CBS National Public Cord Blood Bank

“Did you donate your cord blood?”

Tanya Petraszko MD FRCPC
March 2015
Overview

• What is a stem cell?
• The importance of HLA
• Need for cord blood stem cells
• ‘For all Canadians’
• Building the bank
• How are we doing?
Stem Cell

• Refers to any cell that has the capacity for:
  – Self renewal
  – AND
  – Differentiation

• First discovered in hematopoietic cells but likely in many other tissues
Hematopoietic Stem Cells
3 Sources of Stem Cells
What is the HLA system?

• The major barrier to transplantation:
  – a series of molecules/proteins that all come from a closely linked system of genes
• Their function is to help the organism recognize self from non self
• Gene system is the Human Leukocyte Antigen system (first discovered on white cells)
Why Unrelated Donors?

• HLA Typing: inherited genetic markers

• Only 25% of patients have a match in family

• declining birth rates threaten to reduce this further

Leila,
OneMatch Registrant
& whole blood donor
Table. Calculating the chance of identifying an HLA-matched sibling donor depending on the year of birth of the donor.

<table>
<thead>
<tr>
<th>Donor/patient birth year</th>
<th>Average birth rate (actual)</th>
<th>Sibling Rate (calculated)</th>
<th>Chance of ≥ 1 HLA-matched sibling donor (calculated)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1951 – 1955</td>
<td>3.65</td>
<td>2.65</td>
<td>53.3%</td>
</tr>
<tr>
<td>1956 – 1960</td>
<td>3.88</td>
<td>2.88</td>
<td>56.3%</td>
</tr>
<tr>
<td>1961 - 1965</td>
<td>3.68</td>
<td>2.68</td>
<td>53.7%</td>
</tr>
<tr>
<td>1966 – 1970</td>
<td>2.61</td>
<td>1.61</td>
<td>37.1%</td>
</tr>
<tr>
<td>1971 – 1975</td>
<td>1.98</td>
<td>0.98</td>
<td>24.6%</td>
</tr>
<tr>
<td>1976 – 1980</td>
<td>1.73</td>
<td>0.73</td>
<td>18.9%</td>
</tr>
<tr>
<td>1981 – 1985</td>
<td>1.63</td>
<td>0.63</td>
<td>16.6%</td>
</tr>
<tr>
<td>1986 – 1990</td>
<td>1.62</td>
<td>0.62</td>
<td>16.3%</td>
</tr>
<tr>
<td>1991 – 1995</td>
<td>1.69</td>
<td>0.69</td>
<td>18.0%</td>
</tr>
<tr>
<td>1996 – 2000</td>
<td>1.56</td>
<td>0.56</td>
<td>14.9%</td>
</tr>
<tr>
<td>2001 – 2005</td>
<td>1.52</td>
<td>0.52</td>
<td>13.9%</td>
</tr>
</tbody>
</table>

*Allan et al, BBMT 2009
OneMatch

Canadian Blood Services’ OneMatch Stem Cell and Marrow Network,

• recruits healthy, unrelated, volunteer blood stem cell donors
• Maintains national registry
• conducts searches for patients who need an unrelated blood stem cell transplant
• coordinates the collection and delivery of blood stem cells when a match is found
• NPCBB is part of this
OneMatch Registry and National Public Cord Blood Bank

• OneMatch Registry is the 10th largest registry in the world with over 330,000 donors.
  – *established in 1988.*

• National Public Cord Blood Bank Canada
  – *approved in March 2011*
  – *Go Live 2013-2015*
OneMatch Fast Facts – June 2013

• Searchable donors: 317,810
• Canadian Transplant Centres: 18
• Canadian Collection Centres: 10
• International Registries: 69
  – Over 21,327,461 registrants worldwide
• International Cord Blood Banks: 49
  – Over 580,675 umbilical cord blood units

Francis,
OneMatch Registrant
Q1 2014 Factors: Industry Information
Meeting the Canadian Patient Stem Cell Need, OneMatch
Canadian Unrelated Transplants -Bone Marrow & PBSC-

Fiscal Year

<table>
<thead>
<tr>
<th>Year</th>
<th>Canadian Donor</th>
<th>International Donor</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006/2007</td>
<td>40</td>
<td>138</td>
</tr>
<tr>
<td>2007/2008</td>
<td>33</td>
<td>148</td>
</tr>
<tr>
<td>2008/2009</td>
<td>42</td>
<td>172</td>
</tr>
<tr>
<td>2009/2010</td>
<td>57</td>
<td>191</td>
</tr>
<tr>
<td>2010/2011</td>
<td>52</td>
<td>210</td>
</tr>
<tr>
<td>2011/2012</td>
<td>51</td>
<td>282</td>
</tr>
<tr>
<td>2012/2013</td>
<td>41</td>
<td>232</td>
</tr>
</tbody>
</table>

YTD
Need for Cord Blood Stem Cells

• For all stem cell sources, the racial and ethnic group of the patient strongly influences the likelihood of having a suitable graft identified.

• Growth of the cord blood unit inventory holds more promise than adult donor recruitment in efforts to narrow discrepancy between Caucasions and minority patient groups.

Gragert et al NEJM 2014
## Canadian First Nations, Metis and Inuit Patients

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>6</td>
<td>4</td>
<td>6</td>
<td>4</td>
<td>12</td>
<td>13</td>
</tr>
<tr>
<td>Cancelled</td>
<td>0</td>
<td>39</td>
<td>42</td>
<td>43</td>
<td>49</td>
<td>50</td>
<td>61</td>
<td>71</td>
<td>75</td>
<td>79</td>
<td>95</td>
</tr>
<tr>
<td>Preliminary</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Workup</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

### Number of Aboriginal Patient Searches

![Bar chart showing the number of Aboriginal patient searches from 2003/04 to 2011/12.](chart)
## Canadian Black Patients

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Active</td>
<td>0</td>
<td>6</td>
<td>9</td>
<td>14</td>
<td>15</td>
<td>22</td>
<td>19</td>
<td>21</td>
<td>31</td>
<td>31</td>
<td>44</td>
</tr>
<tr>
<td>Cancelled</td>
<td>0</td>
<td>82</td>
<td>87</td>
<td>91</td>
<td>101</td>
<td>105</td>
<td>119</td>
<td>128</td>
<td>137</td>
<td>152</td>
<td>164</td>
</tr>
<tr>
<td>Preliminary</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Workup</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

### Number of Black Patient Searches

<table>
<thead>
<tr>
<th>Year</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003/04</td>
<td>9</td>
</tr>
<tr>
<td>2004/05</td>
<td>15</td>
</tr>
<tr>
<td>2005/06</td>
<td>16</td>
</tr>
<tr>
<td>2006/07</td>
<td>22</td>
</tr>
<tr>
<td>2007/08</td>
<td>21</td>
</tr>
<tr>
<td>2008/09</td>
<td>23</td>
</tr>
<tr>
<td>2009/10</td>
<td>31</td>
</tr>
<tr>
<td>2010/11</td>
<td>34</td>
</tr>
<tr>
<td>2011/12</td>
<td>44</td>
</tr>
</tbody>
</table>
Ethnic composition of OneMatch

- Caucasian: 71%
- Chinese: 7%
- Other: 4%
- Black: 1%
- Asian: 2%
- Hispanic: 0%
- Aborigina: 1%
- Unknown: 3%
- East Indian: 1%
- Arab / West Asian: 1%
- Filipino: 1%
- Japanese: 0%
- Korean: 0%
- Latin American: 4%
- South Asian: 1%
OneMatch Registrants: May 2014
N=342,224
Cords and Ethnic Diversity

• US National Marrow Donor Program
  – HLA genotypes from 10,000,000+ adult donors and 180,000+ CBU

• Rate of 8/8 match
  – Caucasian European 75%
  – Caucasian of Middle Eastern or North African 46%
  – Asian, Hispanic, Native Americans 27-50%
  – Black Americans of all backgrounds 16-19%

• Due to under representation in donor pool AND increased diversity in the minority groups

  • Gragert et al NEJM 2014
Cords and Ethnic Diversity

• Higher likelihood of match as only 6/6 required
• Likelihood of 6/6 match
  • European descent: 17% adult recipient, 38% child
  • African American: 6% adult, 2% child
  – Likelihood of 4/6 match
    • 80% in ALL adult populations, virtually all in caucasians
    • Virtually all children in all ethnic groups

Gragert et al NEJM 2014
In other words

Likelihood of matched donor for Non Caucasians:

Adult registry donor (8/8)
– 15-30%

Cord blood unit (4/6)
– 80%
Why Cord Blood?

• No risk to mother or newborn baby
• Collected in advance, tested and frozen, ready to use
• More lenient HLA matching - increased chance to find a suitable donor
• Lower incidence of GVHD
• Unit is small, enough for a child or small adult
• 2 CBUs needed for adults
• Cost = ~$40,000/CBU purchased internationally
Cord blood donor found for Quebec woman battling leukemia for second time

Doctors say they have found an umbilical cord for a Mai Duong.
Official Announcement

March 14, 2011
• Ministers of Health approve national, public umbilical cord blood bank
• $48 million investment over eight years.
• Canadian Blood Services is committed to raising $12.5 million for start-up costs.

April 1, 2011
• National Public Cord Blood Bank project began in Ottawa, as per approved model by the Ministers of Health

Mandate
• Bridge the gap of underrepresented ethnically diverse adults on the OM Registry
• Save more lives!
“For All Canadians” Fundraising Campaign

- Over $11.5 million raised to date of $12.5 million
  - Marshall Eliuk of Edmonton
Recognition in the Media

Margaret Atwood
Cord blood shouldn’t be a private matter

Margaret Atwood
Special to The Globe and Mail
Published Monday, Sep. 15 2014, 3:00 AM EDT
Last updated Tuesday, Sep. 16 2014, 7:11 AM EDT
National Public Cord Blood Bank Model

Five collection sites and two manufacturing facilities for processing, storage and distribution.
Cord Blood and Research

- Approximately 15% to 40% of the cord blood units collected are of sufficient volume and/or cell count to be used for transplantation.
Cord Blood for Research Program

- Mothers delivering at The Ottawa Hospital (Civic or General Campus) are given the option to consent to donate their baby’s cord blood to research in the event that the cord blood unit is not bankable.

- Goal: provide researchers across Canada with cord blood units that do not meet the necessary criteria for transplant purposes (non-bankable cord blood units) for biomedical research.

- Cord blood for research products are provided on a cost-recovery basis.

- [www.blood.ca/researchcordblood](http://www.blood.ca/researchcordblood)
Ottawa

Research Consent Rate

2013 - 2014

August: 33%
September: 49%
October: 55%
November: 60%
December: 56%
Cord Blood Banking Process

Seven key processes for cord blood will include capturing and centralizing data on a per unit basis for traceability, searching and matching, information management, ad-hoc queries, reporting, data export and modeling for optimization.
Marketing Objectives

1. To develop strategy to raise awareness of the public cord blood bank among prospects to facilitate recruitment

2. To implement tactics to support recruitment

3. To develop strategy for donor recognition
Recruitment

Our target group is specific and localized, i.e., healthy pregnant women who plan to deliver at the designated collection hospitals:

• Discussions begin during the antenatal period with their health care professional

• Education, information gathering, questions (becoming informed of process in advance of day of delivery)

• Arrive on special day with Permission to Collect form ready

• No advance registration
Who Can Donate?

- Healthy pregnant women, 18 years of age
- Absence of diseases or medical conditions that could be passed on to a recipient
- 34 weeks gestational age
- Single pregnancy, no multiples
- must deliver at one of our designated collection hospitals
Collection Partners

Lois Hole Hospital for Women

Brampton Civic Hospital (WOHS)

BC Women’s Hospital and Health Center

The Ottawa Hospital: Civic & General Campuses
Two Collection Methods

1. Ex-utero: Fully supported by CBS NPCBB designated staff

2. In-utero (supported): All aspects of collection, labelling, packing/shipping by hospital staff
   - CBS NPCBB Nurse Specialist for maternal interview
Ex Utero Collection
Stem Cell Manufacturing Facility:

- Peripheral Blood Apheresis / Bone Marrow: Processing, testing, storage, distribution
  - FACT Accredited / GMP Guidelines
  - Staffing: Charge Technologists and MLTs
    - Manufacturing Equipment

Manufacturing
Sepax System

- Fully-automated, mobile, GMP compliant system for the efficient and reproducible processing of umbilical cord blood
  - bone marrow and peripheral blood
- Hands-free operation — automated, closed, sterile system
- Quick, accurate data tracking
- Consistently high mononuclear cell recoveries
Testing

- Blood cell counts (Pre and Post)

- Purity, Potency, Safety
  - Purity: Microbiology
  - Potency: Stem Cell Counts
    - Flow Cytometer (CD34+ count)
    - CFU Assay (stem cell culture)
  - Safety: Genetic screening, infectious disease testing
    - HLA
    - NIMA
    - ABO

- QC samples – storage
The IPA/NIMA effect

Mother
IMA/NIMA

Father
IPA/NIPA

NIMA = non inherited maternal antigens
NIPA = non inherited paternal antigens
IMA = inherited maternal antigens
IPA = inherited paternal antigens

The mother develops B and T cell immunity against the IPA of the fetus, which is controlled by T reg. PNAS 2012

Likewise, the foetus develops immunity and Tregs against the NIMA. CTL’s and Tregs identified in foetus, cord blood and adults.

Immunity and regulation can be lifelong in both mother and child. PNAS 2009
Identification of an acceptable mismatch with the help of NIMA

Patient A1, A2 - B7, B44

cord blood A1, A3 - B7, B44

mother of CB A1, A2 - B7, B8 NIMA=A2 and B8

Combining the NIMA A2 and/or B8 with the CB phenotype can create e.g. the Virtual CB phenotype: A1, A2 / B7, B44 and 5 other Virtual Phenotypes (VP) if there is 1 substitution, 12 when there are 2 and 8 when there are 3.

HLA typing of the mother can create 26 up to different VPs!!

Slides courtesy of Jon J. van Rood, Leiden University Medical Center and Europdonor Foundation
Transplant-Related Mortality

(Patients ≥ 10 Years Old)

% with TRM (Cum. Incid.)

Years Post-Transplant

0 1 2 3

0 Mismatch 4/22 RR=0.3 P = 0.011

1+2 MM, 1 NIMA 20/41 RR=0.6, P= 0.012

1 MM, No NIMA Match Reference N= 357

2 MM, No NIMA Match Reference N=131

2 MM, 1NIMA Match N= 31

1 MM, 1NIMA Match N=10

PNAS 2009 106 (47) p10952
Cryopreservation

- Volume reduced cord blood unit
- Cryo-protectant added (DMSO)
  - Controlled rate freezing using ThermoGenesis BioArchive freezer
    - Holds up to 3,636 units
- Liquid nitrogen storage (-196°C)
- Inventory controlled / tracked
- Must be stored within 48 hours of collection; can be stored indefinitely
Searching and Matching

- Listed on OneMatch Registry
- Banked inventory of cord blood units
- Cords listed, searched and requested
- Searched both nationally and internationally
- Stem Cell National Systems Solution (IT system)
- Physicians / Clinical Transplant sites request banked cord blood unit
- Build on current OneMatch process
Requested Cord Blood for Transplant

- Manufacturing selects, releases, packs and ships
- Transport – courier
Transplant and Follow-up

• Transplant Follow-up: Outcome Measurement
  - Build upon the current OneMatch process

• Infusion Reactions

• Engraftment Data
  - 100 day follow-up

• Family History – Genetic
Building the NPCBB: Go-live!

- September 30, 2013 – Ottawa
- July 7, 2014 – Brampton
- January 26, 2015 - Vancouver
Ottawa

First collections July 12 and Oct 14, 2012
Brampton

First collection took place on March 4th, 2014
Edmonton

First collection took place on February 24th, 2014
Vancouver

First collection took place on February 18
January 26, 2015

• Banking cord blood units for transplant purposes in Edmonton and Vancouver
Manufacturing
Cryopreservation

Edmonton

Ottawa
### Since Launch

#### 2013-09-30 to 2015-01-31

<table>
<thead>
<tr>
<th></th>
<th>Caucasian</th>
<th>Non-Caucasian</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collected</td>
<td>1348</td>
<td>1656</td>
<td>3004</td>
</tr>
<tr>
<td>In Process</td>
<td>210</td>
<td>291</td>
<td>501</td>
</tr>
<tr>
<td>Not Bankable</td>
<td>1097</td>
<td>1331</td>
<td>2428</td>
</tr>
<tr>
<td>Listed/Searchable</td>
<td>41</td>
<td>34</td>
<td>75</td>
</tr>
</tbody>
</table>
Ottawa

Average CBU Volume (mL)

[Bar chart showing average CBU volume for TOH-General Campus and TOH-Civic Campus from October 2013 to January 2015.]

*Note that this figure includes 2013-09-30.
Brampton

Average CBU Volume (mL)

*Note Brampton Go-live date: 2014-07-07.

2014 - 2015

Canadian Blood Services
*It's in you to give*
Ottawa

Eligible TNC CBUs

TOH-General Campus
TOH-Civic Campus

2013 - 2015

Note that this figure includes 2013-09-30.

Canadian Blood Services
it's in you to give
Brampton

Eligible TNC CBUs

2014-2015

*Note Brampton Go-live date: 2014-07-07.

Canadian Blood Services
it's in you to give
Ethnic composition of OneMatch
Next steps

• $1million required to continue expansion and build inventory

• Spread the word, we need moms
Thank you

- Tanya.Petraszko@blood.ca
- www.campaignforcanadians.ca