Conference on:

PRACTICAL ASPECTS OF DONOR-RECIPIENT MATCHING IN HSCT

December 17\textsuperscript{th}-18\textsuperscript{th}, 2012

Wroclaw, Poland

under the auspices of

Aleksander Marek Skorupa

\textit{The Governor of Lower Silesia}

organized by

- L. Hirszfeld Institute of Immunology and Experimental Therapy, Polish Academy of Sciences (Wroclaw)
- Lower Silesian Center for Cellular Transplantation and National Bone Marrow Donor Registry (Wroclaw)
- Association for the Benefit of Development of Donation of Marrow (Wroclaw)
# CONTENTS

## TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>WELCOME IN WROCLAW</td>
<td>4</td>
</tr>
<tr>
<td>PREVIOUS INTERNATIONAL CONFERENCES</td>
<td>6</td>
</tr>
<tr>
<td>WROCLAW - the host city</td>
<td>9</td>
</tr>
<tr>
<td>ESTHETIC SUPPORT</td>
<td>11</td>
</tr>
<tr>
<td>ORGANIZING COMMITTEE</td>
<td>16</td>
</tr>
<tr>
<td>GENERAL INFORMATION</td>
<td>17</td>
</tr>
<tr>
<td>CONFERENCE PROGRAMME</td>
<td>21</td>
</tr>
<tr>
<td>ABSTRACTS</td>
<td>26</td>
</tr>
<tr>
<td>ACKNOWLEDGEMENTS</td>
<td>61</td>
</tr>
<tr>
<td>LIST OF INVITED SPEAKERS AND CHAIRPERSONS</td>
<td>62</td>
</tr>
<tr>
<td>PARTICIPANTS OF THE ROUND TABLE DISCUSSION</td>
<td>62</td>
</tr>
<tr>
<td>PARTICIPANTS</td>
<td>63</td>
</tr>
</tbody>
</table>
It is great to participate in work opening a new avenue in research which builds knowledge soon to be translated to the clinic. The study on human histocompatibility antigens (HLA) with an outstanding contribution of Jon van Rood and Nobel Prize winners Benaceraff, Snell and Dausset made it possible to understand the rules behind recognition of self and non-self antigens operating in tolerance, surveillance of infections and cancer as well as in the acceptance of transplanted organs. Described associations between HLA alleles and susceptibility to some diseases including autoimmune and autoinflammatory ones and some forms of cancer laid a cornerstone in understanding the pathomechanism of many diseases.

Everything changes, new forms of life appear, new compounds are synthesized each day in unpredictable ways. The immune system adapts due to the incalculable variety of HLA specificity compositions building the genome as well as due to allelic variability of several genes which makes them more or less prone to transcription or more or less efficiently functioning due to the impact of this variability on the primary structure of encoded peptides. Single nucleotide polymorphism of alleles may make a big difference in gene functioning, which is also seen when investigating microsatellite and CNV patterns. This enormous variability makes the process of donor-recipient matching extremely challenging.

The role of genetic features in determining an optimal donor for a given patient will be discussed during the present conference to better understand the matching process, which ultimately may spare lives.

My group here in Wroclaw customizes organization of conferences on immunogenetics with a great hope to improve health care delivery, making it more rational and effective.
We started with a conference in the year 1981 on Genetic Aspects of Asbestos Exposure. Great scientists were with us and great papers were presented, which opened a path for progress. During the following conferences including that summing up the FP5 StemNet project we had the cream of the cream of scientists, whose lectures published in following conference proceedings contribute significantly to the literature as in the verse:

*With a finger wrapped in brown paper*
*I am trying to link the past and the future*
*With blue flame*
*And white smoke rises up*
*into rough clouds* (Magdalena Lange)

We are happy to have at this conference researchers who with unprecedented skill and determination work on improvement of donor-recipient matching, making world-wide cooperation possible. Cooperation within European regions is also very important. Nearby centers exchanging information and opening their technological potential for use in a mutual fashion may make it possible to tailor the treatment approaches according to the genetics of a disease in concert with appreciation of genetic traits of both recipient and donors in transplantation. This is why I am very happy to have a number of participants from our neighbouring countries as well as colleagues from the eastern part of Europe from Moscow to Ankara.

I heartily welcome all of you to Wroclaw.

The winter holiday is just around the corner. Let us enjoy the most charming and festive atmosphere of Christmas time. Happy New Year 2013.

Andrzej Lange
PREVIOUS INTERNATIONAL CONFERENCES

1. “Epidemiological, Immunological and Genetical Aspects of Asbestosis”, 24-26.03.1981 organized by: Institute of Immunology and Experimental Therapy of The Polish Academy of Sciences, Czerska 12, 53-114 Wroclaw, Poland


2. “Molecular biology techniques in clinical immunology and transplantation”, 15-18.12.1993, Wroclaw organized by: Ludwik Hirszfeld Institute of Immunology and Experimental Therapy Commission of Immunotherapy of the Polish Academy of Sciences, Polish Society of Immunology


3. 3rd Central European Transplant Conference “The present and perspectives of immunogenetics and transplantation immunology and clinical aspects of blood/bone marrow transplantation”, 15-17.12.1997, Wroclaw organized by: BMT Unit, K. Dłuski Hospital, Institute of Immunology and Experimental Therapy in 10th Anniversary of its activity

4. “Standardization of Donor-recipient matching in transplantation: the presence and perspectives in Central-East European Associated States”, 28-29.04.2003, Warsaw organized by: Lower Silesian Center for Cellular Transplantation with National Polish Bone Marrow Donors Registry on its 15th Anniversary of transplant activity on behalf of the Polish Society for Immunogenetics, the Institute of Immunology and Experimental Therapy of the Polish Academy of Sciences, Wroclaw, the Institute of Hematology and Blood Transfusion, Warsaw and the STEMNET Consortium


5. “Immunogenetics in haematology and stem cell transplantation”, 8-10.02.2006, Wroclaw organized by: Polish Society for Immunogenetics, Association for the Benefit of Development of Marrow Donation, L. Hirszfeld Institute of Immunology and Experimental Therapy, Polish Academy of Sciences, Lower Silesian Centre for Cellular Transplantation with the National Polish Bone Marrow Donor Registry, Wroclaw, Commission of Transplantology, Polish Academy of Sciences


Experimental Therapy, Polish Academy of Sciences, Lower Silesian Centre for Cellular Transplantation with the National Polish Bone Marrow Donor Registry

Proceeding published:
Transplantation Proceedings, Vol. 42, No 8, October 2010

Organization of scientific symposia serving as a platform for discussion and spreading information is the legacy of our activity. But to avoid unrealistic ambition it is good to remember my daughter Magdalena’s verse inspired by a Polish proverb: *even having an open window you are not flying*, as opposed to the Fly Eagle Fly:

*Window,*
*I am opening,*
*Leaving open*
*and*
*Falling down*
WROCLAW

Wroclaw is situated at a crossroad whose branches link the town with three European capitals: Warsaw, Prague and Berlin. The crossroads location is reflected in the city’s varied history. Founded in the 10th century, Wroclaw has a rich and unique history, reflecting the Polish, Czech and Prussian-German spirit. This crossroads location is reflected by the colour of the town, which you can see looking at buildings, parks and gardens.

This island of churches recalls the time of the Piast Dynasty. The Arch-Cathedral of St. John the Baptist is visible from far away and it is undoubtedly Wroclaw's most precious monument of sacred architecture (note that it is situated in the vicinity of the JP II Hotel). The church has over 1000 years of history, beginning soon after the Emperor Otto III and the Pope Silvestre II established a diocese in Wroclaw. Such an honour was a proof of the city's great importance, as a centre of politics, economy and culture in the region.

A number of turbulent events swept across the town, especially during the Thirty Years' War. Prussia and its successor Germany brought new changes. Wroclaw, under the name Breslau, was the second town of Germany after Berlin and flourished in the fields of art and science. Numerous Nobel Prize winners had their roots in Lower Silesia and they all worked in Wroclaw. Important names strongly associated with the city, like Naisser, Koch, Rokitansky and Hirszfeld, have coloured the map of medical scientific progress.
The German-Polish sense of art and music, as well as perfect and beautiful urbanization of the city, is a heritage by itself, among which classicistic (note the Wroclaw Opera House, which you may visit to enjoy the performance) and modernistic architecture buildings are most worth seeing (please join the City Tour). Not to be missed is the University with a baroque Leopoldine Saal, facing the Odra River bank. The Odra is a river of over a hundred bridges. They witness the progress in engineering and technical skill. You can walk over the Sand Bridge, built in 1861, or drive via new monumental bridges.

The strengths of Wroclaw rely on the multicultural roots, where German perfectionists merged with the Slavic soul, resulting in the beautiful town bridging the nations which proudly becomes the European Capital of Culture in 2016.

Magdalena Lange
ESTHETIC SUPPORT TO THE CONFERENCE WAS LEND BY: BRONISŁAW KRZYSZTOF, JAN BORTKIEWICZ, MAGDALENA LANGE, ADAM CZERMAK, MAGDALENA ZAWARTO BAND, ARS CANTANDI CHOIR

BRONISŁAW KRZYSZTOF

“Bronislaw Krzysztof knows how to translate emotion and energy into the visual with technical proficiency. He has the capability of translating invisible to visible. His surrealistic expression achieved with masterly classical technique makes Bronislaw Krzysztof one of the most unique contemporary sculptors.”

Mashiko New York

“The urge to touch may not be merely a response to perfection of outward form, but sometimes also a reaction to the attractive power of the life within a person or a created object. The artist strives to produce the illusion of that inner life in his creations.

This, I feel, is one of the most important elements in Krzysztof's work. Other contemporary sculptors, including Anthony Gormley and David Mach, also deal with the human figure in their different ways, but they rarely penetrate so far below the surface.”

Huon Mallalieu British Museum, London

JAN BORTKIEWICZ


**MAGDALENA LANGE**

Magdalena Lange is a PhD student conducting research on the bio-art in the Philosophy Departament at the Jagiellonian University in Krakow. She is graduated biotechnologist and art hisotrian. She studied medicine, literature and photography. She is used to write poems, which were published in the annals of literature. Recently she published a separate volume by the Cracow Publishing Company.
ADAM CZERMAK

Adam Czermak (born 21.07.1983) graduated with distinction from the Henryk Wieniawski Secondary Music School in Poznań (2001) and the Ignacy Paderewski Academy of Music in Poznan in the violin class of Prof. Bartosz Bryła. He continued his studies in Austria (Universitaet fuer Musik und darstellende Kunst Graz) with Prof. Yair Klessa and Silvii Marcovici. In 2005 he was awarded a 2-year scholarship of the Opera in Zurich where he studied with Bartłomieja Niziola and Hanny Weinmeister. Moreover Adam Czermak took part in many International Master Classes in Poland, Austria, Germany and Spain where he perfected his skills with such great Professors like Jadwiga Kaliszewska, Miroslaw Lawrynowicz, Jewgenij Bushkow, Eduard Grach, Rene Staar or Grigorij Zyslin.

Adam Czermak is the laureate of main awards in many national and international competitions like the Stanislaw Hajzer Bach Competition in Zielona Góra, the Stanislaw Serwaczynski Competition in Lublin, the International Competition for Young Musicians in Belgium, the International Violin Competition in Schloss Zell an der Pram in Austria. In 2005 he won one award and one gold medal at the European Competition for Young Soloists in Luxembourg.

The artist was the concertmaster of the International Opera Studio in Zurich (Switzerland), Oviedo Filarmonia in Spain and Goettinger Symphonie Orchester in Germany. Since 2010 he has been a concertmaster of Wroclaw Opera. In his career he has cooperated with the most outstanding conductors like Zubin Mehta, Nello Santi, Franz Welser-Moest, Friedrich Haider, Tadeusz Strugała and Jacek Kaspszyk.
Magdalena Zawartko was born on 9th March 1990 in Wroclaw. Vocal tradition in her family (mother Maria Zawartko - alto; father Jarosław Zawartko - bass; sister Joanna Zawartko - soprano) caused that still being a little girl she discovered her love for singing. She graduated from the Karol Szymanowski Secondary Music School in Wroclaw (the violin class of Andrzej Woźnica), where she developed her passion and actively took part in each artistic school project. After finishing school, she continued her studies at the Academy of Music in Wroclaw, Vocal Faculty, where she worked with Prof. Agata Młynarska - Klonowska. Her great love for jazz music caused that she started to attend Jazz Department classes. Meetings with such musicians like Aleksander Mazur, Jacek Niedziela, Piotr Wojtasik, Tomasz Pruchnicki or Piotr Kałużny gave her still more strength for further work. She took part in Jazz Festival “Jazz na kanapie”, where she had very good reviews, Partnership Festival in Lviv, during EURO 2012, for Dalajlama in People’s Hall in 2010. She won an honorable mention award at the Polish Festival of Jazz Improvisation and Interpretation in Chodów. Despite her young age, she is an originator, co-founder and song trainer at Youth Musical Academy in Wroclaw as well as a song teacher in Mikoszów Music Group.
ARS CANTANDI CHOIR

Wroclaw University of Economics Choir
Conductor: Anna Grabowska-Borys

The Wroclaw University of Economics Ars Cantandi Choir started its activity in December 2004. Its members are people with many different interests, who love to sing together and to share their passion for choir music. Ars Cantandi offers broad music themes in its performance venue, both religious and secular. Repertoire includes music of domestic and foreign composers from various ages. The choir performs classical music as well as gospel and popular music. Ars Cantandi has a great number of successful performances at international and national choral festivals and competitions. The choir participates in ceremonies at Wroclaw University of Economic and regularly takes part in Lower Silesian festivals and concerts. Ars Cantandi has performed in Belarus, Ukraine, in Greece and in Italy.

Annually members of the choir participate in musical workshops to improvement of vocal skills during individual voice emissions, analyses of new repertoire and integration of the choir members.

More information about the choir:
http://arscantandi.wroclaw.pl
http://www.facebook.com/ChorUE
ORGANIZING COMMITTEE

Andrzej Lange, president
Mariola Sędzimirska
Sylwia Mizia
Alicja Hetnar
Dorota Dłubek
Emilia Jaskuła
Katarzyna Kościńska
Małgorzata Polak

CONFERENCE OFFICE

Tomasz Borodzicz
Wojciech Borodzicz
Patrycja Bratos
Agata Czuczwaraw
Dorota Dera-Joachimiak
Mieczysław Domagalski
Aleksandra Erbert
Justyna Godyń
Halina Kosatka

Irena Kutera
Joanna Leśniewska
Monika Mordak-Domagała
Jan Ruta
Paulina Skorupa
Barbara Szymczak
Magdalena Szymiczek-Orłowska
Magdalena Trylińska

Lower Silesian Center for Cellular Transplantation and National Bone Marrow Donor Registry

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53-439 Wroclaw, Poland
tel. +48717831375
fax: +48713621512
e-mail: conference2012@dctk.wroc.pl
conference website: www.conference2012.dctk.wroc.pl
GENERAL INFORMATION

Conference Venue:

December 17th
Plenary and Poster Sessions
John Paul II’s Hotel
2, Saint Idzi Street, Wroclaw

December 18th
Plenary and Poster Sessions
John Paul II’s Hotel
2, Saint Idzi Street, Wroclaw

Workshops
Scientific-Medical Incubator of the Lower Silesian Centre for Cellular Transplantation
18, Muchoborska Street,
54-424 Wroclaw
Telephone/fax during the conference: + 48717911990

Shuttle bus (December 18th, 1 am) will be provided to take you from the John Paul II’s Hotel to the Scientific-Medical Incubator of the Lower Silesian Centre for Cellular Transplantation.

The official language of the Conference is English.
Project N R13 0082 06

The conference is a final event of the Project N R13 0082 06: “The implementation and harmonization of immunogenetic examinations assisting the final decision of selection of alternative donor-recipient pairs for allogeneic stem cell transplantation” sponsored by the National Centre for Research and Development.

Lunch, coffee and tea

During the conference session breaks coffee and lunch will be served free of charge to delegates wearing their name badge.

Public Transport

<table>
<thead>
<tr>
<th>Starting Point</th>
<th>Destination</th>
<th>Means of Transport</th>
</tr>
</thead>
<tbody>
<tr>
<td>John Paul II’s Hotel</td>
<td>Dominikański Square Railway Station</td>
<td>Tram line: 9, 17</td>
</tr>
<tr>
<td></td>
<td>Market Square</td>
<td>Tram line: 10</td>
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<tr>
<td></td>
<td>Town Hall</td>
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</tr>
<tr>
<td></td>
<td>Opera House</td>
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</table>

Taxi

You have 10% discount for Taxi line (phone no. +487119191). For the password please ask the Conference Office.
1. John Paul II's Hotel  
2. Town Hall  
3. Opera House  
4. Workshops  
5. Railway Station  
6. Airport
INFORMATION FOR SPEAKERS AND POSTER PRESENTATION

Audiovisual Equipment

The lecture room will be equipped with a computer for PowerPoint presentations. PowerPoint presentations must be handed in via CD-ROM, USB compatible memory stick not later than one hour before the beginning of the session.

Poster Presentations

Posters will be displayed in the Caritas Room on the underground floor. All accepted posters should be 100 cm height and 80 cm width. Posters should be installed on the numbered boards and should display: the title, authors and institutions of origin. Conference staff will provide technical means to install posters.

CONTINUING MEDICAL EDUCATION (CME)

Participants are granted with 15 points of the Continuing Medical Education (CME) system. A certificate of attendance will be available.
# CONFERENCE PROGRAMME

## Sunday, December 16th, 2012  Opera House

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>19:00</td>
<td>Opera House: Performance by the invitation of Primadonna Ms. Ewa Czermak: Cavalleria rusticana by Pietro Mascagni Pagliacci by Ruggero Leoncavallo</td>
</tr>
</tbody>
</table>

## Monday, December 17th, 2012  John Paul’s II Hotel

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:00-8:30</td>
<td>Registration at the John Paul’s II Hotel 2, Sw. Idziego, 50-328 Wroclaw, Poland</td>
</tr>
</tbody>
</table>
| 8:30-8:35 | Andrzej Lange  
Welcome                                                                 |

### 1st SESSION: European Network of Donor-Recipient Matching

**Chairpersons**  
Machteld Oudshoorn (Leiden)  
Andrzej Górski (Warszawa)

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>08:35-09:05</td>
<td>Machteld Oudshoorn (Leiden): How to perform an effective unrelated donor search?</td>
</tr>
<tr>
<td>09:05-09:35</td>
<td>Meral Beksac (Ankara): The role of Killer Immunoglobulin-Like Receptor polymorphisms in HSCT</td>
</tr>
<tr>
<td>09:35-09:55</td>
<td>Mirosław Markiewicz (Katowice): 15 years of allogeneic hematopoietic cell transplantations from unrelated donors in Katowice. Ongoing studies on minor histocompatibility antigens and anti-HLA antibodies</td>
</tr>
<tr>
<td>09:55-10:10</td>
<td>Discussion</td>
</tr>
<tr>
<td>10:10-10:25</td>
<td>Coffee break / Poster viewing</td>
</tr>
<tr>
<td>10:25-10:55</td>
<td>Gerhard Ehninger (Dresden): Donor safety and harvest procedures</td>
</tr>
<tr>
<td>10:55-11:25</td>
<td>Andrzej Górski (Warszawa): Ethical aspects of electronic health</td>
</tr>
<tr>
<td>11:25-11:40</td>
<td>Discussion</td>
</tr>
<tr>
<td>11:40-11:50</td>
<td>Vera Siffnerova (Prague): Strategy for HLA genotyping of unrelated hematopoietic stem cell donors</td>
</tr>
<tr>
<td>Time</td>
<td>Session</td>
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<tr>
<td>11:50-12:00</td>
<td>Irina Pavlova (St. Petersburg): <em>HLA</em>-A, -B antigen and -DRB1* allele frequencies among of volunteer hematopoietic stem cell donors from St. Petersburg</td>
</tr>
<tr>
<td>12:00-13:00</td>
<td>Lunch</td>
</tr>
<tr>
<td></td>
<td><strong>2ND SESSION:</strong></td>
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<td></td>
<td>European Network of Donor-Recipient Matching</td>
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<tr>
<td>Chairpersons</td>
<td>Gerhard Ehninger (Dresden)</td>
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<td></td>
<td>Carlheinz Mueller (Ulm)</td>
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<tr>
<td>13:00-13:30</td>
<td>Carlheinz Mueller (Ulm): <em>Factors contributing to efficient donor procurement</em></td>
</tr>
<tr>
<td>13:30-14:00</td>
<td>David Steiner (Prague): <em>Computer algorithms in the search for unrelated stem cell donors</em></td>
</tr>
<tr>
<td>14:00-14:15</td>
<td>Discussion</td>
</tr>
<tr>
<td>14:15-14:45</td>
<td>Roman Danielewicz (Warszawa): <em>The role and development of Central Potential Unrelated Bone Marrow Donor and Cord Blood Registry in Poland</em></td>
</tr>
<tr>
<td>14:45-15:15</td>
<td>Andrzej Lange (Wroclaw): <em>The level of donor-recipient matching versus major complications and survival post alloHSCT</em></td>
</tr>
<tr>
<td>15:15-15:30</td>
<td>Discussion</td>
</tr>
<tr>
<td>15:30-15:45</td>
<td>Coffee break / Poster viewing</td>
</tr>
<tr>
<td>15:45-16:15</td>
<td><strong>ROUND TABLE DISCUSSION</strong> chaired by Colette Raffoux (Paris)</td>
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<tr>
<td></td>
<td>Mutual Cooperation Between Registries and Transplant Centres - Logistics and Technology</td>
</tr>
<tr>
<td></td>
<td>Participants: Meral Beksc, Ludmila Bubnova, Rita Cekauskiene, Roman Danielewicz, Gerhard Ehninger, Wieslaw Wiktor Jędrezyczak, Andrzej Lange, Carlheinz Mueller, Machteld Oudshoorn, Colette Raffoux, David Steiner</td>
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<tr>
<td></td>
<td>Short introductory talks on EMDIS (5 minutes each): Colette Raffoux, Carlheinz Mueller, David Steiner, Roman Danielewicz, Andrzej Lange</td>
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</tbody>
</table>

Monday, December 17th, 2012  Wroclaw Town Hall

Official Welcome and Concert*

* Supported by the Halina Halska-Fijalkowska Society of Vocal Music Aficionados
# CONCERT

## Program

<table>
<thead>
<tr>
<th>J. S. Bach: Sarabande Gigue Partita d-moll</th>
<th>Adam Czermak - violin</th>
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</thead>
<tbody>
<tr>
<td>V. Monti - Czardas</td>
<td>Adam Czermak - violin</td>
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<tr>
<td></td>
<td>Dominik Mąkosa - piano</td>
</tr>
<tr>
<td>J. Bock - theme from ‘Fiddler on the Roof’</td>
<td>Adam Czermak - violin</td>
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<tr>
<td></td>
<td>Dominik Mąkosa - piano</td>
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<tr>
<td></td>
<td>Grzegorz Piasecki - contrabass</td>
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<tr>
<td></td>
<td>Wojciech Buliński - drums</td>
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<tr>
<td>Jazz standards:</td>
<td>Adam Czermak - violin</td>
</tr>
<tr>
<td>Winter Wonderland</td>
<td>Magdalena Zawartko - vocal</td>
</tr>
<tr>
<td>Santa Claus is coming to town</td>
<td>Dominik Mąkosa - piano</td>
</tr>
<tr>
<td>Holy night</td>
<td>Grzegorz Piasecki - contrabass</td>
</tr>
<tr>
<td>White Christmas</td>
<td>Wojciech Buliński - drums</td>
</tr>
<tr>
<td>Popular music hits:</td>
<td>ARS CANTANDI CHOIR</td>
</tr>
<tr>
<td>Vincent Clarke, arr. Deke Sharon, Anne Raugh - Only You</td>
<td></td>
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<tr>
<td>Seal, arr. Matthusas Becker, Hans van den Brand - Kiss from a Rose</td>
<td></td>
</tr>
<tr>
<td>Wiliam ‘Smokey’ Robinson, Ronald White, arr. Deke Sharon, Anne Raugh - My girl</td>
<td></td>
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<tr>
<td>The most beautiful Christmas Carols:</td>
<td></td>
</tr>
<tr>
<td>arr. Stanisław Niewiadomski - Wśród nocnej ciszy</td>
<td></td>
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<tr>
<td>Romuald Twardowski - Diwa Maryja Cerkow’ Stroiła</td>
<td></td>
</tr>
<tr>
<td>‘Przekażmy sobie znak pokoju’</td>
<td>Soloists and Choir</td>
</tr>
</tbody>
</table>

### Monday, December 17th, 2012

<table>
<thead>
<tr>
<th>20:00-22:30</th>
<th>Gala Dinner</th>
</tr>
</thead>
</table>
### 1st SESSION:
Cord Blood and Autologous Transplantation - the Role and Timing of these Procedures

<table>
<thead>
<tr>
<th>Time</th>
<th>Speaker</th>
<th>Presentation Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>08:00-08:25</td>
<td>Wiesław Wiktor Jędrzejczak (Warszawa)</td>
<td>Perspectives for the use of the cord blood in HSCT</td>
</tr>
<tr>
<td>08:25-08:50</td>
<td>Maria Spyropoulou-Vlachou (Athene)</td>
<td>The role of HLA in cord blood transplantation</td>
</tr>
<tr>
<td>08:50-09:15</td>
<td>Barbara Łukomska (Warszawa)</td>
<td>Neural differentiation and potential use of stem cells from the cord blood for central nervous system transplantation therapy</td>
</tr>
</tbody>
</table>

#### Discussion
09:15-09:30
Katarzyna Bogunia-Kubik (Wroclaw): HLA proficiency testing for Central and East Europe - summary of the XVIII trial

09:45-10:00
Coffee break / Poster viewing

### 2nd SESSION:
Immunological aspects of HSCT

<table>
<thead>
<tr>
<th>Time</th>
<th>Speaker</th>
<th>Presentation Title</th>
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<tbody>
<tr>
<td>10:00-10:25</td>
<td>Grzegorz Dworacki (Poznań)</td>
<td>Morphological patterns and histopathological validation of biopsies in patients following allogeneic hematopoietic stem cell transplantation - standardization attempt</td>
</tr>
<tr>
<td>10:25-10:50</td>
<td>Aleksandra Klimczak (Wroclaw)</td>
<td>Immunopathomorphological features of GvHD in patients transplanted at different levels of matching</td>
</tr>
<tr>
<td>10:50-11:15</td>
<td>Andrzej Lange (Wroclaw)</td>
<td>Immune system network operating post HSCT - outcome and relevance for alloHSCT</td>
</tr>
<tr>
<td>11:15-11:40</td>
<td>Holger Lode (Greifswald)</td>
<td>Post transplant immunotherapy approaches in neuroblastoma</td>
</tr>
<tr>
<td>11:40-11:50</td>
<td></td>
<td>Discussion</td>
</tr>
<tr>
<td>Time</td>
<td>Event</td>
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</tr>
<tr>
<td>----------</td>
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<td></td>
</tr>
<tr>
<td>11:50-12:00</td>
<td>Jacek Nowak (Warszawa): <em>The donor pool and the efficacy of unrelated hematopoietic stem cell donor search process</em></td>
<td></td>
</tr>
<tr>
<td>12:00-13:00</td>
<td>Lunch</td>
<td></td>
</tr>
<tr>
<td>13:00</td>
<td>Transfer (bus provided) to the Center of Research and Education of the Lower Silesian Center for Cellular Transplantation (Muchoborska Street)</td>
<td></td>
</tr>
<tr>
<td>WORKSHOPS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13:30-16:00</td>
<td>Workshops on:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- ‘SBT Resolver / HARPS (Conexio) solutions for routine SBT labs’ - Sami Djoulah, sponsored by POLGEN and OLERUP SSP</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- ‘Standardization for CMV viral load monitoring’ - Mariusz Dadak, sponsored by ROCHE Diagnostics</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- ‘Following reconstitution of CMV immunity by detection of CMV-specific T cells using Dextramers’ - Liselotte Brix, sponsored by Immudex</td>
<td></td>
</tr>
<tr>
<td>16:00-16:30</td>
<td>Coffee Buffet</td>
<td></td>
</tr>
</tbody>
</table>
# ABSTRACTS

<table>
<thead>
<tr>
<th>Title</th>
<th>Author/s (city, country)</th>
<th>Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>THE ROLE OF KILLER IMMUNOGLOBULIN-LIKE RECEPTOR POLYMORPHISMS IN HSCT</td>
<td>Meral Beksaç, Klara Dalva (Ankara, Turkey)</td>
<td>Oral</td>
</tr>
<tr>
<td>THE SAFETY OF UNRELATED DONORS</td>
<td>Gerhard Ehninger, Claudia Rutt, Alexander Schmidt (Dresden, Germany)</td>
<td>Oral</td>
</tr>
<tr>
<td>COMPUTER ALGORITHMS IN THE SEARCH FOR UNRELATED STEM CELL DONORS</td>
<td>David Steiner (Prague, Czech Republic)</td>
<td>Oral</td>
</tr>
<tr>
<td>THE ROLE AND DEVELOPMENT OF CENTRAL POTENTIAL UNRELATED BONE MARROW DONOR AND CORD BLOOD REGISTRY IN POLAND</td>
<td>Roman Danielewicz, Klaudia Nestorowicz (Warsaw, Poland)</td>
<td>Oral</td>
</tr>
<tr>
<td>THE LEVEL OF DONOR-RECIPIENT MATCHING VERSUS MAJOR COMPLICATIONS AND SURVIVAL POST ALLOHSCT</td>
<td>Andrzej Lange (Wroclaw, Poland)</td>
<td>Oral</td>
</tr>
<tr>
<td>IMMUNE SYSTEM NETWORK OPERATING POST HSCT - OUTCOME AND RELEVANCE FOR ALLOHSCT</td>
<td>Andrzej Lange (Wroclaw, Poland)</td>
<td>Oral</td>
</tr>
<tr>
<td>THE ROLE OF HLA IN CORD BLOOD TRANSPLANTATION</td>
<td>Catherine Stavropoulos-Giokas (Athens, Greece)</td>
<td>Oral</td>
</tr>
<tr>
<td>ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATIONS FROM UNRELATED DONORS IN KATOWICE - 15 YEARS OF EXPERIENCE</td>
<td>Miroslaw Markiewicz, Agata Wieczorkiewicz-Kabut, Monika Dzierzak-Mietl, Anna Koclega, Krzysztof Bialas, Patrycja Zielinska, Malwina Malwina, Sławomira Kycz - Krzemien (Katowice, Poland)</td>
<td>Oral, Poster P1</td>
</tr>
<tr>
<td>Title</td>
<td>Authors</td>
<td>Location</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>MISMATCHES OF MINOR HISTOCOMPATIBILITY ANTIGENS AND THEIR INFLUENCE ON RESULTS OF ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FROM SIBLINGS</td>
<td>Monika Dzierzak-Mietla, Mirosław Markiewicz, Urszula Siekiera, Sylwia Mizia, Anna Koclega, Patrycja Ziełinska, Krzysztof Białas, Agnieszka Karolczyk, Sławomira Kyrcz-Krzemien (Katowice, Wrocław, Poland)</td>
<td>Katowice, Wrocław, Poland</td>
</tr>
<tr>
<td>PRESENCE OF ANTI-HLA ANTIBODIES IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FROM HLA-MISMATCHED UNRELATED DONORS</td>
<td>Anna Koclega, Mirosław Markiewicz, Urszula Siekiera, Alicja Dobrowolska, Sylwia Mizia, Monika Dzierzak-Mietla, Patrycja Ziełinska, Sławomira Kyrcz-Krzemien (Katowice, Wrocław, Poland)</td>
<td>Katowice, Wrocław, Poland</td>
</tr>
<tr>
<td>STRATEGY FOR HLA GENOTYPING OF UNRELATED HEMATOPOIETIC STEM CELL DONORS</td>
<td>Ing. Vera Siffnerova, MUDr. Sara Nazarova, Ing. Milena Vrana, RNDr. Marie Dobrovolná (Prague, Czech Republic)</td>
<td>Prague, Czech Republic</td>
</tr>
<tr>
<td>DEMANDS ON INSTRUMENTATION IN HLA GENOTYPING LABORATORY</td>
<td>Hana Klimentova, Renata Macnerova, Vera Siffnerova, Milena Vrana, Marie Dobrovolná (Prague, Czech Republic)</td>
<td>Prague, Czech Republic</td>
</tr>
<tr>
<td>HLA-A, -B ANTIGEN AND DRB1* ALLELE FREQUENCIES AMONG OF VOLUNTEER HEMATOPOIETIC STEM CELL DONORS FROM ST. PETERSBURG</td>
<td>L. Bubnova, I. Pavlova, J. Sokolova, V. Bakay, L. Ivanova (St. Petersburg, Russia)</td>
<td>St. Petersburg, Russia</td>
</tr>
<tr>
<td>DONOR SEARCHES IN CENTRAL POTENTIAL UNRELATED BONE MARROW DONOR AND CORD BLOOD REGISTRY IN POLAND</td>
<td>Klaudia Nestorowicz, Roman Danielewicz (Warsaw, Poland)</td>
<td>Warsaw, Poland</td>
</tr>
<tr>
<td>THE DONOR POOL AND THE EFFICACY OF UNRELATED HEMATOPOIETIC STEM CELL DONOR SEARCH PROCESS</td>
<td>Elżbieta Graczyk-Pol, Anna Marosz-Rudnicka, Renata Mika-Witkowska, Marta Rogatko-Koroś, Agnieszka Długokęcka, Joanna Dziopa, Agnieszka Golec, Jacek Nowak (Warsaw, Poland)</td>
<td>Warsaw, Poland</td>
</tr>
<tr>
<td>Title</td>
<td>Authors</td>
<td>Type</td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------</td>
<td>---------------</td>
</tr>
<tr>
<td>TH17 MEDIATED IMMUNITY AND ASSOCIATIONS WITH NOD2/CARD15 MUTATIONS IN aGVHD AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION</td>
<td>Aleksandra Klimczak, Emilia Jaskula, Andrzej Lange (Wroclaw, Poland)</td>
<td>Oral, Poster P10</td>
</tr>
<tr>
<td>25TH ANNIVERSARY OF MARROW TRANSPLANT ACTIVITY IN WROCLAW LOWER SILESIAN CENTER FOR CELLULAR TRANSPLANTATION WITH NATIONAL BONE MARROW DONOR REGISTRY</td>
<td>Andrzej Lange, Mariola Sędzimirksa, Krzysztof Suchnicki, Janusz Lange, Dorota Duda, Sylwia Mizia, Jolanta Bochenśka, Małgorzata Polak, Barbara Szymczak (Wroclaw, Poland)</td>
<td>Poster P12</td>
</tr>
<tr>
<td>LYMPHOCYTE SUBPOPULATIONS RECOVERY POST ALLOHSCT AND HERPES VIRUSES REACTIVATION INFLUENCED THEMSELVES IN A MUTUAL FASHION</td>
<td>Janusz Lange, Daria Drabczak-Skrzypek, Dorota Dłubek, Emilia Jaskuła, Dariusz Wołowiec, Andrzej Lange (Wroclaw, Poland)</td>
<td>Poster P13</td>
</tr>
<tr>
<td>IL-10 and IL-6 PROMOTER POLYMORPHISMS INFLUENCE THE OUTCOME OF PATIENTS AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION</td>
<td>Emilia Jaskuła, Dorota Dłubek, Sylwia Mizia, Mariola Sędzimirksa, Krzysztof Suchnicki, Janusz Lange, Monika Mordak-Domagała, Andrzej Lange (Wroclaw, Poland)</td>
<td>Poster P14</td>
</tr>
<tr>
<td>HLA PROFICIENCY TESTING FOR CENTRAL AND EAST EUROPE - SUMMARY THE XVIII TRIAL</td>
<td>Katarzyna Bogunia-Kubik, Andrzej Lange (Wroclaw, Poland)</td>
<td>Oral, Poster P15</td>
</tr>
<tr>
<td>ANALYSIS OF THE INCIDENCE OF ANTINUCLEAR ANTIBODIES IN POST ALLOHSCT SETTING WITH RESPECT TO HLA TYPE AND THE DEGREE OF DONOR-RECIPIENT MATCH</td>
<td>Krzysztof Suchnicki, Przemysław Zdziarski, Eliza Turlej, Andrzej Lange (Wroclaw, Poland)</td>
<td>Poster P16</td>
</tr>
<tr>
<td>Title</td>
<td>Authors</td>
<td>Poster</td>
</tr>
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<td>----------------------------------------------------------------------</td>
<td>-------------------------------------------------------------------------</td>
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</tr>
</tbody>
</table>
THE ROLE OF KILLER IMMUNOGLOBULIN-LIKE RECEPTOR POLYMORPHISMS IN HSCT
Meral Beksaç¹,² and Klara Dalva³
¹Department of Hematology, Ankara University Unrelated Donor Registry and Cord Blood Bank, Ankara, Turkey
²Ankara Tip Fakultesi Hematoloji Bilim Dalı, Cebeci Yerleskesi, Dikimevi, 06620 Ankara, Turkey
³HLA Typing Laboratories, Department of Hematology, Ankara University School of Medicine, İbni Sina Hospital, Sihhiye, 06100 Ankara, Turkey

Despite all efforts to improve HLA typing and immunosuppression, it is still impossible to prevent severe graft versus host disease (GVHD) which can be fatal. GVHD is not always associated with graft versus malignancy and can prevent stem cell transplantation from reaching its goals. Overall T-cell alloreactivity is not the sole mechanism modulating the immune defense. Innate immune system has its own antigens, ligands, and mediators. The bridge between HLA and natural killer (NK) cell-mediated reactions is becoming better understood in the context of stem cell transplantation. Killer immunoglobulin-like receptors (KIRs) constitute a wide range of alleles/antigens segregated independently from the HLA alleles and classified into two major haplotypes which imprints the person's ability to suppress or to amplify T-cell alloreactivity. This paper will summarize the impact of both activating and inhibitory KIRs and their ligands on stem cell transplantation outcome. The ultimate goal is to develop algorithms based on KIR profiles to select donors with maximum antileukemic and minimum antihost effects.

Presentation: Oral

THE SAFETY OF UNRELATED DONORS
Gerhard Ehninger, Claudia Rutt, Alexander Schmidt
TU Dresden, DKMS Deutsche Knochenmarkspenderdatei

Introduction: Donor follow-up is indicated to detect potential long-term risks for allogeneic stem cell donors.
Materials and Methods: We sent a follow-up questionnaire to 15,456 donors of peripheral blood stem cells (PBSC) or bone marrow (BM) within a retrospective study design. Donors were asked for their general health conditions (question #1), hospitalization or long-term medical treatment since donation and the underlying disease (#2), prescription drugs taken regularly or for at least 4 week since donation (#3) and for their willingness to donate again (#4).
Results: With 12,559 responses, we achieved an overall return rate of 81.3% leading to 30,777 observation years for PBSC donors (n=8,730),
23,037 for BM donors (n=3,556) and 1,414 for donors of both PBSC and BM (n=273). The median (average) time since donation of responding donors was 3.3 (4.2) years.

Most donors (95.1% of PBSC, 96.0% of BM and 92.2% of PBSC+BM donors) assessed their health conditions as very good or good (comparison of PBSC and BM donors: χ² test, p=0.03). In univariate analysis, PBSC donors showed significantly less often indicators for health-related problems according to questions #2 and #3 than BM donors (χ² tests, p Multivariate analysis, however, did not confirm these differences). As the PBSC sample included significantly more male.

In total, 85 malignancies were reported within the project, thereof 50 in 48 PBSC donors, 31 in BM donors and 4 in donors of both PBSC and BM. Six cases of hematological malignancies are included: 2 cases of Hodgkin’s disease (both in PBSC donors), plasmocytoma (PBSC donor), AML (BM donor), Non-Hodgkin lymphoma (BM donor), CLL (donor of both PBSC and BM). Through donor center practice, we got notice of 21 further donor malignancies, 5 of those were hematological: Hodgkin’s disease (PBSC donor), plasmocytoma (PBSC donor), AML (donor of both PBSC and BM), and 2 cases of CML (1 PBSC donor, 1 BM donor).

The observed standard incidence ratio (SIR) for all malignancies and all donors of 0.99 (95% confidence interval: 0.79-1.24) suggests that underreporting does not substantially affect the quality of the collected data on malignancies. Corresponding SIR values for PBSC and BM donors are 1.12 (0.82-1.50) and 0.84 (0.56-1.19), respectively.

A higher-than-expected incidence of malignant melanoma could be observed in BM donors (SIR=3.02, 95% confidence interval 1.38-5.73, based on 9 reported cases). As a correlation between BM donation and the development of malignant melanoma seems not to be plausible, a type I statistical error may be the most probable explanation for this result. Furthermore, we observed lower-than-expected incidences of lung cancer (SIR=0.15, 95% confidence interval 0.00-0.82) and malignant neoplasms of lips, oral cavity and pharynx (SIR=0.00, 95% confidence interval 0.00-0.75). A correlation between malignancy development and a lack of health-conscious behavior is well-known for these malignancies. One might, therefore, hypothesize that stem cell donors show more often health-conscious behavior than the general population.

No increased incidences of leukemia, non-Hodgkin lymphoma, plasmocytoma or Hodgkin’s disease compared to age- and gender-adjusted incidences of the German population could be observed in PBSC, BM or PBSC+BM donors. The respective SIR values with 95% confidence intervals for PBSC donors are 0.00 (0.00-2.62), 0.00 (0.00-1.72), 3.59 (0.11-20.02) and 2.46 (0.30-8.89). Based on these data, a threefold or stronger increase of the leukemia risk through PBSC donation can be excluded with an error probability of 0.05.
The high number of observation years supports the relevance of our study. A detailed analysis of malignancies allowed us to narrow down a potential increase of leukemia risk after PBSC donation that has been discussed in the literature. In summary, we found no evidence that PBSC or BM donation might be unsafe procedures.

**Conclusion:** Our study shows that retrospective stem cell donor follow-up projects may be valuable complements in addition to prospective donor follow-up that often suffers from high drop-out rates.

**Presentation:** Oral

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**COMPUTER ALGORITHMS IN THE SEARCH FOR UNRELATED STEM CELL DONORS**
David Steiner
Department of Cybernetics, Czech Technical University in Prague

Hematopoietic stem cell transplantation (HSCT) is a medical procedure in the field of hematology and oncology, most often performed for patients with certain cancers of the blood or bone marrow. A lot of patients have no suitable HLA-matched donor within their family, so physicians must activate a “donor search process” by interacting with national and international donor registries who will search their databases for adult unrelated donors or cord blood units (CBU). Information and communication technologies play a key role in the donor search process in donor registries both nationally and internationally. One of the major challenges for donor registry computer systems is the development of a reliable search algorithm. This work discusses the top-down design of such algorithms and current practice. Based on our experience with systems used by several stem cell donor registries, we highlight typical pitfalls in the implementation of an algorithm and underlying data structure.

**Presentation:** Oral

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**THE ROLE AND DEVELOPMENT OF CENTRAL POTENTIAL UNRELATED BONE MARROW DONOR AND CORD BLOOD REGISTRY IN POLAND**
Roman Danielewicz, Klaudia Nestorowicz
Polish Transplant Coordinating Center Poltransplant

**Introduction:** According to change in transplant law since 2011 there is one Central Potential Unrelated Bone Marrow Donor and Cord Blood Registry (CBMR Poltransplant) in Poland instead of six previously independent registries. CBMR Poltransplant is registered in BMDW as PL5.
Former registries were changed to Donor Centers (DCs) that must have accreditation of Ministry of Health. Currently there are 13 DCs in Poland. DCs should transfer their data immediately to CBMR Poltransplant. This is possible due to the access to registry database and software which is continuously improved.

**Materials and Methods:** Development of DCs and the numbers of donors data transferred to CBMR Poltransplant will be discussed during presentation. Part of the donors were recruited by DCs basing on their own resources, but large number of donors in last few years was recruited with the help of state budget (e.g. from National Program of Development of Transplantation Medicine - 24568 donors in 2011, 17729 in 2012). Currently there are 111000 of donors in CBMR. PL5 register, after changing its role from DC to Central Register, has transferred almost 50 000 of donors to be handled by DCs established in 2011.

**Results:** Data of Polish donors in CBMR Poltransplant were searched by search centers from UK, Poland, Germany, Turkey, USA and others. Since 2001 more than 4167 searches were carried out in our register. This year we had 1052 searches, more than 350 CTs and 71 requests for stem cell collection. This is 35% increase of searches from 2011, 75% increase of CTs and 136% increase of collections. CBMR Poltransplant is coordinating and financing searches for Polish recipients. In 2012 almost half of donors accepted for transplantation for Polish recipients are from our DCs (in 2011 only 38%).

**Conclusion:** Despite organizational problems centralization of bone marrow donors registries in Poland and support of development of DCs are resulting in vast increase of donors number and increased percentage of Polish donors providing help to Polish patients.

**Presentation:** Oral

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THE LEVEL OF DONOR-RECIPIENT MATCHING VERSUS MAJOR COMPLICATIONS AND SURVIVAL POST ALLOHSCT

Andrzej Lange¹,²

¹Department of Clinical Immunology, Institute of Immunology and Experimental Therapy, Polish Academy of Sciences, Wroclaw, Poland
²Lower Silesian Center for Cellular Transplantation with National Bone Marrow Donor Registry, Wroclaw, Poland

A breakthrough in hematopoietic stem cell transplantation was achieved when the role of HLA in matching donor-recipient pairs became known and was further substantiated by the progress in technology enabling accurate determination of HLA specificities. The other crucial step was accomplished when a search of potential donors worldwide became readily available (BMDW, EMDIS). In the process of donor-recipient matching 5 loci
specificities determined at the allele level are routinely used. However, even having these tools and more than 12 million donors worldwide we are still failing to find perfectly matched donors for more than 20% of potential recipients. This is due to the presence of rare alleles or rare linkage disequilibrium between DR and DQ and/or B and C specificities. Therefore, it is important to know whether matching at different loci plays a similar role in shaping the outcome of HSCT influencing the risk of acute graft-versus-host disease (aGvHD) and overall survival. Our work, together with those of others, supports the following conclusions:

(i) patients receiving transplants from donors with at least one mismatch at the allele or antigen level tended to have worse 2-year survival than those 10/10 matched,
(ii) locus A mismatches have a more deleterious effect on overall survival and increase the risk of aGvHD compared to those in B or C loci,
(iii) a negative effect of locus DR mismatches is seen in overall survival and in the frequency of aGvHD but DQ mismatches are better tolerated,
(iv) length of matching adversely affects survival,
(v) matching for DP specificities should consider the level of matching and the putative role of so-called permissive and non-permissive mismatches.

In making the final decision also other factors including donor CMV serostatus may be considered. CMV reactivation constitutes one of the main threats post HSCT. Up to thirty percent of patients post HSCT suffer from CMV reactivation/infection. We documented that recipients receiving a transplant matched at a level lower than 10/10 are more susceptible to CMV reactivation/infection. Independently of the level of matching, CMV IgG seropositivity of recipients with concomitant seronegativity of donors constitutes a risk factor of CMV reactivation. IgG negativity in donors favors the outcome of HSCT if recipients are also CMV IgG negative. CMV IgG seronegative donors’ lymphocytes poorly generate IFNgamma when confronted with CMV peptides, which reflects a lack of CMV peptide recognition. The risk of CMV reactivation is increased in IgG CMV + patients receiving a transplant from a seronegative donor. CMV immune competence of donors may reduce the risk of CMV reactivation. Data presented here should be considered in relation to the clinical situation of patients and biological features of a potential donor including age and gender and if used during donor selection may facilitate this process, providing some rationale behind the undertaken decision.

Presentation: Oral
The use of hematopoietic stem cell transplantation (HSCT) as a rescue procedure after high dose chemotherapy still constitutes a major field of medical activity. HSCT using autologous cells is not possible if the marrow in spite of the primary chemotherapy is colonized by malignant cells and also when stem cells harboring life-threatening mutations have to be replaced. In the allogeneic setting employed, identical twins and siblings having the same chromosome 6 as recipients substantially differ with respect to the outcome. Matched sibling transplantations are associated with the risk of GvHD, which is rarely seen if at all in the identical twins setting. However, the other side of the coin shows a lack of graft potential to keep down cancer cells providing that they are responding to immunological surveillance. Allogeneic transplantation may play a significant role as a cancer immunotherapy procedure. The situation became even more complex when due to small size families the need for unrelated donor transplantations substantially increased. Again we learned that optimal matching based on 5 loci specificities determined at the high resolution level results in a similar survival as seen in a matched family donor setting. However, the advantage associated with the graft vs leukemia effect is counterbalanced with a higher risk of aGvHD and a slow immune reconstitution with a higher incidence of infectious complications including viruses, bacteria and fungi. Knowing these threats a great effort was undertaken, by researchers and medical staff, to implement preemptive and prophylactic measures preventing consequences of the drawbacks associated with unrelated donor HSCT. In the present talk the following points will be discussed.

1. Reconstitution of the immune system starts with the expansion of transplanted lymphocytes at different stages of differentiation. They do their job according to the competence. The presence of IgG CMV antibodies in donors is associated with the ability of lymphocytes to produce IFNgamma upon CMV peptide challenge, which benefits the recipients with a lower rate of reactivation and better survival. The IFNgamma encoded gene physiologically differs from person to person with a single nucleotide substitution which if present in promoter or intron 1 regions may influence the pace of transcription. Indeed, individuals having an IFNgamma allele associated with a higher generation potential are less susceptible to CMV and EBV reactivation, with a positive effect on survival.
The same influences the risk of aGvHD, which means that the whole situation is rather complex.

2. Both aGvHD and infectious complication risk depends on the conditioning regimen toxicity. The latter apparently depends on the intensity of this procedure, but is also modified by genetic features of genes encoding strong pro-inflammatory cytokines TNF\(\alpha\) and IL-6. Defined nucleotide substitution patterns of both genes influence the susceptibility of transplanted patients to toxic injury and in addition polymorphic features of IL-6 genes control this gene transcription process, resulting in higher or lower CRP production to confront infections. Again these features shape the risk of aGvHD (IL-6 G allele).

3. Just after manifestation of conditioning regimen toxicity fades aGvHD becomes clinically apparent in a majority of transplanted patients. This process varies in intensity and is welcome if associated with the graft vs leukemia effect but must be controlled so as not to exert a life-threatening deteriorating effect. Hope lies in the activity of T regulatory cells which naturally arise during an active immune response including alloreactivity to keep it under control. Treg lymphocytes try to control immune response cells, being in a higher proportion in blood than immune function exerting cells; however, if they do not expand enough, aGvHD becomes clinically apparent. We found that the gene of IL-10, known from its regulatory potential, is characterized by different SNP constellations and patients carrying ACC haplön constellation suffer less frequently from aGvHD. IL-6 CC low producer genotype and IL-10 GCC high producer haplotype associate with a lower risk of aGvHD. Importantly, patients carrying this haplotype had a higher proportion of FoxP3+ lymphocytes in blood at all early observation points post HSCT.

4. The presence of mutations in the NOD2/CARD15 gene influences the recognition of bacteria wall constituents (e.g. muramyl dipeptide - MDP), which finally results in cytokine generation deregulation favoring aGvHD. Notably, we found that the presence of NOD2/CARD15 mutations resulted in a decrease of the number of IL-17 producing lymphocytes in blood likely marginalized at the tissue site where they exert strong pro-inflammatory activity.

In conclusion, improving our knowledge on pathophysiology of aGvHD and that of immunodeficiency in unrelated donor transplanted patients will enable tailoring of immunosuppression and supportive therapy given as prophylactic or as pre-emptive measures.

**Presentation:** Oral
THE ROLE OF HLA IN CORD BLOOD TRANSPLANTATION
Catherine Stavropoulos-Giokas
Hellenic Cord Blood Bank, Biomedical Research Foundation Academy of Athens (BRFAA), 4 Soranou Efessiou Street, 115 27 Athens, Greece

The experience of the last 20 years indicates that cord blood transplantation is a valid alternative to Bone Marrow (BM) and PBSC transplants for patients suffering from malignant or non-malignant diseases, who do not have a matched sibling donor or a matched volunteer unrelated donor. A low rate of Graft versus Host Disease (GVHD) in the presence of higher HLA disparity, represents the main advantage of the umbilical cord grafts, while delayed engraftment due to limited cell dose is still the major drawback [1]. CB is a viable source particularly for racial and ethnic minority patients whose genetic variations are not included in unrelated volunteer donor registries [2].

The role of HLA mismatches in CBT remains unclear as most transplants have been selected on low resolution class I HLA typing and allelic level class II typing. In malignant diseases, HLA mismatching is partially overcome by increasing the cell dose. Recent data on associations between HLA disparity and survival, support that there is a direct association between the number of donor-recipient HLA mismatches and the risk for GVHD [3].

Unrelated Cord Blood Transplantation in Children
The Cord Blood Transplantation Study (COBLT) [4], has reported the clinical outcomes of unrelated donor umbilical cord blood transplantation in pediatric patients with hematologic malignancies, and suggest selecting CB units that are at least 4 of 6 by LR typing at class I loci and HR typing at HLA-DRB1. Even if HR matching decreases GVHD, overall survival may not be affected because of competing contributions of GVHD and graft-versus-Leukemia.

In patients with hemoglobinopathies, the risk factors like the donor/recipient mismatching and cell dose, are probably amplified by the effect of multiple transfusion exposures, that might sensitize the recipient to donor alloantigens or in the case of SCD the cytokine milieu of the disease might interfere with engraftment.

Unrelated Cord Blood Transplantation in Adults
The first unrelated cord blood transplantation was performed in 1996 and since then, more than 20,000 patients have undergone CB transplantation. In the adult setting the use of a 4-6/6 match CB is considered the equivalent of a 7/8 allele matched unrelated donor when a fully matched donor is unavailable [5, 6].

Intense efforts have been made to determine the “permissive” HLA mismatches that do not increase post-transplant risks. Including HLA mismatch direction in search procedures permits easy identification of grafts with unidirectional mismatches, allowing to give priority to graft-
versus-host direction only (GVH-O) and to avoid rejection direction only (R-O) grafts [7].

Since the identification of HLA-C as a classical transplantation antigen, donor mismatching for HLA-C has been shown to be a risk factor after myeloablative, non-myeloablative, unrelated donor, cord blood, marrow and peripheral blood stem cell transplantation [8].

There is data analyzing the impact of administering a CB unit that shares a non inherited maternal HLA antigen (NIMA) with a mismatched HLA antigen in the recipient, for patients with hematologic malignancies treated with CB transplantation [9], which may define “permissive” HLA mismatches.

There is currently little clinical evidence suggesting an important clinical impact for HLA-DR-DQ or DP matching for CB transplantation as well as other non HLA loci like Minor Histocompatibility antigens, Killer immunoglobulin-like receptors (KIR), Cytokines, Chemokines and immune response genes.

Double CB transplantation
In order to overcome cell dose limitations, improve engraftment rates and immune reconstitution, a strategy consisting of administering two partially matched CB grafts called double CBT (dCBT) has been implemented. In almost all dCBT outcomes [10], single-unit dominance is observed. No relationship was found between CB/recipient match and unit dominance, even at the allelic (HR) level: a better HLA matched unit at high resolution was not more likely to become the dominant unit. Although no consensus has yet been reached concerning intra-unit HLA match in dCBT, current practice is to maximize matching of the two units to the recipient at the antigen-level for HLA-A and -B, and at the allele-level for DRB1 with a minimum of 4/6 match.

Cord Blood Unit Selection
With the number of cryopreserved CB increasing and the better understanding of the factors influencing transplant outcome (cell dose, HLA match, CD34+ dose etc), a need has arisen for better strategies regarding unit selection.

NMDP strategy [12] for cord blood unit selection indicates that all patients should receive a cell dose of >2.5 x 10⁷ NC/kg. In case of double CBT, each CB should have a cell dose of >1.5 x 10⁷ NC/kg. Moreover, the patient should receive a 4/6 or better A, B, DR HLA match. A very important parameter, is to avoid HLA mismatches at loci in which patients have preformed HLA antibodies. It has also been suggested that if maternal typing is available, a CB with a NIMA-shared antigen should be preferred. Extended HLA matching may yield better outcomes after cord blood transplantation, although HLA match does not predict survival nor the predominant cord.

Considering the additional increasing molecular understanding of most diseases, allogeneic stem cell transplantation is headed towards a next generation of transplantation procedures: the individual adaptation in
terms of graft source, engineering, and post-transplant immune interventions depending on the type of disease and underlying genetic alterations of donors and patients. Cord Blood, with its immediate availability and the possibility of having genotypically well characterized units, is a prime candidate for prospective applications combining the beneficial effects of several allogeneic transplantation strategies.

2. Gluckman E, Choice of donor according to HLA typing and stem cell source. Hematopoietic Stem Cell Transplantation; The EBMT handbook; 6th edition, 2012, ch.6: 90-107

**Presentation:** Oral
ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATIONS FROM UNRELATED DONORS IN KATOWICE - 15 YEARS OF EXPERIENCE
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Introduction: Transplant Center in Katowice (CIC:677) has 15 years of experience in performing allogeneic hematopoietic cell transplantations from unrelated donors (allo-UD-HCT). Analysis of logistical data related to this activity is presented.

Materials and Methods: Data of 558 first allo-UD-HCTs performed between years 1997-2012 were included into analysis.

Results: A vast majority of patients, 552[99%] were Polish (PL), whereas the most donors, 423[76%], were foreign (F). An increasing contribution of PL donors, in 3 consecutive 5-year spans, was observed: 12%, 20% and 30%, respectively. Interestingly, in the last 2 years it was as high as 38%.
Number of donations provided by registries of PL donors were as follows: PL1-9[6%], PL2-7[5%], PL3-33[24%], PL4-13[10%], PL5-46[34%] and DKMS.PL6 (donors center recruiting in Poland for ZKRD)-27[20%].
Donations from F donors were provided by: Germany-312[74%], USA-34[8%], UK-19[4%], Czech Republic-16[4%], Italy-13[3%], France-6[1%], the Netherlands and Israel- 5 each [1%], plus 7 other European and 2 oversea countries [HLA typing and matching of donor-recipient pairs was performed in the following laboratories: Medigen-266[48%], DCTK-150[27%], IHiT-114[20%], CSKWUM and Olomouc (Czech Republic)- 14[2.5%] each. All of them, but 40 (incompletely typed before the year 2006), were high resolution determined in HLA-A,B,C,DRB1,DQB1 loci. The donor-recipient matching accuracy was: 376[67%] fully matched donors, 160[31%] single- and 12[2%] double-mismatched donors in HLA-A (26), HLA-B (20), HLA-C (91), HLA-DRB1 (3), and HLA-DQB1 (30). Mismatched HLA loci were homozygous in 25[14%] donors and 12[7%] recipients. The percentage of fully HLA- matched donors was higher in PL [88%] than in F [61%] donors.

Conclusion: Donor-recipient matching quality significantly improved and the number of domestic allo-UD-HCTs substantially increased within last 10 years, what had a great impact on transplantation activity and results.

Presentation: Oral, Poster P1
MISMATCHES OF MINOR HISTOCOMPATIBILITY ANTIGENS AND THEIR INFLUENCE ON RESULTS OF ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FROM SIBLINGS

Dzierzak-Mietla Monika, Markiewicz Miroslaw, Siekiera Urszula¹, Mizia Sylwia², Koclega Anna, Zielinska Patrycja, Bialas Krzysztof, Karolczyk Agnieszka, Kyrcz-Krzemien Slawomira

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Introduction: Minor histocompatibility antigens (MiHA) are polymorphic peptides presented in context of HLA molecules that in case of donor/recipient mismatch may influence outcomes of allo-HCT. The goal of this study was to identify alleles of 11 MiHA in sibling donor/recipient pairs and to analyze the impact of immunogenic MiHA mismatches on results of allo-HCT.

Materials and Methods: The study group consisted of 62 pts (34 women, 28 men), median age 38(14-59) yrs, and their HLA-matched sibling donors (30 women, 32 men), median age 35(14-60) yrs. Allo-HCTs were performed for AML, ALL, MDS, CML and NHL in yrs 2000-2008. Alleles encoding 11 MiHAs: HA-1, HA-2, HA-3, HA-8, HB-1, ACC-1, ACC-2, HwA-9, HwA-10, UGT2B17 and HY were tested with use of Dynal AllSet mHA typing kit and PCR-SSP method. Only immunogenic MiHA mismatches determined with use of dbMinor database were evaluated.

Results: Median time from diagnosis to allo-HCT was 0.62(0.24-12.91) yrs, median follow-up was 3(0.04-10) yrs. Immunogenic MiHA mismatches were observed in 42 (68%) donor/recipient pairs: unidirectional GVH- or HVG-directed in 18 each and bi-directional in 6 pairs. Autosomally-encoded GVH-directed MiHAs influenced OS, which after 4 years was 76% in pts with and 53% in pts without disparities. Acute GVHD observed in 27 pts, including 24 serious (III-IV), and chronic GVHD observed in 25 pts, including 12 extensive, was influenced by GVH-directed disparities of HY. GVH-directed disparities of HY also adversely affected OS and DFS. Mismatches of MiHAs in the HVG direction, both autosomal and with restricted tissue distribution, decreased probability of relapse.

Conclusion: Immunogenic disparities of MiHAs were identified in 2/3 of HLA-matched sibling donor-recipient pairs, distribution of GVH- and HVG-directed mismatches of autosomally encoded MiHAs and HY was similar. Mismatches of HY significantly influenced incidence of serious acute and extensive chronic GVHD and decreased OS and DFS.

Presentation: Poster P2
PRESENCE OF ANTI-HLA ANTIBODIES IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FROM HLA-MISMATCHED UNRELATED DONORS

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Introduction: The clinical significance of anti-Human Leukocyte Antigen Antibodies (anti-HLA Abs) is well known in solid organ transplantation and transfusional medicine, but in allogeneic hematopoietic stem cell transplantation (allo-HSCT) it has not been finally defined. The purpose of this study was to detect anti-HLA Abs before and after allo-HSCT from HLA-mismatched unrelated donors (UD).

Materials and Methods: We examined 53 pts with acute leukemia: 20(37%) lymphoblastic and 33(63%) myeloblastic, who received allo-HSCT from partially HLA-mismatched UD. HLA- A, B, C, DR, DQ alleles were PCR-typed. Single HLA antigen or allele mismatch was present in 32(60%) or 13(24%)pts, double antigenic or allelic mismatch in 3(5.6%) or 3(5.6%)pts, respectively, and combined antigenic/allelic HLA mismatches in 2(3.7%)pts. Anti-HLA A, B, C, DR, DQ and DP antibodies were identified in ELISA-based DynaChip Technology using microchips spotted with purified HLA antigens immobilized on the surface of the glass chip.

Results: Anti-HLA Abs were detected in 24(45%) pts before allo-HSCT: against class I, II or both in 8(33%), 5(20%) and 11(45%)pts, respectively. Following allo-HSCT, anti-HLA Abs were detected in 37(69%) pts: against class I, II or both in 15(40%), 6(16%) and 16(43%) pts, respectively. In 9(17%) pts anti-HLA Abs were not detected neither before nor after allo-HSCT. Anti-HLA Abs directed against the class of mismatched HLA antigens were detected in 10 pts before and in 20 pts after allo-HSCT. Although we did not identify donor- or recipient- allele specific anti-HLA Abs, detected anti-HLA Abs belonged to the same CREG (Cross-Reactive Group) as the mismatched HLA antigen in 3 pts before and 5 pts after allo-HSCT.

Conclusion: Our preliminary results indicate that anti-HLA Abs are present pre- and post-transplant in mismatched allo-HSCT recipients and thus may be potentially responsible for the occurrence of transplant-related complications, what warrants further investigation.

Presentation: Poster P3
STRATEGY FOR HLA GENOTYPING OF UNRELATED HEMATOPOIETIC STEM CELL DONORS
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Introduction: Hematopoietic stem cell transplantation (HSCT) is part of standard treatment protocols for hematological, oncohematological and metabolic diseases. Human leukocyte antigen (HLA) matching is considered to be an important factor in therapy success. In terms of HSC compatibility of donor and recipient, five HLA loci are tested at high resolution (HR) level.

Materials and Methods: The EFI (European Federation for Immunogenetics) standards specify HR level which is sufficient to determine the degree of HLA match for HSCT. This level is defined as a four-digit identification of alleles with all ambiguities distinguished in exon 2 and 3 for HLA class I and exon 2 for HLA class II and all null alleles excluded.

Results: Patient samples without HLA-identical related donors are typed in class I loci (A, B, C - exons 2, 3, 4) and in class II loci (DRB1 - exon 2, DQB1 - exon 2, 3). Results are forwarded to a transplant coordinator and further to unrelated donor registries. Based on the preliminary search, samples of potentially suitable donors are ordered from national registries as well as from foreign ones (after an approval of a patient health insurance company). Typing results from the registries are completed and confirmed at HR level. Typing is performed to preferentially exclude potential differences, potential mismatches are consulted with transplantologists whether to complete the result or stop typing. Due to high polymorphism of HLA system and thus the difficulty finding a fully HLA-identical HSC donor, functional differences between alleles (P group in HLA class I) are taken into consideration while reporting results.

Conclusion: Established quality management system (our HLA laboratory is accredited by the Czech Institute for Accreditation according to ČSN EN ISO / IEC 17025 and 15189 norms), the activity in compliance with EFI standards (accreditation since 2007) and cost-effective approach allow us to cover testing by public health insurance.

Presentation: Oral, Poster P4
DEMANDS ON INSTRUMENTATION IN HLA GENOTYPING LABORATORY
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Introduction: Genotyping of HLA-A, -B, -C, -DRB1 and -DQB1 loci to determine histocompatibility for hematopoietic stem cell transplantation (HSCT) is performed by polymerase chain reaction with sequence-specific primers (PCR-SSP) and sequence-based typing (SBT).

Materials and Methods: The key to successful HLA polymorphism detection by above mentioned methods is to have a good quality DNA in an amount of 150 - 200 ul with minimum concentration 20 ng / ul. For this purpose our laboratory uses an automatic DNA extraction and purification device iPrep from Qiagen. Critical parameters for its selection were fully automated parallel processing of up to 13 samples, excellent yield and high quality of purified DNA. The measurement of DNA concentration is performed on spectrophotometer NanoDrop that has the advantage of fast processing and a small amount of the sample needed.

Results: The next step in sample processing is PCR reaction. Technical parameters of PCR cyclers must comply with requirements of diagnostic kits used according to the manufacturer instructions listed in package leaflets. Our laboratory uses PCR-SSP kits from Olerup We also use an electrophoretic gel system from the same company - the format is compatible to Biometra documentation system and graphics of SCORE evaluation software. The continuity of systems used reduces the potential for errors.

Conclusion: For SBT we use the 8-capillary genetic analyzer ABI 3500. The analyzer is fully automated: all the steps from sample injection to data analysis (sequencing, fragment analysis, forensic applications) are automatic. The advantages over former types of analyzers are also automatic monitoring of supplies consumption, including batch number and expiration date, as well as monitoring of planned device maintenance. Additionally ABI 3500 has a unit for placement of two plates which allows better utilization of working time of the analyzer for sequencing and fragment analysis.

Presentation: Poster P5
HLA-A, -B ANTIGEN AND -DRB1* ALLELE FREQUENCIES AMONG OF VOLUNTEER HEMATOPOIETIC STEM CELL DONORS FROM ST.PETERSBURG

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Introduction: Cohort of volunteer hematopoietic stem cell donors of Blood Banks of Russia includes the populations from various Russian regions (St. Petersburg, Samara, Kirov, Rostov-upon-Don, Nizhny Novgorod, Chelyabinsk). Now in Russia there are 8 administrative regions. In each region live people of different nationalities. In the present study we have performed HLA typing of volunteer hematopoietic stem cell donors from St.Petersburg. The majority of the population of north-west region, in which St.-Petersburg is located, is Russian.

Materials and Methods: HLA typing was performed in volunteer hematopoietic stem cell donors Blood Banks of Russia from St.Petersburg (A and B loci - 1198 persons; DRB1 loci 450 persons). All these persons are active blood donors. Two different methods were used for HLA tying: HLA-A, -B antigen were studied using CDC; HLA-DRB1* alleles (low resolution) were studied using PCR-SSP method. HLA typing was performed in Russian Center of Tissue Typing (EFI accredited laboratory).

Results: Typing of volunteer hematopoietic stem cell donors from St.Petersburg revealed 17 antigens for HLA-A locus with A2 (48,9%), A3 (28,7%), A1 (20,8%) as the most frequent ones. The least frequent of antigen were A43 (0,1%), A36 (0,2%), A34 (0,5%). The results of HLA-B typing showed the presence of 30 antigens. The most frequent were B7 (26,8%), B35 (20,9%), B12 (18%). The least frequent of antigen were B65 and B42 (both - 0,1%), B63 (0,2%), HLA-DRB1 typing showed the presence of 13 allele groups, among which were prevailing DRB1*15 (14,45%), DRB1*13 and DRB1*07 (both - 13,89%), DRB1 *01(13,22%). DRB1*10 (1,22%), DRB1*09 and DRB1* 14 (1,56%) were the least frequent.

Conclusion: These data may be useful for studies “HLA and diseases”, population studies as well as for transplantation purposes.

Presentation: Oral, Poster P6
DONOR SEARCHES IN CENTRAL POTENTIAL UNRELATED BONE MARROW DONOR AND CORD BLOOD REGISTRY IN POLAND
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Introduction: Since 2011 there is one Central Potential Unrelated Bone Marrow Donor and Cord Blood Registry (CBMR Poltransplant) in Poland instead of six previously independent registries. CBMR affiliated in BMDW as PL5 is cooperating with other registries worldwide, including NMDP (USA). There are 13 DC in Poland which transfer their data to CBMR Poltransplant using improved registry’s database and software. Currently there are 111000 of donors in CBMR.

Materials and Methods: Data of Polish donors are searched by centers from UK, Poland, Germany, Turkey, USA and others. This year we had already more than 1025 search requests, more than 350 CTs and 71 requests for stem cell collection from PL5. The number of searches is dynamically increasing along with the growing number of donors. This is clearly shown in data of registry and 13 Donor Centers. Poltransplant is coordinating searches for Polish patients requiring BM transplant. This has grown almost threefold since 2001 (respectively 162 in 2001, 525 in 2012 till October). More than 3600 searches for Polish patients were carried out in our register during last 12 years (exact numbers will be presented in details on poster).

Results: Currently in Poland we have 4 search centers that are contracted by CBMR Poltransplant for the task. While in 2011 number of Polish donors matched for Polish BMTx was not exceeding 38%, in 2012 almost half of donors accepted were from Polish DCs. On the poster we will discuss in details the number of searches from Polish transplant centers. While activity of those centers is not equal, together they fully cover the needs of Polish tx centers.

Conclusion: Increasing number of donors in Polish CBMR Poltransplant and efficient system of donor-recipient matching is resulting in increased number of Polish donor-Polish recipient matches.

Presentation: Poster P7
THE DONOR POOL AND THE EFFICACY OF UNRELATED HEMATOPOIETIC STEM CELL DONOR SEARCH PROCESS

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Introduction: The availability of matched unrelated hematopoietic stem cell donor (UD) in domestic and international registries is crucial for hematopoietic stem cell transplantation (HSCT) treatment in patients with lack of matched family donor (MFD). In 2006 the number of Polish donors in registry was not satisfactory. 35 173 donors (including 18 449, 52% ABDRB1 typed donors) were submitted to BMDW database. An increment dynamics of Polish registries was high, especially in 2010 and 2011 (146 749 and 285 074 donors, respectively), with 90% ABDR typed donors. Respective numbers of all BMDW donors, ABDR typed donors and % were as follows: 2006 - 10 700 000, 7 100 000 (66%); 2010 - 14 900 000, 12 800 000 (86%) and 2011 - 18 600 000, 16 800 000 (87%).

Materials and Methods: We compared the efficiency of UD search procedures conducted in consecutive 2006-2011 in Poland for N=2424 patients.

Results: Between 2006 and 2011 an appropriate donor have been found for 1474 (61%) patients in need of HSCT (range from 48% to 83% in 2006 and 2011, respectively, OR=5.07; 95%CI 3.6-7.2; p=7,3x10^-20). The percent of patients for whom an appropriate donor was found in Polish and BMDW-reporting registries was similar and highly determined by increased numbers of ABDR typed donors (coefficient of determination, r^2= 0.75; p=0.027).

The successful finding of ethnically matched donor of European, Polish ancestry during all the period of 6 years was determined stronger by the number of BMDW reported donors than Polish donors (r^2=0.96, p=0,00047 and r^2=0.86, p=0,0080, respectively) but during last 3 years (2009/2010/2011) it was diversely determined depending on a search center. In Institute of Hematology and Transfusion Medicine search center the increased fraction of Polish donors was significantly determined by the increased number of donors with Polish ethnicity (r^2=1.00, p=0.026) and became not significantly determined by external BMDW-reported registries (r^2=0.98, p=0.062). In remaining Polish search centers the fraction of Polish donors found for Polish patients in 2006-2011 was not significantly determined by the number of Polish donors (r^2=0.79, p=NS).

The successful finding of fully (10/10 allelic specificities) matched donor was significantly dependent on the search center. The highest % of patients with 10/10 donors was achieved by the search centers of Institute of Hematology and Transfusion Medicine and the Central Clinical Hospital
of Warsaw Medical University (82% and 77%, respectively, p=NS). Two remaining search centers less efficiently submitted to transplant centers fully matched donors than the leading center (72%, p=0.0014 and 64%, p=0.000000032). In 2011 for 11% of patients submitted to our search center an acceptable donor could not be found. For 92% of remaining patients a perfectly matched donor (10/10) and for 8% of patients 9/10 donor was found. These donors were accepted for transplantation in collaborating transplant clinics.

**Conclusion:** Finding optimal UD is a desired task dependent on the number of donors available in donor registries. Enriched resources of ethnically matched donors and broad typing (at least at HLA loci A, B and DRB1 at intermediate resolution level) efficiently increased the efficacy of bone marrow donor search procedures. Final effectiveness of search process is highly dependent on search algorithm and the experience of search center staff.

**Presentation:** Oral, Poster P8

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**LITHUANIAN BONE MARROW DONOR REGISTRY - EXPERIENCE OF 2004-2011**

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**Introduction:** Lithuanian Bone Marrow Donor Registry (LBMDR) was established in Hematology, Oncology and Transfusion Medicine Center of Vilnius University Hospital Santariskiu Klinikos (VUHSK) in 2004. LBMDR facilitates unrelated donor search for 2 transplant centers - VUHSK (for adults) and Children’s Hospital, Affiliate of VUHSK (for children).

**Materials and Methods:** All data about unrelated bone marrow donors (UD), searches and transplantations are collected in LBMDR database and analyzed further.

**Results:** LBMDR actively recruits voluntary bone marrow donors. 1422 new donors were recruited in 2011. By the end of 2011, 6579 volunteer donors (0.22% of Lithuanian population) have been registered to LBMDR. All donors are HLA-A, B, C, DRB1 typed. Most of the donors (47%) belong to 26-35 year old age group. LBMDR facilitated 25 donations from LBMDR donors (6 donations abroad and 19 for patients, treated in Lithuania). Registry initiated 378 unrelated donor searches for national patients in 2004-2011. 340 of searches further proceeded with 94% success rate. 25
searches were canceled due to patient’s reasons. Suitable unrelated donor was found for 321 patient. Acceptable donor was not found for 19 (6%) patients. 10/10 HLA matched donor was found for 226 (70%), 9/10 for 84 (26%) and 8/10 for 11 (3%) patients.

Unrelated donor bone marrow transplantations were performed for 237 patients: 33 children and 204 adults. 175 of them received peripheral blood stem cells, 62 - bone marrow. Most of patients (105) were transplanted for acute myeloid leukemia. 27 patients were further treated with donor lymphocyte infusion.

**Conclusion:** LBMDR is one of world’s UD registries, facilitating unrelated donor searches, donations and transplantations in cooperation with other registries worldwide.

**Presentation:** Poster P9

**TH17 MEDIATED IMMUNITY AND ASSOCIATIONS WITH NOD2/CARD15 MUTATIONS IN aGVHD AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION**

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**Introduction:** Damage of the gastrointestinal tract during the acute phase of GvHD plays a major role in the amplification of this systemic disease after hematopoietic stem cell transplantation (HSCT). The role of genetic background and effector cells migration into the target tissues is currently investigated in the pathobiology of aGvHD.

**Materials and Methods:** A total of 219 patients were evaluated for the presence of NOD2/CARD15 gene mutation using single nucleotide polymorphism technique (SNP) by assessing polymorphism of SNP8, SNP12 and SNP13. Thirty five gastrointestinal biopsies taken from patients with clinical symptoms of aGvHD were analyzed by immunocytological staining for the presence of cellular infiltrates (CD3, CD4, CD8, CD138) including detection of IL-17, FOXP3.

**Results:** The NOD2/CARD15 gene mutation was assessed in 11% of HSCT recipients, in 13% of HSCT donors and in 5.5% when both donor and recipient have gene mutated. The cumulative incidence of transplant-related mortality was 64% and 35% when recipient or donor (respectively) were affected with NOD2/CARD15 gene mutation. If the mutation involved both recipient and donor this proportion increases to 75%. NOD2/CARD15 gene mutation was also associated with susceptibility to severe GvHD
grade III-IV and this affected 36% of patients when both recipient and donor were involved compared to 25% when recipient and 29% when donor have gene mutated and 16% without gene mutation. In all biopsies gut epithelium was damaged by cellular infiltrates composed predominantly with CD8+ T-cells and proportion of IL-17 producing cells. When donor and recipient were carrier NOD2/CARD15 gene mutation severe lesions in the gut epithelium were associated with abundant infiltration of IL-17+ cells compared of the ones without gene mutation. **Conclusion:** NOD2/CARD15 gene mutation is associated with severity of intestinal aGvHD. Patients affected with NOD2/CARD15 gene mutation have worse prognosis for posttransplant outcome and survival compared to these without gene mutation.

**Presentation:** Oral, Poster P10

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**PROJECT N R13 0082 06 - THE INVOLVEMENT OF THE DIFFERENT INSTITUTIONS SHOWN BY NUMBER OF PROCEDURES PERFORMED**

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**Background:** In the year 2009 a Polish Donor-Recipient Matching Study Group started its activity focusing on the implementation and
harmonization of HLA typing and assessing the usefulness of cytokine gene polymorphism detection in the process of unrelated donor-recipient matching for HSCT. Within this project in the years 2010-2011 three hundred sixty consecutive donor-recipient pairs matched in three Polish institutions and then transplanted in cooperating hospitals were reported to the coordinator.

**Donor-Recipient HLA Matching:** All individuals were typed using genetic technology which included techniques of a high-resolution potential (sequence-based and PCR-SSP) at the stage of confirmatory typing, finally documenting the level of matching between donors and recipients. HLA labs in service had Polish accreditation and they participated in the quality control workshops. Three centers were involved in search and confirmatory typing; one of them had EFI (European Federation for Immunogenetics) accreditation while the other two had the Polish accreditation and participated in the HLA Proficiency Testing for Central and East Europe.

Two hundred and forty-eight (69%), 58 (16%) and 54 (15%) pairs were studied in the Lower Silesian Center for Cellular Transplantation with National Bone Marrow Donor Registry, the Department of Hematology, Medical University of Warsaw, and the Institute of Hematology and Transfusion Medicine, respectively.

**Transplant Centers:** Seven transplant centers participated in the study. All of them were granted with European Bone Marrow Transplantation Group (EBMT) accreditation for unrelated donors transplantation.

**Data Collection:** A standard questionnaire described each patient and donor pair and included follow-up data. The questionnaire was adapted from the Med-A (Minimum Essential Data) data collection form of EBMT extended by information on conditioning regimen toxicity, post transplant chimerism, Herpes and Polyoma viruses post-transplant infection/reactivation, and HLA specificities. All data were collected and registered using the MS Office Access database.

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**Presentation:** Poster P11
25TH ANNIVERSARY OF MARROW TRANSPLANT ACTIVITY IN WROCLAW
LOWER SILESIAN CENTER FOR CELLULAR TRANSPLANTATION AND
NATIONAL BONE MARROW DONOR REGISTRY
Andrzej Lange, Mariola Sędzimirska, Krzysztof Suchnicki, Janusz Lange, Dorota Duda, Sylwia Mizia, Jolanta Bocheńska, Małgorzata Polak, Barbara Szymczak on behalf of colleagues actively involved in daily work and the progress made
Lower Silesian Center for Cellular Transplantation and National Bone Marrow Donor Registry, Wrocław, Poland

History Background: The Division of Immunotherapy and Bone Transplantation was established in 1986 in cooperation with the Institute of Immunology and Experimental Therapy of the Polish Academy of Science in Wrocław. The Division started with autologous transplantations followed by allogeneic ones and since the year 1997 unrelated donor transplantations have been performed. The Division became an independent institution under the name of the Lower Silesia Center for Cellular Transplantation with National Bone Marrow Donor Registry (LSCCT & NBMDR) - since 24th of January 2002.
The LSCCT & NBMDR is the longest operating bone marrow transplant center in Poland. The center has performed over 1000 transplantations in children and adults with the use of all bone marrow stem cells or PBPC in autologous and allogeneic including haploidentical and non-related donor fashions.

Transplant Activity: A number of transplantations were pioneering on the worldwide scale including treatment of children with immunodeficiencies and Fanconi anemia, triple transplantation in SCLC patients, the use of elutriation for modified transplant material in the haploidentical donor setting, the use of PBPC in unrelated donor transplantations.
Our institution is proud of the activity of the National Bone Marrow Donor Registry and its HLA lab, which has been granted with the European Federation for Immunogenetics accreditation and the transplant center has the accreditation of the NMDP.
The institution is active in international cooperation and research, which is seen in its active participation in 150 scientific papers and in the area of regenerative medicine. The project on revascularization of ischemic legs started in 2003 with successful continuation more recently extended to the treatment of patients with infarction of the femur. Having a clean room facility, it is about to start cell therapy in aGvHD and CMV reactivation.

Presentation: Poster P12
LYMPHOCYTE SUBPOPULATIONS RECOVERY POST ALLOHSCT AND HERPES VIRUSES REACTIVATION INFLUENCED THEMSELVES IN A MUTUAL FASHION

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Introduction: Immunological recovery post alloHSCT is influenced by the conditioning regimen, cellular profile of transplant material and further post transplant is shaped by environmental factors. CMV, EBV and HHV-6 predominately infect lymphoid cells and also influence thymic and bone marrow microenvironment.

Materials and Methods: We followed 44 patients (age 1 to 64 median 45 yr., 21 ric/mac, 21/23 , sib/mud 21/23, BM/PBPC 4/40) for the pace of lymphocyte recovery at 4 consecutive time points beginning when the number of lymphocytes in blood exceeded 200 cells/μl after transplantation (median day 35 range 31-53). We used the method of flow cytometry to determine lymphocytes of CD4(+), CD8(+), CD20(+) profile and CD4+ T cell subsets: Central memory (CM) CD4+CCR7+CD45- and Effector memory (EM) CD4+CCR7-CD45+. CMV, EBV and HHV-6 copies were measured in blood with the use of QT-PCR.

Results: It appears that:
• Herpes viruses reactivations were seen in 27 (61%) patients, HHV-6 in 11 patients, EBV 15 and CMV in 4 patients. HHV-6 reactivation occurred rather early after transplantation and was followed by reactivation in 8 cases.
• At the beginning of immune recovery CD4+lymphocyte and their EM subset were lower in patient with CMV copies when compared to those without them (CD4+ cells 44/μl vs 120/μl p=0,066 M-W U test) (CD4+EM cells 25/μl vs 75/μl p=0,088 M-W U test).
• Three weeks later the presence of HHV-6 was associated with a decrease in number of CD4+ cells, CD4+ CM and CD4+EM cells for patients with HHV-6 copies when compared to group without HHV-6 copies, which was independent of aGvHD manifestation. (CD4+ cells 93 /μl vs 190/μl; p=0,044 M-W U test); (EM cells 41/μl vs 142/μl; p=0,015 M-W U test) (CM cells 6 /μl vs 18/μl; p=0,015 M-W U test)
• All CMV infected patients survived and showed an increase in CD8(+) lymphocytes in comparison with those lacking CMV infection 5-6 weeks after transplant. (182 k-k/μl vs 535 k-k/μl p=0,017 M-W U test)
• Patients having EBV copies had higher proportion of CD20(+) cells when compared to those lacking EBV copies (19 /μl vs 9/μl; p=0,077 M-W U test).
Conclusion: Low lymphocyte CD4(+) and CD4+ EM count precedes CMV and results from HHV-6 infection. HHV-6 infection leads to a decrease of lymphocyte CD4+CM count.

Presentation: Poster P13

IL-10 AND IL-6 PROMOTER POLYMORPHISMS INFLUENCE THE OUTCOME OF PATIENTS AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION
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Introduction: It is known that polymorphism of cytokines gene influences transcription and may change the primary structure of encoded peptides. Allelic variants characterize with different transcription pace (when polymorphic site is situated in the untranslated regions) or different function if exons are involved in the polymorphic change. Acute GvHD reflects a balance between pro-inflammatory and regulatory cytokines.

Materials and Methods: We evaluated the impact of IL-10 (rs18000896, -1082 G/A; 18000871, -819 C/T; rs18000872, -592 C/A) and IL-6 (rs1800795: -174 G/C) gene polymorphisms in donors and recipients genome on the outcome of HSCT in 246 patients (F/M: 108/138) grafted from unrelated (138), and from sibling (108) donors.

Results: We found that patients carrying IL-10 ACC haplotype had a lower frequency of aGVHD (grade II-IV) as compared to the recipients with other haplotypes (32/129 vs 41/106, p=0.024). Protective effect of the recipient ACC haplotype on aGvHD depended on the extent of disparity: being absent in sibling (8/53 vs 9/47, p=ns), but seen in unrelated donors transplantations (24/76 vs 31/58, p=0.013).

Similarly, IL-6 polymorphism influenced the aGvHD risk in unrelated donors transplantation but not in sibling transplantation. Homozygosity G/G in donors constituted the risk factor of aGvHD. Patients grafted from donors having GG homozygous polymorphism of IL-6 had more frequently aGVHD (grades>0) (31/61 vs 58/160, p=0.065) with more significantly impact in MUD transplantation (27/37 vs 38/86, p=0.006). Recipient having homozygous C/C genotype on position -174 of the IL-6 gene had more frequently CMV IgG before transplantation (50/52 vs 150/184 p=0.008). Patients with ACC haplotype had higher proportions of FoxP3+ lymphocytes in CD4+ population in blood in three consecutive observations post HSCT (mean [95CI]: 5.625% [4.208-7.043] vs 3.37% [1.569-5.175], p=0.022; 5.10%
Conclusion: Promoter region of IL-10 and IL-6 polymorphisms influences the risk of aGvHD and Herpes viruses reactivation/infection. The effect of IL-10 polymorphic features associate with the impact on Treg lymphocyte proportions in blood.

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Presentation: Poster P14

HLA PROFICIENCY TESTING FOR CENTRAL AND EAST EUROPE - SUMMARY THE XVIII TRIAL
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The HLA Proficiency Testing for Central and East Europe is organized under the auspices of the Polish Society for Immunogenetics. Since 1999, when we started our activity, over 50 HLA laboratories from 13 countries have participated in our External Proficiency Testing scheme. Our standardization workshop covers serological typing of HLA class I antigens and DNA typing at the low and high resolution level of HLA class I (A, B, C) and class II loci (DRB1, DQB1 and DPB1) and has over 30 HLA laboratories participating every year.

Thirty-eight laboratories participated in the last XVIII trial (in year 2012), including 22 participant from Poland and 16 from abroad (Czech Republic, Hungary, Lithuania, Romania, Russia, Serbia, Slovenia, Turkey). Seventeen laboratories submitted the results of HLA class I typing by serology, 32 participated in HLA class I DNA typing and 32 participated in HLA class II DNA typing including 10 and 14 laboratories that sent the results of HLA class I and II high resolution typing, respectively. Comparison of the percentage of laboratories that successfully (with no or only one discrepant result) completed their typings, showed that only one laboratory was unsuccessful. Its erroneous results were associated with typing of the DQB1 alleles at the low resolution level. All the other categories of this standardization trail were successfully completed.

In conclusion, although some doubtful results are still observed a continuous improvement is seen with respect to both serology and DNA typing.
Recent progress in the field of genetics and HLA offers the possibility to investigate the relationship with the patomechanism of the disease. An increased relative risk of developing a number of auto-immune / auto-inflammatory diseases in persons carrying certain HLA specificities is a well described phenomenon. Studies outside of the transplantation setting had focused on the immune responses to self-antigens as a result of HLA dependent antigen presentation - this mechanism is also important in the terms of finding a ‘perfect donor - recipient match’, when one of the most important complications of alloHSCT is Graft vs Host Disease (GvHD), a pathology closely resembling auto-immune / auto-inflammatory or systemic connective tissue diseases. Cumulative incidence shows that survival of transplant recipients matched for 10/10 HLA alleles is similar to the survival of recipients of fully matched related transplantations, this however may leave important immunologic phenomena unnoticed . In this study we took a close look at the post transplant development of antinuclear antibodies (ANAs), their possible relationship with: (1) type of donor, degree of HLA match and (2) the presence of certain - ‘disease-linked’ HLA specificities.

74 adult patients (age 16 to 60 y, median 42 y; 41 females, 33 males) suffering from haematological malignancies and aplastic anemia (AML/ALL - 47 cases, CML - 18, SAA - 3, MP - 6) were transplanted in years 1989 to 2011 from matched related (45) and unrelated (29; 23 matched 10/10 alleles, 6 matched 9/10) donors. Patients were routinely followed during the observation period and screened for the presence of anti nuclear antibodies (ANAs), by means of the fluorescence intensity which was described as: none (0), weak (+) or strong (++/+++). (I) 41 patients (53%) presented with strong positive test, 17 pts (22%) showed weak fluorescence while in 19 pts (25%) no Abs were detected. Peak of fluorescence intensity was seen at mean +1399 day post HSCT
(+100 to +5891; time period of chronicGvHD). Comparing ANAs incidence in related vs unrelated groups: (i) related: ANA=0 (15%), ANA=(+) (27%), ANA=(++++) (58%); (ii) unrelated: ANA=0 (37%), ANA=(+) (16%), ANA=(++++) (47%). However comparing the results within unrelated donor group: matched vs unmatched: ANA=0 (33% vs 60%), ANA=(+) (11% vs 40%), ANA=(++++) (56% vs 0,0). cGvHD incidence in all patients was: cGvHD(+)=45%, cGvHD(-)=35%.

(II) 50 patients were tested for HLA-connected relative risk of developing Sjogron syndrome (SS), autoimmune hepatitis (AIH) or systemic lupus erythematous (SLE). 39 patients presented with strong positive results of antinuclear autoantibody fluorescense test. 10 patients revealed SLE-antinuclear antibody pattern (5 had anti-histone Abs, 4 had anti-dsDNA Abs), two of them were DR3-positive, one was DR2. Two patients had SS-type antibodies (one of them was DR3-positive), one was positive with respect to anti mitochondrial Abs. Within group with strong positive ANA only one pts had the 'ancestral haplotype' with DR4 (neither type I diabetes nor SLE or SS-pattern Abs were detected). Four patients were carriers of HLA B27 - none of them suffered from ankylosing spondylitis, arthritis or acute anterior uveitis. It should be noted that HLA background provides a susceptibility but does not predict who will eventually develop autoimmune phenomena. 4-fold higher SLE-antinuclear antibody pattern in DR3-negative patients prompt possible therapeutic strategies in managing severe autoimmune disorders. It remains to be seen whether: (i) the 'perfect match' enables immune reactivity in the style of autoimmunity, (ii) autoimmunity is facilitated by some other yet undiscovered genetic modality, (iii) patients with poorly matched donors receive as standard stronger immunosupresion preventing not only GvHD but also processes leading to ANAs formation.

Presentation: Poster P16
CCR5 GENE POLYMORPHISM AFFECT THE RISK OF GVHD AFTER ALTERNATIVE TRANSPLANTATION OF HAEMATOPOIETIC STEM CELLS - POLISH DONOR-RECIPIENT STUDY GROUP


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CCR5 recognizes beta chemokines (including CCL2 - CCL5) and is expressed on cells involved in haematopoietic reconstitution and immune response. The 32bp deletion mutation (delta32 polymorphism) within the CCR5 gene results in a non-functional chemokine receptor. Our previous studies showed that the CCR5 polymorphism and expression were associated with the incidence of acute graft-versus-host disease (aGvHD) and EBV reactivation in transplant recipients (Bogunia-Kubik et al. 2006, 2007). The present multicenter study aimed to analyze the effect of the CCR5 deletion on the transplant outcome from alternative donors. Three hundred and sixty patient-donor pairs were investigated and typed for the CCR5 alleles. It was found that:

Recipients homozygous for the 32bp deletion more frequently suffered from aGvHD than patients lacking this mutation (5/10 vs. 34/313, p=0.001 and 2/10 vs. 15/313, p=0.034, for grade III-IV and IV aGvHD, respectively). These patients characterized also with worse overall survival (12% vs. 52%, p=0.145). Moreover, patients grafted from delta32 homozygous donors more frequently presented with aGvHD (3/8 vs. 15/318, p=0.001 for grade III-IV and grade IV aGvHD).

Logistic regression analysis considering recipient age, donor-recipient gender relation, 10/10 HLA match and the recipient CCR5 polymorphism confirmed the role of the CCR5 delta32 homozygosity as an independent risk factor of grade III-IV aGvHD (OR=8.823, p=0.002). In this analysis donor-recipient compatibility was shown to play a protective role (OR=0.421, p=0.022). Similar analysis considering donor CCR5 polymorphism confirmed the role of donor homozygous genotype with the
delta32 deletion (OR=6.512, p=0.048) as an independent factor increasing the risk of grade IV aGvHD. It appeared that delta32 homozygous genotype, independently whether present in patient or recipient, constitutes a risk factor of severe aGvHD complications after transplantation from alternative donors. Supported by the National Centre for Research and Development grant N R13 0082 06.

**Presentation:** Poster P17

**DONOR AND RECIPIENT CXCL12 GENE POLYMORPHISM AFFECTS THE OUTCOME OF ALTERNATIVE TRANSPLANTATION OF HAEMATOPOEITIC STEM CELLS - POLISH DONOR-RECIPIENT STUDY GROUP**


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We have previously documented the effect of the CXCL12 (SDF-1) (3’UTR-801-G>A) gene polymorphism on the mobilization potential of CD34+ cells and haematological recovery after transplantation (Bone Marrow Transplant 2009, Transplant Proc 2010). In the present study the results of the CXCL12 genotyping were related with the alternative transplant outcome of 360 patients transplanted in 7 Polish institutions. Toxic complications were less frequently observed in patients grafted from donors carrying the CXCL12-3’A allele (42/79 vs. 105/151, p=0.014 and 24/79 vs. 73/151, p=0.009 for grade II-IV and III-IV, respectively). Logistic regression analyses showed that donor CXCL12-3’A allele (OR=0.509, p=0.022 and OR=0.473, p=0.013 for grade II-IV and III-IV toxicity) and younger age of recipients (OR=0.980, p=0.036 and OR=0.981, p=0.040, respectively)
were independently protective while donor-recipient gender relation and 10/10 HLA match were not significant.

The incidence of aGvHD grades I-IV was lower in patients having A allele (52/119 vs. 113/204, p=0.043) and AA homozygous genotype (6/25 vs. 159/298, p=0.005). Logistic regression analysis considering recipient age, donor-recipient gender relation, 10/10 HLA match and the recipient CXCL12 polymorphism confirmed the role of the A allele as an independent factor associated with a decreased risk of aGvHD (OR=0.591, p=0.030) similarly to HLA compatibility (OR=0.421, p=0.072). These relationships were also seen for aGvHD when AA homozygosity was considered (AA genotype OR=0.257, p=0.006; HLA match OR=0.621, p=0.063). Of note, patients having A allele post HSCT were less prone to early Herpes virus reactivation as observed for HHV-6 (2/34 vs. 19/69, p=0.026).

These results imply that the CXCL12-3'A allele variant in donors makes patients less prone to toxic complications and early post-transplant HHV6 reactivation but if present in recipients decreases the risk of aGvHD.

Supported by the National Centre for Research and Development grant N R13 0082 06.

Presentation: Poster P18
ACKNOWLEDGEMENTS

We wish gratefully acknowledge with thanks the support offered by exhibiting companies

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<table>
<thead>
<tr>
<th>Abbott Molecular</th>
<th>Gilead</th>
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<tbody>
<tr>
<td>Amgen</td>
<td>Janssen</td>
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<td>AOP ORPHAN</td>
<td>Novartis</td>
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<td>AstraZeneca</td>
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<td>Braun</td>
<td>Pierre Fabre</td>
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<td>Polgen</td>
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<td>Fresenius Medical Care</td>
<td>Roche</td>
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Ehninger, Gerhard (Dresden) invited speaker; chairman
Górski, Andrzej (Warszawa) invited speaker; chairman
Jędrzejczak, Wiesław Wiktor (Warszawa) invited speaker; chairman
Klimczak, Aleksandra (Wrocław) invited speaker
Lange, Andrzej (Wrocław) president; speaker
Lode, Holger (Greifswald) invited speaker; chairman
Łukomska, Barbara (Warszawa) invited speaker
Markiewicz, Mirosław (Katowice) invited speaker
Mueller, Carlheinz (Ulm) invited speaker; chairman
Oudshoorn, Machteld (Leiden) invited speaker; chairman
Raffoux, Colette (Paris) invited speaker; chairman
Spyropoulou-Vlachou, Maria (Athene) invited speaker; chairman
Steiner, David (Prague) invited speaker

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