


One Haplotype Matched Bone Marrow/Hematopoietic Stem Cell Transplants

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Common assumptions

- The better the HLA match, the better the outcome
- Identical twin is best
- HLA matched sibling, great
- Unrelated matched, good
- Not a match, graft-vs-host disease (GVHD)



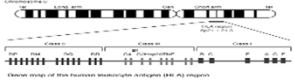

**HLA is highly variable at
the individual and
population levels.**

How do we get variation?

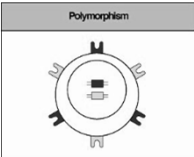



How do we get variation?

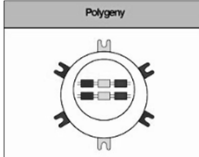

- Polygenic – several genetic loci or genes
- Polymorphic – many different alleles at any given genetic loci

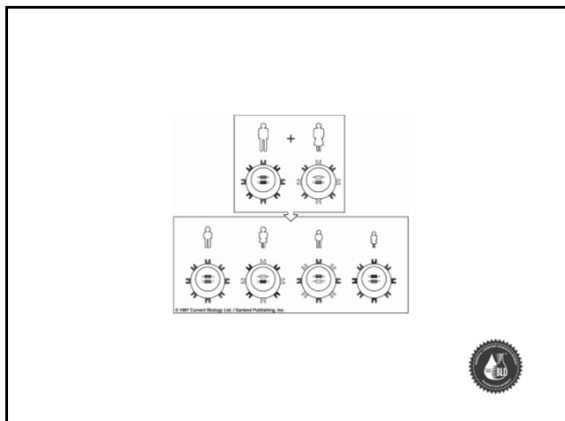



Polymorphism


Polygeny




Mom – A1, A2, B7, B8, DR1, DR4
 Her gametes could be: A1, B7, DR1
 A1, B8, DR4
 A1, B8, DR1
 A1, B8, DR4

 A2, B7, DR1
 A2, B7, DR4
 A2, B8, DR1
 A2, B8, DR4




Mom A1, A2, B7, B8, DR1, DR4
 Dad A30, A31, B27, B35, DR8, DR17


 Son 1 A1, A30, B7, B27, DR1, DR8
 Son 2 A1, A31, B7, B35, DR1, DR17
 Son 3 A2, A30, B8, B27, DR4, DR8
 Son 4 A1, A30, B7, B27, DR1, DR8




Mom A1, A2, B7, B8, DR1, DR4
 Dad A30, A31, B27, B35, DR8, DR17
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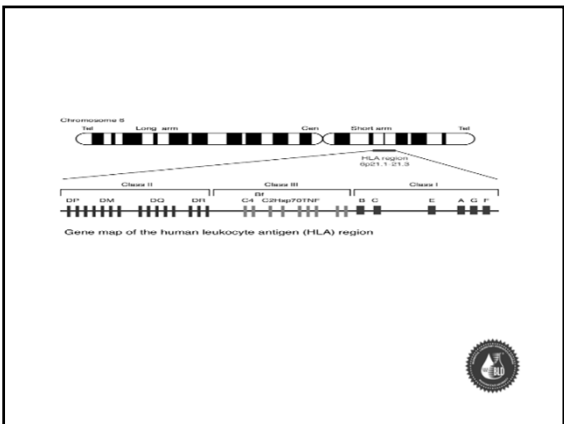
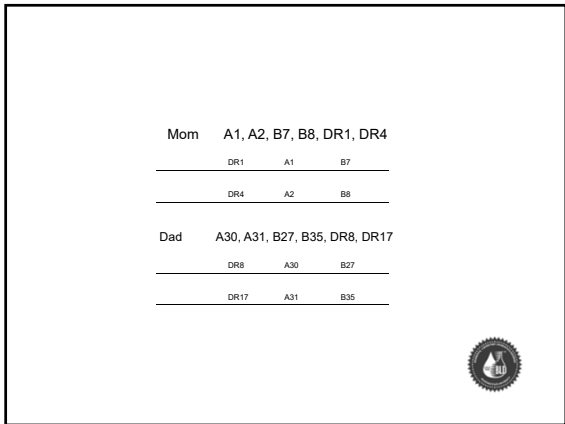
Mom A1, A2, B7, B8, DR1, DR4
 Dad A30, A31, B27, B35, DR8, DR17
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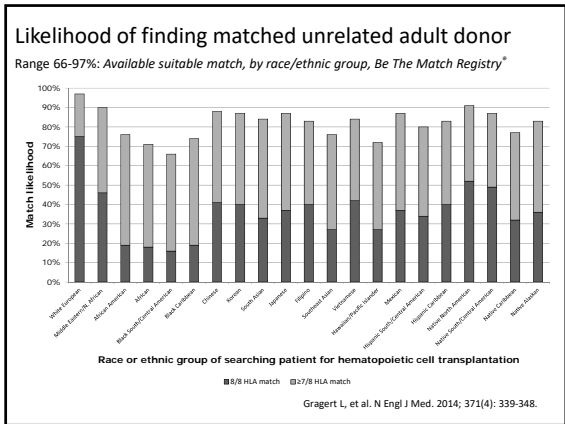
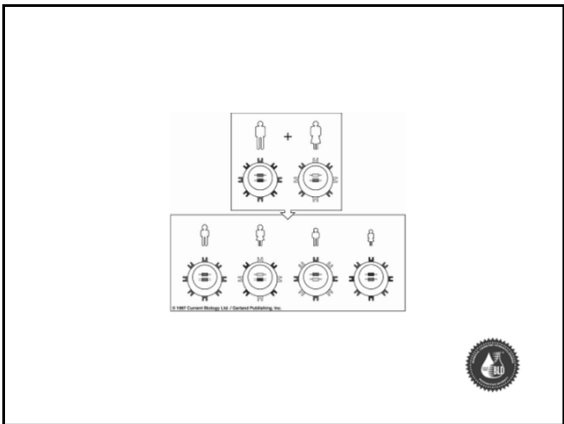
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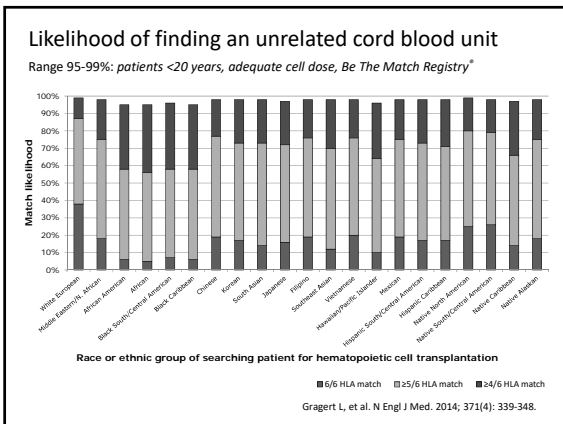


Numbers of HLA Alleles:


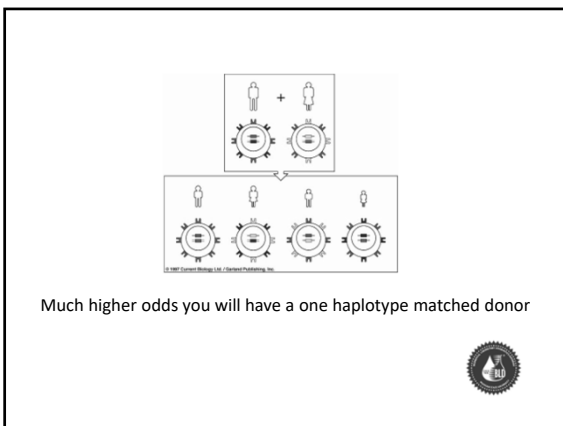
- HLA Class I Alleles 13,680
- HLA Class II Alleles 5,091
- HLA Alleles 18,771


IMGT 7/24/2018





If you don't have a matched related donor, the median time for to search for a matched unrelated donor is about 50 days.

- ### Risks
- Graft vs Host Disease (GVHD)
 - Liver, skin, mucosa, GI tract
 - Grades I-IV
 - Acute or Chronic
 - Treat with immunosuppressants
 - Avoid by T cell depleted grafts
- 


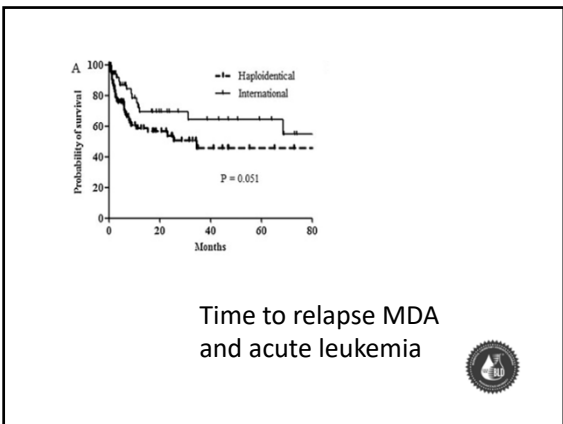
Outcomes

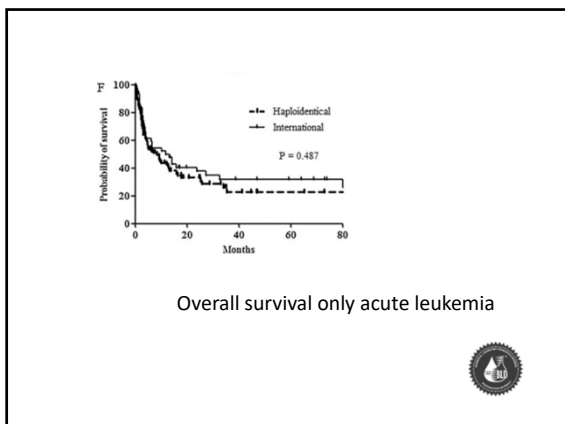
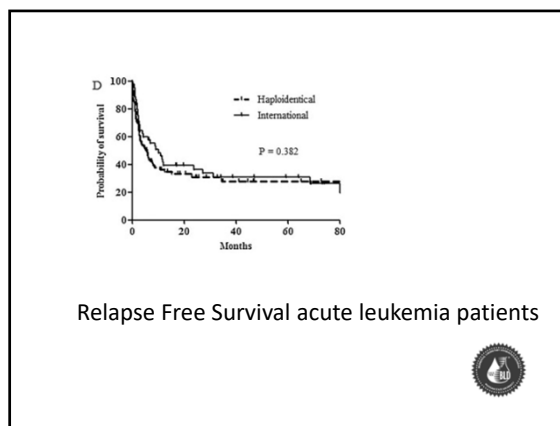
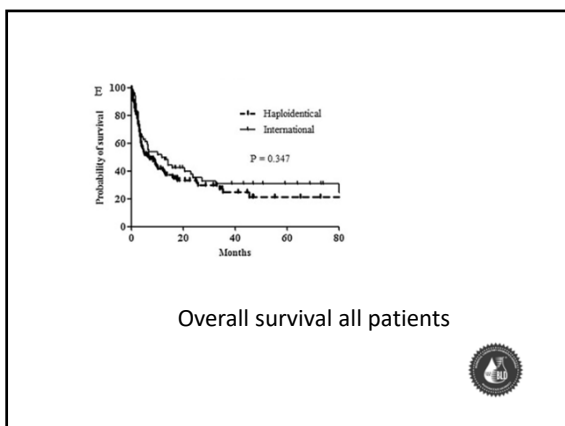
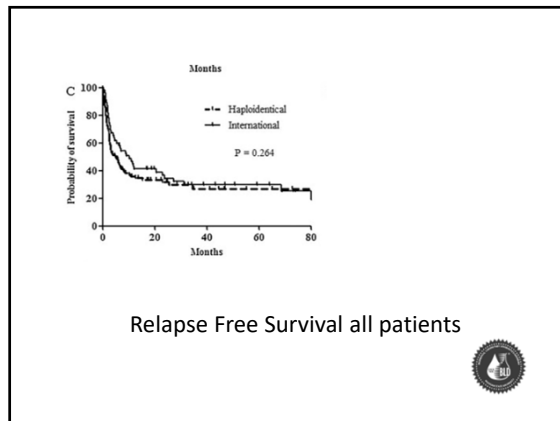
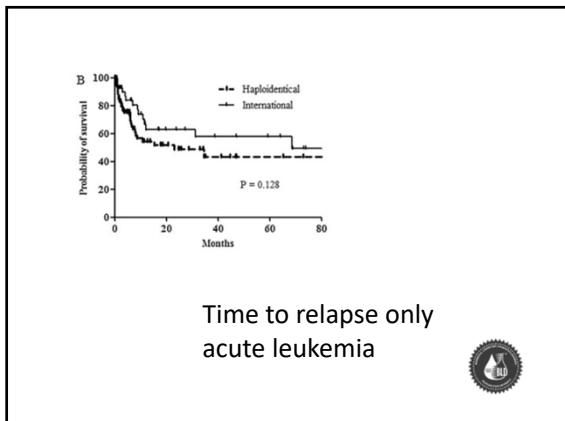
Leukemia Research
Volume 69, June 2018, Pages 31-38

Which donor is better when a matched donor is not available domestically? Comparison of outcomes of allogeneic stem cell transplantation with haploidentical and international donors in a homogenous ethnic population

Hyunkyoung Park ¹, Yoo Jin Lee ¹, Sang-Jin Shin ², Jayoun Lee ³, Silvia Park ⁴, Inho Kim ⁴, Joon-ho Moon ⁵, Hyeon Lee ⁶, Jun Ho Jang ⁴, Sung-Soo Yoon ⁴, Youngil Koh ⁴, ^{1,2,3,4,5,6}

121 haploidentical – 55 unrelated matched donors
MDS and acute leukemia recipients




Costs


Bone Marrow Transplantation

Article | Published 09 March 2018

Cost-effectiveness analysis of haploidentical vs matched unrelated allogeneic hematopoietic stem cells transplantation in patients older than 55 years

Mathias Debals, Genevieve Carole Saint, Catherine Faucher, Rajae Touzani, Claude Lemerle, Christian Chabannon, Sabine Fauri, Raynier Devillier, Samia Harbi, Luis Castagna, Laurence Caymans, Didier Blaise & Anne-Gaëlle Le Correlier 

29 Haploidentical and 63 Matched unrelated



Haplo-related vs unrelated

- Total for unrelated:
 - 67K – 399K
- Total for Haplo-related:
 - 56K – 242K



Haplotype matching

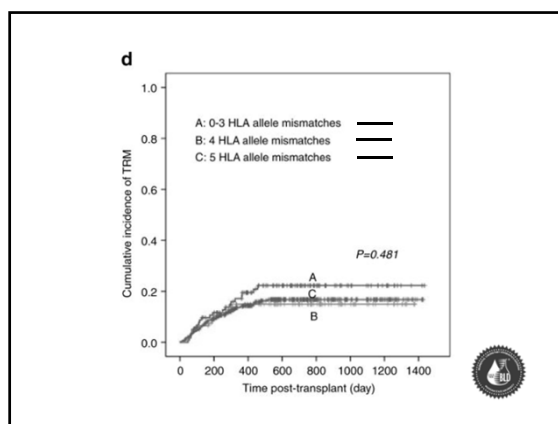
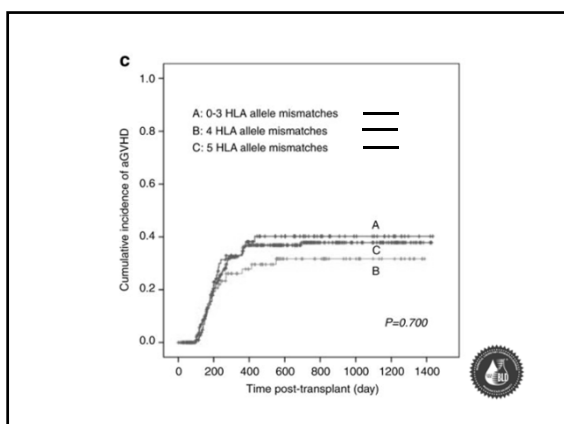
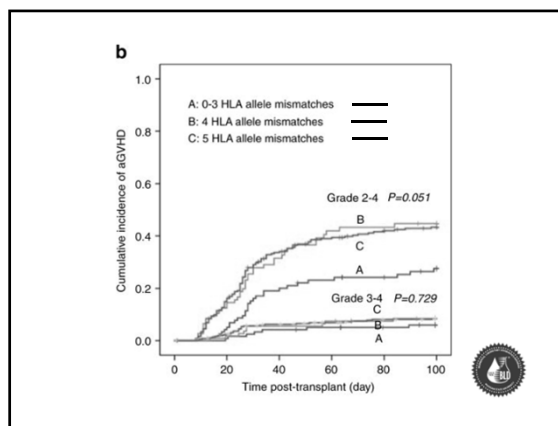
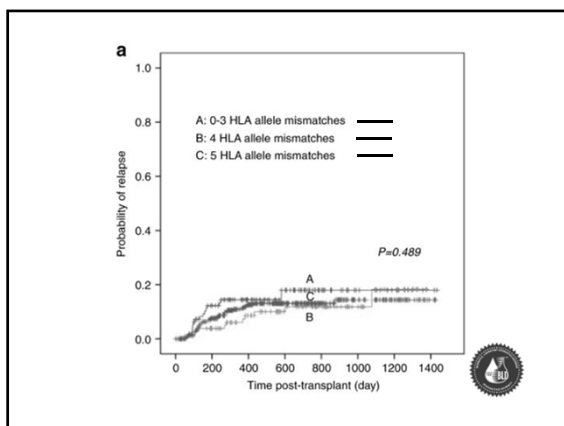
Bone Marrow Transplantation

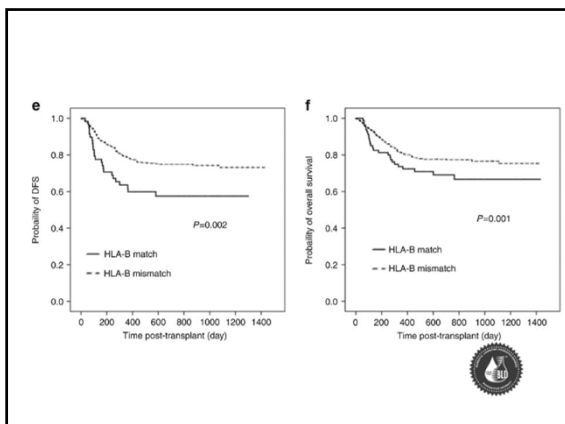
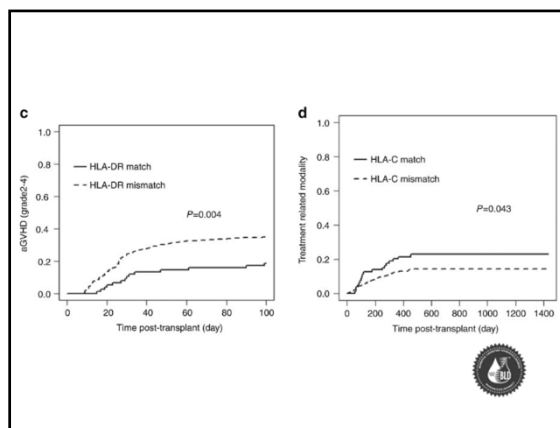
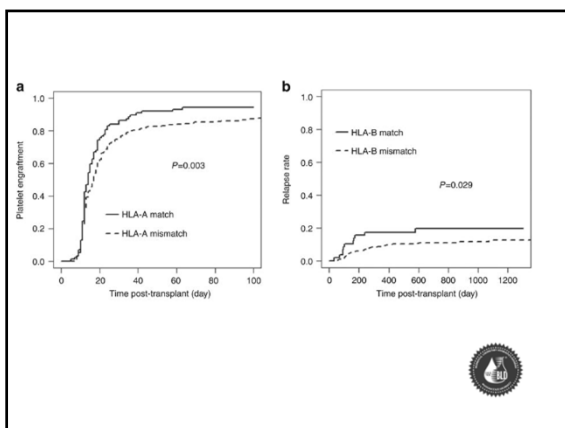
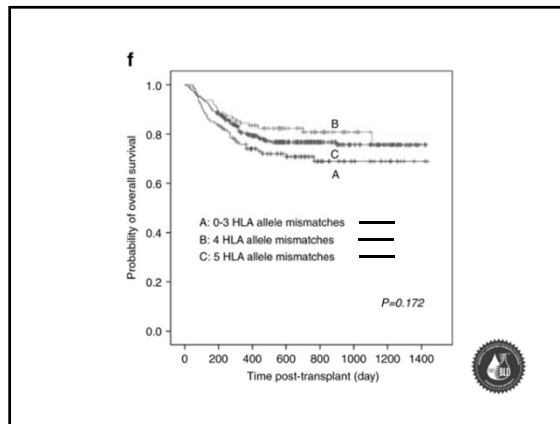
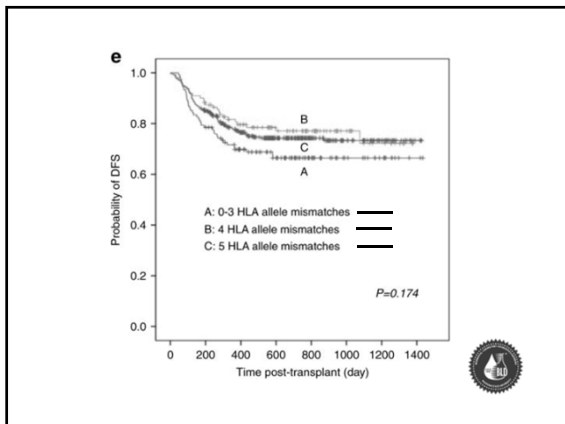
Article | Published: 15 January 2018

Impact of HLA allele mismatch at HLA-A, -B, -C, -DRB1, and -DQB1 on outcomes in haploidentical stem cell transplantation

Ming-Rui Huo, Xu-Ying Pei, Dan Li, Ying-Jun Chang, Lan-Ping Xu, Xiao-Hui Zhang, Kai-Yan Liu & Xiao-Jun Huang

595 MDS and leukemia recipients – all haploidentical transplants





Age matters

- Older recipients with younger donors have better outcomes
 - Superior survival
 - Decreased GVHD
- 40 years old is the magic number for recipients
- 35 years old for the donor

Donor age determines outcome in acute leukemia patients over 40 undergoing haploidentical hematopoietic cell transplantation

Jonathan Canaan¹, Bipin N Savani², Myriam Labopin^{3,4}, Xiao-jun Huang⁵, Fabio Ciceri⁶, William Arcese⁷, Yener Koc⁸, Johanna Fischer⁹, Didier Blaise¹⁰, Zafer Gülbasi¹¹, Maria Teresa Van Lint¹², Benedetto Bruno¹³, Mohamad Mohty¹⁴ and Arnon Nagler¹⁵


Graft vs. Leukemia (GVL)

Leukemia (2016) 36, 447-455
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www.nature.com/lwa


ORIGINAL ARTICLE
Is there a stronger graft-versus-leukemia effect using HLA-haploidentical donors compared with HLA-identical siblings?

O Ringden¹, M Labopin², F Ciceri³, A Wiktorski⁴, A Bacigalupo⁵, W Arcese⁶, A Ghavamzadeh⁷, RM Hantelaj⁸, C Schmidt⁹, A Nagler^{10,11} and M Mohtai¹¹ for the Acute Leukemia Working Party of the European Group for Blood and Marrow Transplantation

9815 matched sibling transplants
864 haplotype matched transplants



- No real advantage most likely due to use of immunosuppressants in haploidentical




Disadvantages

Rambam Maimonides Med J, 2014 Oct 29;5(4):e0028. doi: 10.5041/RMMJ.10162. eCollection 2014 Oct.

Hematopoietic stem cell transplantation-50 years of evolution and future perspectives.


Henig J¹, Zuckerman T².

- Need higher dose 13.8 million cells/kg vs 5
- Higher rate of non-engraftment
- Higher transplant related mortality due to infection caused by delayed immune reconstitution



Advantages

- Most everyone has a donor under this paradigm
- Less time to transplant
- Equivocal outcomes




Questions?

