Leukemia and Stem Cell Transplant: Why Your Donation Matters

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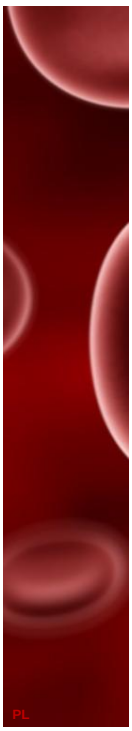
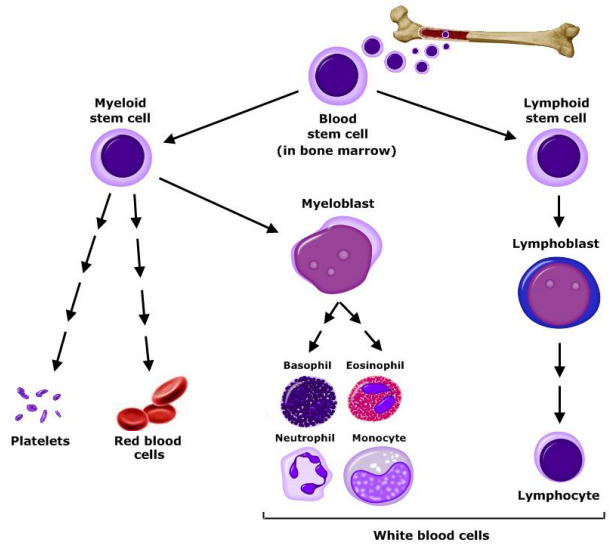


What are stem cells?

- Stem cells are cells that can mature and develop into many other kinds of cells
- Stem cells in the bone marrow generate all types of blood cells:
  - Red blood cells (carry oxygen)
  - White blood cells (fight infection)
  - Platelets (help clotting)

Blood cell development

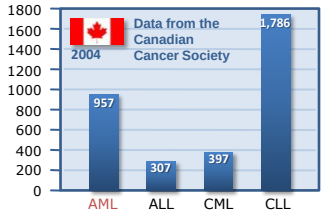


What is leukemia?

- Leukemia is a malignant cancer affecting the bone marrow and blood
  - All leukemias develop from a stem cell in the bone marrow that grows and multiplies uncontrollably
  - Leukemia cells eventually crowd out normal bone marrow cells, causing problems with normal blood cell production

Leukemia

- The four most common types of leukemia in adults are:
  - acute myelogenous leukemia (AML)
  - acute lymphocytic leukemia (ALL)
  - chronic myelogenous leukemia (CML)
  - chronic lymphocytic leukemia (CLL)
- Acute leukemias progress more rapidly, and need to be treated more urgently



Leukemia treatment

- Treatment for leukemia is individualized for each patient and may include one or more of:
  - Chemotherapy
  - Radiation therapy
  - Stem cell transplantation

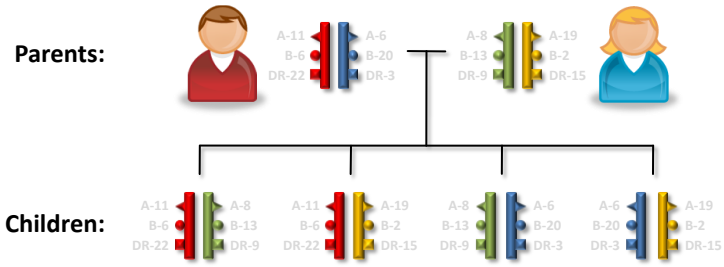
Stem cell transplant

- In order to perform a stem cell transplant, a suitable source of stem cells must be found
- This means finding a donor whose stem cells are similar to (**"match"**) the patient's cells
- "Matching" means having the same (or similar) pattern of *HLA markers*

What is HLA?

- All cells in our body have markers on their surface that identify them as belonging to itself ("self")
- On blood cells, these are called *"human leukocyte antigens"* **(HLA)**
- These HLA markers prevent our immune systems from attacking our own cells

HLA in families

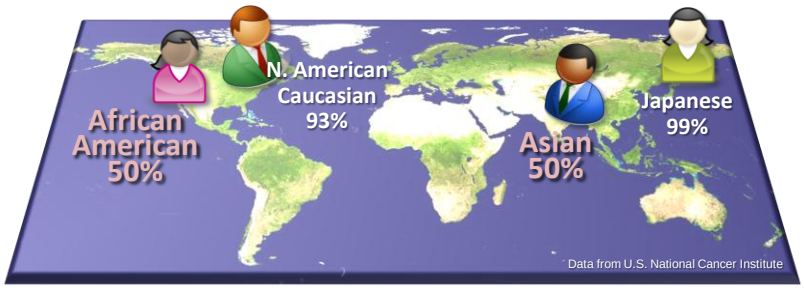


- We inherit **half** our HLA markers from each parent (we share only **50%** of markers with each parent)
- Each full sibling has a **25%** chance of matching another (identical twins are 100% match)
- Only 30% of patients find a family match; **70% depend on unrelated matched donors**

HLA in populations

- Patients are more likely to find a stem cell match within their own ethnic communities
  - **HLA patterns tend to be more similar within ethnic groups**
- National and international registries of HLA markers (stem cell registries) are searched to find matches for patients

Matching in populations



- South-Asians (and other minorities) are underrepresented in stem cell registries
- Patients from these ethnic groups are *much less likely* to find suitable donors

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Canadian registry

- OneMatch Stem Cell and Marrow Network, managed by Canadian Blood Services
- At this time, >230 000 people have registered, but only 5 000 of these (2%) are South Asian
- www.onematch.ca

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OneMatch registration

- **Online:**
  - Go to website (www.onematch.ca) read detailed information, and follow instructions to register
- **Phone:**
  - 1-888-2DONATE (236-6283)
- Either method is **free**

one match
stem cell and marrow network

OneMatch registration

- Donors in Canada must be:
  - Between **17-50** years of age
  - In generally **good health**
  - Committed to donating to **any patient**
- Keep in mind that those who join the registry do so for **all patients in need**, not just one patient

one match
stem cell and marrow network

OneMatch registration

- If registering online, you will be contacted by phone for follow-up questions and to confirm interest
- Within 2-3 days, you will receive a **cheek swab kit** by mail
- Swabs are used to collect cell samples from the inside of your cheek, for DNA analysis of your HLA markers

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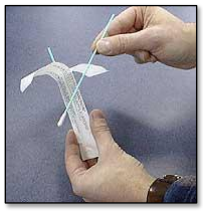
OneMatch registration

- The kit contains detailed info on how to collect a sample



- The process is simple, and takes 10-15 minutes to complete

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OneMatch registration

- Once your sample is received by OneMatch, it is analyzed and results are entered into the database in about 3 weeks
- Please keep OneMatch notified of changes in your contact info, so they can reach you, if you are found to be a match

OneMatch registration

- If you are found to match with a patient in need of stem cell transplant, OneMatch will then contact you
- Average time on the registry until activation is **7 years**
- Donation could be for Canadian or international patients

Blood stem cell therapy

- Stem cell transplant can help cure **many diseases:**
  - **Cancers:** leukemias, lymphomas
  - **Bone marrow diseases:** sickle cell anemia, thalassemias, aplastic anemia
  - **Immune system disorders**
  - **Genetic/metabolic diseases**

Donation procedures

- There are two viable sources of stem cells from donors:
  - Peripheral blood stem cell **(PBSC)**
  - **Bone marrow**
- PBSC collection is now **the most common method**
  - Presently, PBSC is used in more than $^{2}/_{3}$ of stem cell collections
  - Recovery time is **only a few hours**

Donation procedures

- The **transplant physician** must decide which strategy of stem cell collection to use
- Donors have the right to accept or refuse the strategy, but...
  - Donors should consider what they are prepared to give (even before registering)

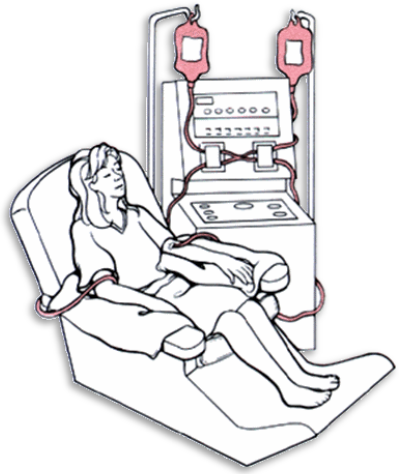
PBSC collection

- The donor receives 4-5 days of G-CSF* injections
  - This growth factor increases the number of stem cells in the blood
  - Possible side effects include:
    - Mild bone pain, fever and/or chills
    - Nausea and/or vomiting
    - Local irritation at injection site
  - These go away 2-3 days after stopping the injections

*G-CSF: granulocyte colony stimulating factor

PBSC collection

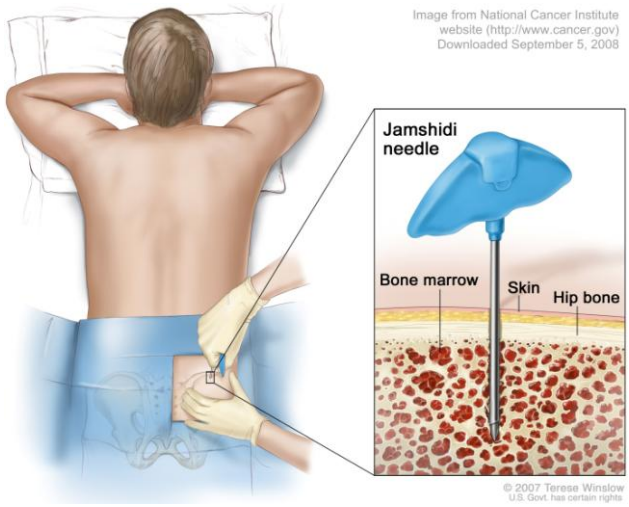
- The donor is connected to an **apheresis** unit
- This machine separates stem cells out from the blood, then **immediately returns the rest back to the donor**



Bone marrow harvest

- For bone marrow donation, the donor is given a general (or regional) anaesthetic
- A special needle is inserted into the back of the hip bone, and about 1L of marrow is extracted
- **Bone marrow replenishes itself within 4-6 weeks**

Bone marrow harvest



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Bone marrow harvest

- The most common side effect is **pain** in the hip bones at the site(s) of collection
- However, this pain is easily managed, and usually lasts **a few days**
- Donors are back home **the same day**

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Cord blood donation

- Stem cells from **umbilical cord blood** are another potential source for transplant
- Parents of a new baby may decide to donate cord blood:
  - **Public** registries: stem cells may be given to anybody in need (free process, helps the greater community)
  - **Private** registries: stem cells are saved for possible future need of the donor ($$, low likelihood of personal need)

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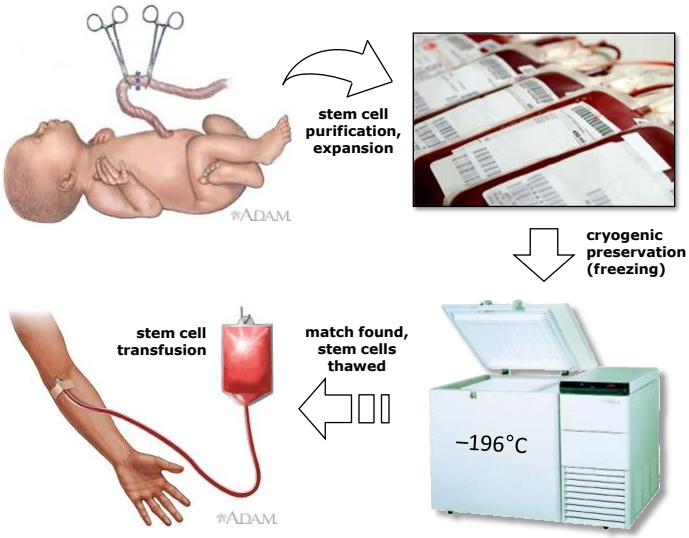
Cord blood donation



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Cord blood donation

- OneMatch does not currently offer umbilical cord blood donation services
- In Canada, two **public** registries are available at this time:
  - Alberta Cord Blood Bank, available nationally (www.acbb.ca)
  - Héma-Québec, at Montréal hospitals (www.hema-quebec.qc.ca)

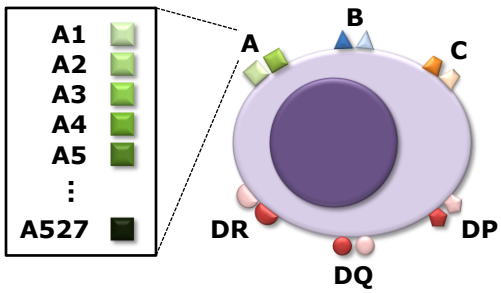
Other ways to help

- **Consider:**
  - Blood and blood product donation
  - Financial gifts
- **1-888-2DONATE (236-6283)**
- **www.bloodservices.ca**

Canadian Blood Services
it's in you to give

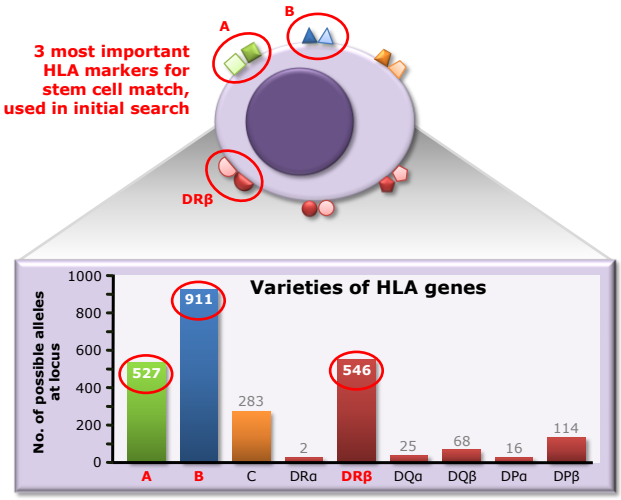
Resource slides

HLA markers



- There are **six** major types of HLA markers, inherited in **pairs**
- Each type can have *hundreds* of variants, thus *trillions* of potential combinations of all 6 pairs
- This is why it can be very difficult to find a matched donor for a given patient

Important HLA markers



Data adapted from U.S. National Cancer Institute and IMGT/HLA Database

U.S. registry

- The National Marrow Donor Program (NMDP)
- Currently, ~7 million registered stem cell donors; 450 000 (6%) are Asian
- Asians contributed 3 800 out of nearly 70 000 cord blood units (5%) in the registry
- www.marrow.org

Indian Registries

- A few small registries exist:

Asian Indian Donor Marrow Registry
Professor N.K. Mehra, Dr. U. Kanga
Dept. of Transplant Immunology and Immunogenetics
All India Institute of Medical Science
Ansari Nagar
110029 New Delhi

Tel: +91-11-265-88-588
Fax: +91-11-265-88-663
Email: narin98@hotmail.com

(Member of BMDW international registry)

Department of Transfusion Medicine
Dr. Sunil B. Rajadhyaksha
Tata Memorial Hospital
Dr. Ernest Borges Road
400012 Parel, Mumbai

Tel: +91-22-2417-7000
Tel: +91-22-2417-7096
Fax: +91-22-2414-6937
Email: ombts@vsnl.com

(Not yet a member of BMDW international registry)

- Independent recruiters:
  - MatchPia: www.matchpia.org
  - South Asian Marrow Association of Recruiters: www.samarinfo.org

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International registry

- Bone Marrow Donors Worldwide currently has 12,441,390 stem cell donors available
- 59 donor registries from 43 countries, 40 cord blood banks from 25 countries
- www.bmdw.org

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Sources of transplants

Canadian patients: unrelated stem cell transplants

Source	2003	2004	2005	2006	2007	2008*
Bone marrow	107	90	76	67	54	14
PBSC†	69	89	103	132	123	43
Cord	12	21	48	46	66	20
DLI‡	4	8	5	12	12	2
PBSC+Marrow	0	0	1	0	0	0
Total	**192**	**208**	**233**	**257**	**255**	**79**

*2008 (January-April 14), †PBSC: peripheral blood stem cells, ‡DLI: donor leukocyte infusion

one match
stem cell and marrow network

Timeline

1956: E.D. Thomas (Cooperstown, NY) performs first successful human bone marrow transplant (BMT) between identical twins

1958: J. Dausset (Paris) identifies first of many HLA antigens

1968: R.A. Good (Minnesota) performs first successful BMT from matched, related (non-twin) donor

1973: First successful matched, unrelated BMT performed at Sloan-Kettering Cancer Centre (New York)

1974: Anthony Nolan Trust (UK) starts first dedicated bone marrow registry

1980: Dausset, B. Benacerraf, and G.D. Snell win Nobel for discovery of HLA

1986: National Bone Marrow Donor Registry started in USA, first donor match made in 1987

1988: E. Gluckman (Paris) successfully transplants cord-blood stem cells, for a patient with Fanconi anemia

1989: Unrelated Bone Marrow Donor Registry started in Canada*; Bone Marrow Donors Worldwide (BMDW) established

1990: Thomas and J.E. Murray win Nobel for work in transplant biology

1995: Bensinger *et al.* transplant peripheral blood stem cells to treat hematological malignancies, demonstrate superiority to BMT

*The UBMDR came under the auspices of Canadian Blood Services in 1998, and became OneMatch in 2007

South Asia

- **Total population: 1,525,673,058**

- India
  1,147,995,898
- Pakistan
  172,800,051
- Bangladesh
  153,546,901
- Nepal
  29,519,114
- Sri Lanka
  21,128,773
- Bhutan
  682,321

Projected 2008 data from US Census Bureau (http://www.census.gov)