



# Stem Cell Donor Matching for Patients of Mixed Race

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# Motivation

If Nick Glasgow were white, he would have a nearly 90 percent chance of finding a matching bone marrow donor who could cure his leukemia. But because the 28-year-old bodybuilder is one-quarter Japanese, his doctor warned him the outlook was grim. Glasgow's background, he said, would make it impossible to find a match, because a match usually comes from a patient's own ethnic group. "The doctor didn't say it was slim-to-none. He didn't say it would be hard. He said `zero chance,'" Glasgow's mother,..., recalled.

-Associated Press, 27 May 2009

# Motivation

- Friends and family of Mr. Glasgow organized a web-based campaign to recruit potential donors
- Focus of recruitment was on those of mixed European-Japanese background
- The punch line:

Found **two** matching potential donors within one month

# Questions Posed

- Mr. Glasgow's chances of finding a match were obviously not zero. What were they?
- To what extent are individuals more likely to find a match within their "own" ethnic group? How do we define "own"?
- Is there an economic case for aggressive recruitment of new potential donors of mixed race?

# Bone Marrow Transplants

- Many diseases of the blood can be potentially cured by a hematopoietic stem cell (bone marrow) transplant
- This involves destruction of the patient's bone marrow and its replacement with bone marrow from a donor
- The new bone marrow replenishes the blood with non-diseased cells

# Matching Patients with Donors

- In order to be successful, patient and donor must be adequately “matched”
- In solid organ transplants:
  - Match blood type to prevent rejection of graft by recipient
  - Rarest blood type is in 7% of population
- In hematopoietic stem cell transplants:
  - Match HLA type to prevent rejection of recipient by the graft (GVHD)

# Many HLA Types

- More than 10 million distinct types, even at a relatively gross level of matching
- Probability of matching a sibling is 25%
  - Approximately 30% of needy patients have a matching sibling
- Approximately 4,000 patients per year in United States who could benefit from a transplant, but have no matching sibling

# Matching Probabilities by Race

	Caucasian	African-American	Asian	Hispanic
Caucasian	1/8,000			
African-American	1/133,000	1/127,000		
Asian	1/270,000	1/2,000,000	1/37,000	
Hispanic	1/45,000	1/370,000	1/370,000	1/39,000

**Note:** Table entries give the probability that a randomly selected member of the row race matches a randomly selected member of the column race.

## Other Facts:

- 50% of Caucasians belong to groups with a prevalence less than 1 in 100,000
- 20% of Caucasians belong to groups with a prevalence less than 1 in 1,000,000

# Marrow Donor Registries

- To solve this matching problem, registries of willing donors have been established
  - Determine HLA type and store along with contact information
- A needy patient's type can be compared to those in the registry
- A matching registrant will be asked to donate

# NMDP Registry, 2009

Race or Ethnicity (Self-Identified)	Number in Registry
American Indian/Alaska Native	90,000
Asian	550,000
Black or African American	600,000
Native Hawaiian or Other Pacific Islander	11,000
White	6,000,000
Multiple Race	250,000
Hispanic or Latino	800,000
<b>Total</b>	<b>8,301,000</b>

**Source:** 2009 NMDP Facts and Figures, accessed at [http://www.marrow.org/NEWS/MEDIA/Facts\\_and\\_Figures/2009 Facts and Figures Final 20031210.pdf](http://www.marrow.org/NEWS/MEDIA/Facts_and_Figures/2009_Facts_and_Figures_Final_20031210.pdf)

# NMDP Registry Imputations

- Best available HLA data (from NMDP) divided into the following categories:
  - Caucasian
  - African-American
  - Asian
  - Hispanic
- Need to impute number of registrants for each of these groups, plus each mixed-race combination

# NMDP Registry Imputations

- Caucasian:
  - White, AI/AN
- African-American
  - Black or African American
- Asian
  - Asian, Native Hawaiian or Other Pacific Islander
- Hispanic
  - Hispanic or Latino

# NMDP Registry Imputations

- The “multiple race” category was divided among the six biracial combinations in proportion to their 2000 US Census numbers

# Imputed NMDP Registry

Racial Group	Imputed Number in Registry
White	6,090,000
African-American	600,000
Asian-American	561,000
Hispanic	800,000
African-American, White	43,700
Asian-American, White	50,900
Hispanic, White	92,500
African-Amer., Asian-Amer.	8,000
African-American, Hispanic	44,600
Asian-American, Hispanic	10,400

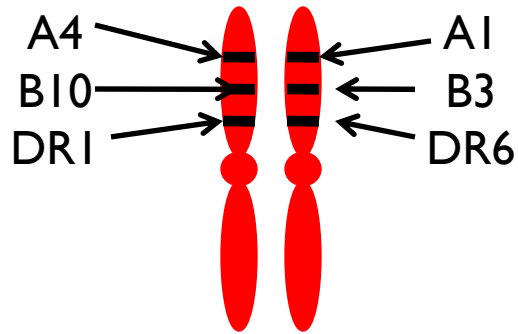
# Imputed NMDP Registry

Racial Group	Imputed Number	Probability Available	Effective Number
White	6,090,000	0.57	3,471,300
African-American	600,000	0.27	162,000
Asian-American	561,000	0.35	196,350
Hispanic	800,000	0.34	272,000
African-American, White	43,700	0.42	18,400
Asian-American, White	50,900	0.46	23,400
Hispanic, White	92,500	0.46	42,100
African-Amer., Asian-Amer.	8,000	0.31	2,500
African-American, Hispanic	44,600	0.30	13,600
Asian-American, Hispanic	10,400	0.34	3,600
<b>Total</b>	<b>8,301,000</b>		<b>4,205,250</b>

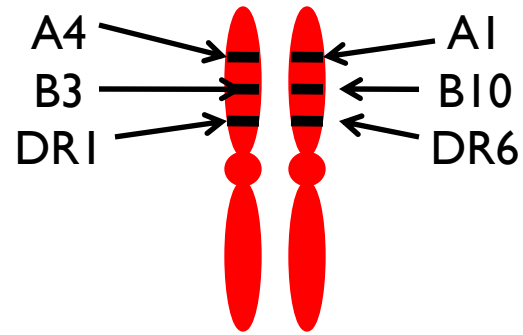
# Matching Patients and Donors: Haplotypes and Phenotypes

- A **haplotype** describes the combination of alleles on a particular chromosome
- Each individual has two haplotypes, one from each parent
- Patient-donor compatibility depends upon the **phenotype**, which is the union of the two haplotypes

# Phenotype Matching



**Phenotype:**  
A1,A4,B3,B10,DR1,DR6



**Phenotype:**  
A1,A4,B3,B10,DR1,DR6

These two individuals are of matching phenotype, but do not share the same haplotypes.

# Probability of having no match

- Let  $p_i^x$  be fraction of the population of racial group  $x$  that is type  $i$ .
  - We estimate these values using recent data on haplotype distributions from Kollman, et al. (2007)
- Probability that a person of type  $i$  has no match in the registry is

$$p_i^0 = \prod_x (1 - p_i^x)^{R_x}$$

- Probability that a randomly selected person of racial group  $y$  has no match in the registry is

$$\sum_i p_i^y p_i^0$$

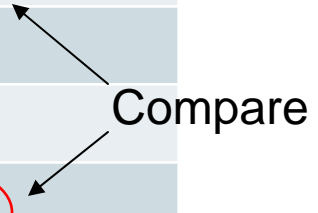
# Match Probabilities

Racial Group	Probability of Match in Registry
White	0.93
African-American	0.58
Asian-American	0.77
Hispanic	0.82
African-American, White	0.71
Asian-American, White	0.80
Hispanic, White	0.87
African-Amer., Asian-Amer.	0.50
African-American, Hispanic	0.65
Asian-American, Hispanic	0.72

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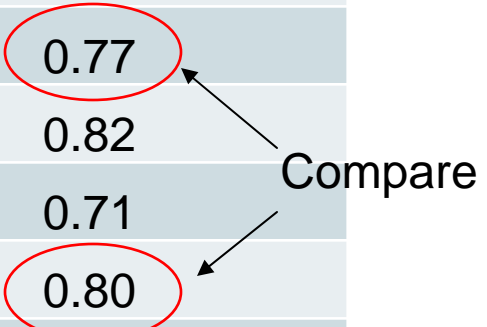
Compare



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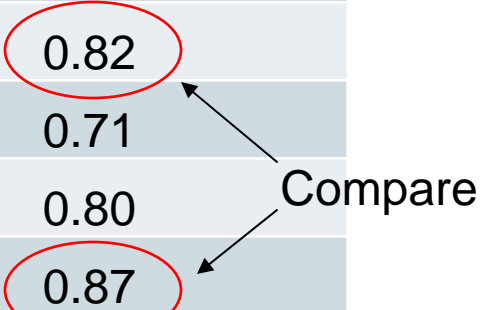
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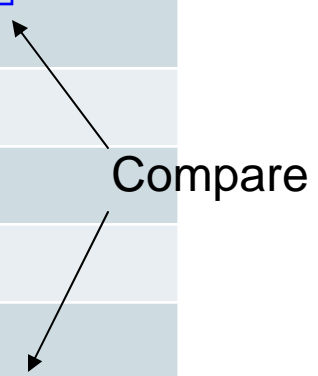
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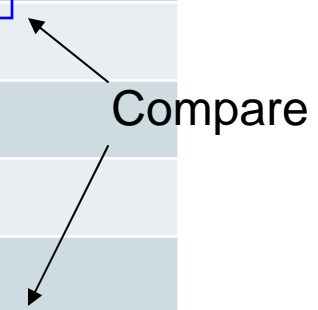
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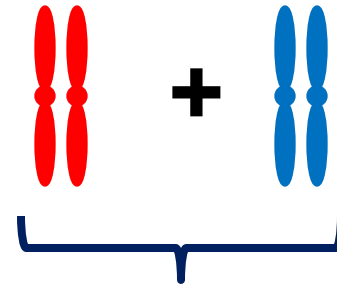


# More Complex Mixed Racial Backgrounds

- Given the distribution of types for biracial individuals, we can calculate type distributions for persons of more complex mixed racial background.
- This calculation is simplified by the fact that the HLA alleles carried by any individual are inherited from just two grandparents.

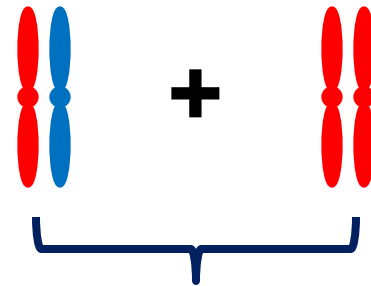
# Mixed Race HLA Genetics

In the first generation, a person with two red types has children with a person of two blue types.

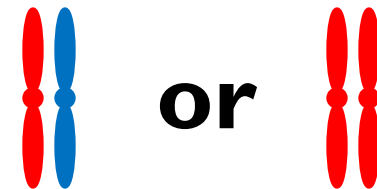


All children in the second generation will have one red type and one blue type.

Suppose one of these has children with someone with two red types.



The children in the third generation have a 50% chance of having two red types and a 50% chance of having one red and one blue type.



# Match probabilities for complex mixed races

- If, for example, the parents are White and Asian-American/White ([Glasgow](#)) we can calculate the probability that their child will have a match as  $.5(0.93)+.5(0.8)=0.865$
- Similar computations can be made for all possible pairs of multi-racial parents.

# Benefits From Adding Registrants

- The increase in match probability for a person of race  $y$  that results from adding a registrant of race  $x$  is

$$G_{xy}(R) = \sum_i p_i^x p_i^y p_i^0(R)$$

- Adding one more person to the registry only results in an additional transplant if a patient of that type is in need of a transplant.
- Multiply  $G_{xy}(R)$  by the number of persons of race  $y$  who will seek transplants during the year to get the probability that adding a person of race  $x$  to the registry will result in an additional transplant to a person of race  $y$  during that year.

# Annual Number of Patients Seeking Transplants by Race

Racial Group	Number
White	3,401
African-American	392
Asian-American	205
Hispanic	425
African-American, White	10
Asian-American, White	16
Hispanic, White	22
African-Amer., Asian-Amer.	3
African-American, Hispanic	10
Asian-American, Hispanic	3

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# Probability that an Additional Registrant will be a Unique Match for a Patient Requiring a Transplant Over a One Year Period by Race of Registrant and Race of Recipient

Registrant Race	Race of Recipient									
	W	Af	As	H	Af-W	As-W	H-W	Af-As	Af-H	As-H
W	3.78	0.42	0.19	0.54	0.02	0.02	0.03	0.00	0.01	0.00
Af	3.63	23.42	0.27	2.47	0.22	0.03	0.08	0.05	0.25	0.01
As	3.09	0.51	7.97	0.93	0.02	0.23	0.04	0.03	0.02	0.05
H	4.28	2.28	0.45	5.04	0.06	0.04	0.12	0.02	0.13	0.02
Af-W	5.48	8.25	0.34	2.46	0.31	0.04	0.11	0.05	0.21	0.01
As-W	5.00	0.67	2.85	1.08	0.03	0.49	0.05	0.04	0.03	0.06
H-W	4.48	1.38	0.35	2.21	0.05	0.04	0.10	0.01	0.05	0.01
Af-As	4.89	7.12	2.41	2.81	0.20	0.24	0.09	0.46	0.22	0.10
Af-H	4.84	9.56	0.45	5.47	0.22	0.04	0.12	0.06	0.45	0.02
As-H	4.80	1.48	3.48	2.78	0.04	0.34	0.09	0.09	0.07	0.16

**Note:** All entries are  $\times 10^{-5}$

# Probability that an Additional Registrant will be a Unique Match for a Patient Requiring a Transplant Over a One Year Period by Race of Registrant and Race of Recipient

Registrant Race	Race of Recipient									
	W	Af	As	H	Af-W	As-W	H-W	Af-As	Af-H	As-H
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Af	3.63	23.42	0.27	2.47	0.22	0.03	0.08	0.05	0.25	0.01
As	3.09	0.51	7.97	0.93	0.02	0.23	0.04	0.03	0.02	0.05
H	4.28	2.28	0.45	5.04	0.06	0.04	0.12	0.02	0.13	0.02
Af-W	5.48	8.25	0.34	2.46	0.31	0.04	0.11	0.05	0.21	0.01
As-W	5.00	0.67	2.85	1.08	0.03	0.49	0.05	0.04	0.03	0.06
H-W	4.48	1.38	0.35	2.21	0.05	0.04	0.10	0.01	0.05	0.01
Af-As	4.89	7.12	2.41	2.81	0.20	0.24	0.09	0.46	0.22	0.10
Af-H	4.84	9.56	0.45	5.47	0.22	0.04	0.12	0.06	0.45	0.02
As-H	4.80	1.48	3.48	2.78	0.04	0.34	0.09	0.09	0.07	0.16

**Note:** All entries are  $\times 10^{-5}$

# Probability that an Additional Registrant will be a Unique Match for a Patient Requiring a Transplant Over a One Year Period by Race of Registrant and Race of Recipient

Registrant Race	Race of Recipient									
	W	Af	As	H	Af-W	As-W	H-W	Af-As	Af-H	As-H
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**Note:** All entries are  $\times 10^{-5}$

# Probability Additional Registrant Will be a Unique Match Over a One Year Period by Race of Registrant

Racial Group	Probability of Unique Match	
	To Own Race	To Any Race
White	3.8	5.0
African-American	23.4	30.4
Asian-American	8.0	12.9
Hispanic	5.0	12.4
African-American, White	0.3	17.3
Asian-American, White	0.5	10.3
Hispanic, White	0.1	8.7
African-Amer., Asian-Amer.	0.5	18.5
African-American, Hispanic	0.4	21.2
Asian-American, Hispanic	0.2	13.3

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# Benefit-Cost of New Registrants

- Benefits: Value of lives saved, which depends upon:
  - Number of potential transplants
  - Change in match probability induced by new registrants
  - Survival benefit of transplant
  - Value of statistical life (\$6.5 million)
- Costs:
  - HLA typing of new registrants
  - Cost of additional transplants performed

# Benefit-Cost of New Registrants

	Benefit	Cost	B/C
White	\$1,300	\$297	4.4
African-American	\$8,100	\$800	10.1
Asian-American	\$3,400	\$446	7.6
Hispanic	\$3,300	\$455	7.3
African-American, White	\$4,600	\$549	8.4
Asian-American, White	\$2,700	\$371	7.3
Hispanic, White	\$2,300	\$376	6.2
African-Amer., Asian-Amer.	\$4,900	\$623	7.9
African-American, Hispanic	\$5,700	\$627	9.1
Asian-American, Hispanic	\$3,600	\$450	8.0

# Summary

- The situation of mixed-race individuals in need of bone marrow transplants may not be as dire as some have suggested
- There is a strong economic case to be made for expanding the size of the registry among all racial and biracial groups
  - Benefits to adding mixed race individuals comes primarily from other races
- African-Americans remain the group least likely to find a match and with the highest benefit-cost ratio for adding more registrants

Thank You