMatch and the Australian Bone Marrow Donor Registry have been using OptiMaS since 2012 and 2013 respectively. In 2016, the Search & Match Service of the World Marrow Donor Association (WMDA) started to use OptiMaS on the global comprehensive hematopoietic stem cell database (BMDW).

Apart from the OptiMatch® search engine, the OptiMaS framework uses solely open-source software. It fully supports the EMDIS matching preferences, is compliant with the WMDA HLA Nomenclature Guidelines and successfully completed the WMDA comparative reference validation of HLA matching algorithms.

High quality haplotype frequencies (HF) are the basis for matching probabilities between patients and potential donors. This study highlights the impact of population specific HLA-A, -B, -C, -DRB1 and -DQB1 HF on the match prognoses for donors from three different donor populations: German donors of Turkish origin (ASSW), Gift of Life registry donors (GL) mainly of Jewish descent and NMDP donors mapped to the category Hispanic (HI). We compared the performance of the population specific HF with the global consensus haplotype frequency set. The 10/10 (full HLA) matching probabilities have been assessed by analyzing the results of confirmatory typing (CT) results with weighted linear regression and by the area under the receiver operating characteristic curve (AUC). We could consider 728 (ASSW), 302 (HI) and 1273 (GL) CTs for this analysis. All three populations do benefit from population specific haplotypes. The regression coefficient improved between 0.03 and 0.09. The AUC improved between 0.01 and 0.03 which is significant for \( \alpha = 0.05 \).

The importance of population specific HF for matching probabilities could be underlined in this study. However, HF from a broad population sample can provide valuable information regarding the prospects of an unrelated donor search and the actual (number of) donors to select, if population specific HF are not available. The power of the matching probabilities validation is hampered by the small numbers of high resolution CT results in many donor populations.
A Council Advisory Group Enhances Communication and Relationships Between Network Members and National Marrow Donor Program (NMDP) / Be the Match Senior Leadership and Board of Directors (BOD)

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Aims:
The world of hematopoietic cell transplantation is challenging, requiring all aspects of a network to communicate. Registries serve as the central point, necessitating its understanding of all components, from recruitment to transplant. Registry leadership may consider leveraging an advisory group who represent the full network complement to provide advice and guidance.

Methods:
In 2011, the NMDP Council Advisory Group (CAG) expanded from a 3-member board, confined to contracted donor centers and transplant centers, to a 10-member group. This re-designed group consists of expert representatives from transplant, donor, recruitment, apheresis, and marrow collection centers, cord blood banks, and a Chair and Vice Chair. The Chair serves as a NMDP BOD voting member. The CAG’s prime objective is to serve as a liaison among the Council, NMDP leadership, and the BOD. This group also strives to identify opportunities for improvement in network operations, assist in resolution of issues posed by Council Members, and provide input for the annual Council Meeting content. To evaluate the impact of the expanded CAG, an analysis of accomplishments has been performed.

Results:
To achieve its primary objective of increasing visibility as a reminder that the members represent the Network, the CAG has sponsored webinars applicable to all, including topics on donor availability, social media, change management, and network performance. Monthly, the CAG requests comments from the Network, which are discussed in detail and responded to personally by CAG representatives. From October 2012 to September 2017, 246 comments were received, an average of 50 per year. As a result, CAG has been a strong voice for Recruitment and Donor Centers regarding network performance management to meet the needs of transplant centers. Other significant changes include the addition of ABO typing at recruitment and modifications to the formal search process. The CAG has also influenced the content of the Transplant Center quarterly survey, registry software changes, marketing materials, and the creation of the updated marrow collection video.

Conclusions:
CAG’s engagement has led to a stronger connection between the registry and the Network. Advice from the CAG has led to network system improvements that ultimately impact the transplant center and patient. This specific advisory group has positively influenced all aspects of the NMDP network and may serve as a model for other registries.
Confirmatory Typing – Donors Living Abroad

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¹Cellex Medical Services GmbH, Cologne
²NMDP Be The Match, Minneapolis

What happens when a donor is located in a different country from where they originally registered and is requested for CT?

**Aim:**
To reduce the amount of time from CT request to draw date and to expedite the patients search. Also, making the process as convenient as possible for the donor.

**Method:**
The NMDP and Cellex, a contracted partner, developed a project to organize donors who are requested for CT while living in Europe.

The following was considered:
- Country specific regulations
- Registry specific guidelines and forms, i.e. consent, HHQ, etc...
- Well trained staff
- Bilingual staff when needed

**Pilot Process:**
- **NMDP:** Locates donor
  Info session and HHQ
  Informs the TC
  If donor agrees, then all information is sent to Cellex.
- **Cellex:** Informs donor of next steps
  Schedules blood draw in country where donor is located
  Sends required material (health questionnaire, blood draw sets)
  Organizes blood sample shipment to lab
  Medical evaluation based on the health questionnaire and the laboratory results
  Sends results to the NMDP
  Follow-up on the donor’s feedback
- **NMDP:** Sends results to the TC
Results:
In 12 months: 13 CT requests were organized

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>Completed successfully</td>
</tr>
<tr>
<td>2</td>
<td>Cancelled by TC</td>
</tr>
<tr>
<td>1</td>
<td>Donor switched to country specific registry</td>
</tr>
<tr>
<td>2</td>
<td>In progress</td>
</tr>
</tbody>
</table>

- 3 of them went directly to WU upon return to US!
- The donors were located in 8 different European countries.
- On average, the requests were completed within 18 days after the first donor contact.

During these runs several problems were faced:

<table>
<thead>
<tr>
<th>Problem</th>
<th>Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Language problems of donors and involved parties such as surgeries, hospitals or couriers</td>
<td>Essential documents translated in different languages</td>
</tr>
<tr>
<td>Donors living in areas without access to transportation</td>
<td>Ordering a transport service if necessary</td>
</tr>
<tr>
<td>Donors having no access to mails</td>
<td>Different information ways – letters, SMS</td>
</tr>
</tbody>
</table>

- 9 donors gave a positive feedback as they were still able to help although not located in their homeland
- 1 donor didn't answer the question.

Conclusion:
The results demonstrated that it is feasible to perform a CT-request in a timely manner with donors located abroad; it is a benefit for patients in need as well as for donors being requested.
Work-up and Donation - Donors Living Abroad

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What happens when a donor (allogeneic or autologous) is located in a different country from where they originally registered and is requested for Work-up?

**Aim:**
To perform the Work-up and collection in the timeframe requested by the TC and to make the process as convenient as possible for the donor.

**Methods:**
NMDP and Cellex, a contracted partner, developed a project to organize donors who are requested for a Work-Up while living abroad.

The following was considered:
- Country specific regulations
- Registry specific guidelines and forms i.e. consent, HHQ, etc...
- Well trained staff
- Bilingual staff when needed

**Pilot Process:**
- **NMDP:**
  - Locates donor
  - Info session and HHQ
  - Informs TC
  - If the donor agrees, then information is sent to Cellex

- **Cellex:**
  - Schedules dates
  - Provides all necessary paperwork
  - Makes all travel arrangements for the donor and companion
  - Performs PE and organizes blood sample shipment (US lab, TC)
  - Performs PBSC (including stimulation), bone marrow or lymphocyte collection
  - Organizes product transport
  - Donor follow-up after donation
Results:
During the last 36 months, 47 requests were handled that way. 32 were completed successfully. Half of the cancellations were patient related, the other half was due to non-clearance; 6 donors were not available due to personal time reasons and only one donor wanted to switch to another registry.
The donors were located in 10 different European and non-European countries.

The follow-up showed a very positive result:
- All donors were very satisfied with the work of NMDP and Cellex
- All donors reported felt sufficiently informed and would repeat

During these runs only a few resolvable problems turned up:
- donors living in remote areas with little access to transportation
- customs problems

Conclusion:
The results demonstrated that it is not necessary to do the organization, PE and donation in the country where the donor is registered. It was possible to perform the entire process abroad within the patient-relevant timeframe with donors feeling well informed and being taken care of.
Conceptual Model of Bone Marrow Donors Registry

Lucie Houdova¹, Robert Pergl², Milos Fetter¹

¹University of West Bohemia, NTIS - New Technologies for the Information Society, Pilsen
²Czech Technical University in Prague, Department of Software Engineering, Prague

Aims:
Interoperability on expert, technical and organizational levels is a key factor for registries cooperation. One of the key preconditions for interoperability is a precise definition of terms, relationships and rules between them. Providing an ontological analysis, namely the use of appropriate foundational ontologies and languages, serve to ensure this.

Methods:
The presented ontological model is based on the Czech National Marrow Donors Registry domain knowledge, in accordance to the applicable international standards. Ontological analysis was performed with the use of Unified Foundational Ontology (UFO), i.e. a foundational ontology based on the results of research in cognitive science (linguistics, psychology, philosophy, anthropology and neuroscience) and mathematics, especially modal logic.

Results:
In the proof-of-concept solution, demonstrating the potential of the method, is included a description of the transplantation process for unrelated donation of bone marrow, peripheral blood stem cells and donor lymphocytes.

The analysis results consist of two models:
1. Structural conceptual model according to UFO-A processed in the form of a diagram in the OntoUML language.
2. Behaviour conceptual model according to UFO-B processed in the form of a simplified process diagram. The original notation is easy to understand even for non-technical users.

The model deals with the three mentioned levels: expert level (search, evaluation of patient-donor compatibility, examinations – HLA typing, IDM, ... and HSC donations), technical (structure of exchanged data in databases) and organizational (model defines responsibilities and coordination of individual executive units like donor centers, etc.). In addition, WDMA-related standards are listed in the text in each situation in the process model.

Moreover, the methodology of organic interconnection of the structural and behavioral model was created as a simulation implemented in the form of a web application.

Conclusion:
The application can serve as a tool for a comprehensive presentation of knowledge for registry staff, in terms of processes, acquired records, and application of WMDA standards. This work was supported by ELIXIR CZ internal project.
Full Speed Ahead: Improving Performance of Hap-E Search, a Probabilistic Matching Algorithm Based on Haplotype Frequencies

Christine Gnahm\textsuperscript{1}, Alexander Schmidt\textsuperscript{1}, Jan Hofmann\textsuperscript{1}

\textsuperscript{1}DKMS gemeinnützige GmbH, Tübingen

**Aim:**
In 2012, DKMS developed a search algorithm called Hap-E Search. Based on HLA-A, -B, -C, -DRB1 and -DQB1 haplotype frequencies, it provides 10/10, 9/10 and 8/10 matching probabilities of all potential donors to a patient. Hap-E Search 2.0 is a complete revision of the search kernel to meet the challenges of searching more than seven million registered donors with different typing profiles in terms of typed loci and typing resolution.

**Methods:**
Abandoning the former tree-based approach, Hap-E Search 2.0 pre-calculates information on donor genotypes. This information is constantly updated to the current state of the donor database. To improve performance, all donors with the same HLA-typing and ethnicity are mapped to one representative donor. For these representatives, potential donor genotypes according to underlying haplotype data are calculated and stored, as well as their cumulated frequency.

The donor-patient matching consists of several steps: First, all potential 10/10 and 9/10 donor matches based on antigen recognition domains are selected. Then, potential patient genotypes are determined, as well as genotypes having one or two mismatches to them. Fast calculation of matching probabilities is possible by intersecting these 0/1/2 mismatch patient genotypes with the pre-calculated donor genotypes. For genotypes that cannot be built from haplotype data, we assume a minimal frequency to estimate the matching probability.

Our algorithm supports WMDA conform treatment of alleles with expression-level suffices, as well as mismatch counting for homozygous loci.

**Results:**
HapE Search 2.0 outperforms the old search kernel in terms of runtime by at least an order of magnitude. The performance gain increases for expensive searches that yield several thousand potential matches.

The algorithm was evaluated with the WMDA matching validation (task 3). We obtained identical match probabilities compared to the consensus data for all donor-patient pairs except one, where we observed a deviation of 1% in the 9/10 probability (87% instead of 88%), which was due to rounding. On average, the search for 1,000 patients in 10,000 donors took 6.8 s per search.

**Conclusion:**
With the new approach, performance of Hap-E Search 2.0 is tuned to allow for a more efficient workflow within DKMS quality programs, as well as to improve user experience of our external service "Donor Navigator".
OneMatch Operational Improvement Initiative Results in Decreased Time from Verification Typing Request to Sample Shipment

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¹Canadian Blood Services, OneMatch Stem Cell and Marrow Network, Ottawa

The World Marrow Donor Association (WMDA) has defined a panel of key performance indicators for hematopoietic stem cell registries to measure success in delivery of essential services. It is recommended that 75% of donor samples requested for verification typing (VT) be collected and shipped to the requesting centre within 14 calendar days to expedite identification of a suitable donor for transplant, however data from registries participating in the WMDA Annual Questionnaire shows that only 73% (2015) and 74% (2016) of VT samples were remitted within recommended timelines. In recent years, OneMatch has met this target only 60% (2015) and 48% (2016) of the time, prompting comprehensive review of donor management processes. Registry staff engaged in a process improvement initiative to review practices surrounding donor management at VT. A subset of 60 VT transactions fulfilled during each of the past two years during periods of increased donor demand and heightened VT shipment efficiency (83% and 62% of samples shipped within 14 days, respectively) were analyzed to develop a procedural optimization strategy. A positive correlation between completion of donor contact within one day of VT request and ability to ship samples within 14 days was identified, thus revision of processes surrounding initial donor contact and scheduling of health screening questionnaire and blood sample collection were proposed. Challenges to completing initial donor contact within one day included increased VT demand, staff resource constraints, and the vast geographical distribution of Canadian donors. In April 2017, procedural changes including revision of donor contact policies, staff re-education and continued competency, and introduction of a donor contact timeline tracking mechanism were implemented. Staff operational hours were staggered to accommodate donors across Canadian time zones at initial contact and appointment scheduling, and donors are now offered several immediate appointment options for consideration. These changes have led to a rapid, dramatic improvement in VT sample shipment times: an average time of 13.5 days was achieved for 413 VT requests fulfilled during the eight month post-implementation interval with 293 (71%) samples shipped within 14 days. OneMatch continues to approach the WMDA target and to explore additional opportunities for procedural improvement as part of our commitment to excellence in registry service provision.
Prometheus Light - Free On-Line Donor Registry Software

David Steiner¹, Albert Mustafin¹

¹Steiner, Praha 10

Aims.
Many small registries are eager to share their donors with the world/community, but don’t have proper tools to do so. In order to submit donors to BMDW, the data should be submitted in a proper format, which in turn requires some IT knowledge, hardware infrastructure, software and data validation tools that are not necessarily in place in a medical facility. In order to join EMDIS network even more complex software has to be implemented.

Steiner Ltd. has developed Prometheus software for management of stem cell donor registries. It has been deployed in 40 registries around the world. It covers quite a lot of functionality from adult donor and cord blood bank data management, patient management, search process, EMDIS, transplant and collection records, donor/patient follow up, etc. and is hosted by registry itself. Prometheus software has helped many small and middle-size registries to deploy professional registry management software.

However for some small and start-up registries such tool is too complex and we also understand that not every registry can afford to buy software. They just need to start IT operations at minimum costs. For them, we have developed a new web based tool "Prometheus Light".

Methods:
We came up with an idea to share our expertise by building an online tool that would allow small registries, at minimum configuration, to enter their donors in a predefined format to an online database that has a possibility to export those donors to BMDW database.

Prometheus Light is a web based registry software that has been developed in Java programming language using state-of-the-art programming frameworks, such as Hibernate, Spring and Vaadin that bring high level of security and stability of the system. Security measures cover European GDPR requirements.

Results:
We have implemented the functionality and deployed the system in the professional cloud data centre in Germany. Small and start-up registries are welcomed to start using it at no implementation costs. They don’t have to invest into own hardware infrastructure, but only access to the internet and a web browser is needed.

Conclusions:
Prometheus Light is ready-to-use cloud based registry software system that covers basic functionality for small and start-up donor registries. It is provided at no implementation costs.
P-49-37-2: Registries: Management and Innovative (IT) Solutions
Friday June 29, 2018 | 15:30 – 16:00

Prometheus Search Service

David Steiner¹, Albert Mustafin¹
¹Steiner, Praha 10

Aims:
Steiner Ltd. provides Prometheus software for management of stem cell donor registries that has been deployed in 40 registries around the world. These registries have the same needs like large organizations regarding the upfront donor search system: they want to have possibility to integrate private data of own donors with global search results of other registries, apply own filtering and sorting rules, add recommendations for their clients (transplant centers) and print search results into own report templates.

Methods:
Prometheus Search Service is deployed in a professional cloud data centre in Germany in secure environment. The server hosts a database with a copy of Prometheus data - we use only the subset of the data that is being exported to BMDW. No personal information. We have implemented real-time data synchronization.

The server provides various functions and interfaces:
1. Upload of data to BMDW using new REST API. This way we can set up regular (e.g. daily) full data synchronization with BMDW. We will also be ready for differential updates, when they are introduced by BMDW.
2. Integration and data exchange with systems of large registries. For example, some registries regularly export data to NMDP, where they are listed in NMDP upfront search system.
3. Search Service API for Prometheus software. Prometheus software then integrates search results with private data, offers extensive sorting and filtering options and customized search reports.
4. Prometheus Search Service uses Prometheus search algorithm. We are ready to integrate the Service with the BMDW/OptiMatch Search Service API, when it is available.

Results:
The Prometheus Search Service is used by Prometheus applications that are deployed at individual registries. The search functionality has been deployed to the first registries in 2017. In February 2018 already 10 registries participate in the project.

Thanks to real-time synchronization, a new donor added to the local Prometheus database in one registry can be immediately found by other Prometheus users. Donor record updates are visible as well.

Conclusions:
The upfront donor search is being used by large registries (NMDP, ZKRD) for many years. Prometheus Search Service is a new implementation of an upfront donor search in the Prometheus software. It is secure platform that simplifies donor search and allows integration with BMDW and systems of large non-Prometheus registries.
Innovative Management of Repeat Cytomegalovirus Testing of Hematopoietic Stem Cell Donors

Ying Li, David Winstone, Guy Parkes

1NHS Blood and Transplant, Stem cell donation and transplantation, Bristol

Introduction:
The British Bone Marrow Registry (BBMR) is a panel of blood donors who have volunteered to become hematopoietic stem cell donors. All blood donors are Cytomegalovirus (CMV) typed when joining the BBMR, to allow CMV status to be taken into consideration when transplant centres are selecting potential donors for a patient. However, due to transfusion/passive transfer of antibody or failure of testing in a seronegative BBMR donor, it could be CMV false positive; due to hypogammaglobulinaemia or failure of testing in a previously infected BBMR donor, it could be CMV false negative. Therefore, it would be beneficial to have the most up-to-date CMV status of donors.

Methods:
BBMR successfully launched a CMV campaign in 2015 and started repeat CMV testing when BBMR donors attend their blood donation sessions later that year. An automated report containing BBMR donors blood donation details (sample number and date bled) is sent to our testing laboratory. Once CMV testing is completed, results are transferred automatically to our LIMS system and then made available via BMDW (Bone Marrow Donor Worldwide) for searches.

Results:
29% (n=102,960) of BBMR donors are active blood donors, the automated process allowed us to complete the repeat CMV testing for 93% (n=95,316) of the active donors. 0.6% (n=601) donors had historical false CMV positive. 0.5% (n=471) donors had historical false CMV negative or seroconverted.

Conclusions:
CMV is a common virus affecting an estimated 50-60% of the UK population and is dormant in most healthy people. It remains one of the most important complications after allogeneic hematopoietic stem cell transplantation (HSCT). Previous studies have shown that, besides HLA match, matching the CMV status of the donor and the patient can have a significant benefit on patient survival. To our knowledge, we are the first stem cell registry to carry out repeat CMV testing and make the most up-to-date CMV status of donors searchable via BMDW.