

Accessing the HaploStats Program August 04, 2011

HaploStats (<http://www.HaploStats.org>) is provided by the National Marrow Donor Program (NMDP) Bioinformatics group (see <http://bioinformatics.nmdp.org/>) as a tool facilitating access to haplotype frequency information relative to specific HLA types found in the U.S. population. This application accesses the same frequency tables used to generate match probabilities in NMDP search reports.

Methods Used to Estimate Haplotype Frequencies

HaploStats information has been compiled from the NMDP registry database using the methods outlined in Maiers, M., Gragert, L., and Klitz, W. “[High resolution HLA alleles and haplotypes in the US population](#)”, *Human Immunology* (2007) 68, 779-788. The information accessed by HaploStats is an expansion of the original published haplotype dataset. The North American Indian race/ethnicity group has also been added to the current HaploStats data. Statistical characteristics of the dataset are presented in Table 1.

Table 1.

Summary of Haplo-Stats A-B-DRB1 haplotype sampling characteristics among five US census population categories.

Racial/ ethnic Group	Total sample size (2N)	Number of Haplotypes with n>=1	% of sample in the top 100 haplotypes	% of haplotypes estimated with n>1
AFA	9,178	2,780	31	98.5
API	7,348	1,977	39	99.0
CAU	54,874	4,522	46	99.2
HIS	9,960	2,858	35	98.6
NAM	3,174	1,063	45	98.0
Overall	84,534	13,200	39	98.7

How to Use HaploStats

Filling in the input screen

HLA information can be entered into the HaploStats application for any combination of HLA-A, B, C, DRB1/3/5 or DQB1 loci. The HLA can be entered as (see Table 2 for examples):

- Old (version 2) or new (version 3) nomenclature
- Any level of allele nomenclature detail (for example B*15:01:01:01)
- serology
- NMDP allele codes
- low resolution codes such as A*01:XX
- P and G group nomenclature suffixes are not available for lookup at this time

Table 2.		
Acceptable Formats for Entering Allele Information into HaploStats		
Format	HLA-B types	Alleles Included in the HaploStats Search
Old Nomenclature (Version 2)		
4 Digit Allele Code	0801	B*08:01
Serology	21	B*49:01-49:05, 50:01, 50:02, 50:04
NMDP Code	15CDF	B*15:01, 15:26N, 15:28, 15:32, 15:33
XX Allele Code	13XX	B*13:01-13:06, 13:07N, 13:08Q, 13:09-13:24
New Nomenclature (Version 3)		
4 Digit Allele Code	08:01	B*08:01
Serology	21	B*49:01-49:05, 50:01, 50:02, 50:04
NMDP Code	15:CDF	B*15:01, 15:26N, 15:28, 15:32, 15:33
XX Allele Code	13:XX	B*13:01-13:06, 13:07N, 13:08Q, 13:09-13:24

For homozygous loci, it is only necessary to fill in one of the “Type” fields. Once all HLA information has been entered in the appropriate fields for the desired loci, click the <Submit Query> button to retrieve haplotype information.

HaploStats output

- For low resolution codes, all possible related combinations, where there is frequency data available, will be displayed in the results (Note: haplotype frequencies are displayed as percentages for readability).
- HaploStats reports "individual haplotype frequencies" as a percent and "haplotype pair frequencies" in scientific notation.
- Depending on which loci have had information entered, a list of all observed (A-B-DRB1), (B-C), (DRB1-DRB3), (DRB1-DRB5) and (DRB1-DQB1) haplotype frequencies is displayed.
- Haplotype frequency and rank information is broken out by broad race/ethnicity groups: Caucasian (CAU), African American (AFA), Asian Pacific Islander (API), Hispanic (HIS) and North American Indian (NAM).
- Additionally, a list of all possible observed (A-B-DRB1), (B-C), (DRB1-DRB3), (DRB1-DRB5) or (DRB1-DQB1) haplotype pair combinations and their frequencies is provided. Haplotype pair frequency information is broken out by the same broad race/ethnicity groups.
- New to HaploStats as of April 2011. Global HLA Haplotype Maps are available for any haplotype highlighted in blue, indicating a hyperlink, in either the “(A-B-DRB1) Individual Haplotype Frequencies” list or the “(A-B-DRB1) Haplotype Pair Frequencies” grid. These maps were developed in collaboration with consenting registries listing donors in Bone Marrow Donors Worldwide (BMDW) (<http://www.bmdw.org>) and are a product of the 16th International HLA and Immunogenetics Workshop (IHIWS) Registry Diversity Project http://www.16ihw.org/projects/maiers_diversity.html. Not all A-B-DRB1 haplotypes reported in HaploStats will have maps available. Only the top 40,000 A-B-DRB1 haplotypes, according to BMDW registries contributing to individual country frequency calculations, had maps created. In addition, US frequencies depicted in the maps were developed from a more current cohort and do not match exactly the frequency values reported in the HaploStat frequency tables. See figure III for an example of Global HLA Haplotype Maps.

- **Note that all allele codes entered at a resolution higher than the protein level of nomenclature will have haplotype frequencies rolled up to protein level (as estimated by Maier, M., Gragert, L., and Klitz, W. in “[High resolution HLA alleles and haplotypes in the US population](#)”, *Human Immunology* (2007) 68, 779-788.)** For example, the estimated frequency for haplotypes containing the allele A*02:05:49 will be represented by the frequency of the observed and related haplotypes containing A*02:05.

For an example of HaploStats HLA entry and display screens, see figures I, II and III.
 For comments and questions about HaploStats, please send correspondence to Bioinformatics@NMDP.org

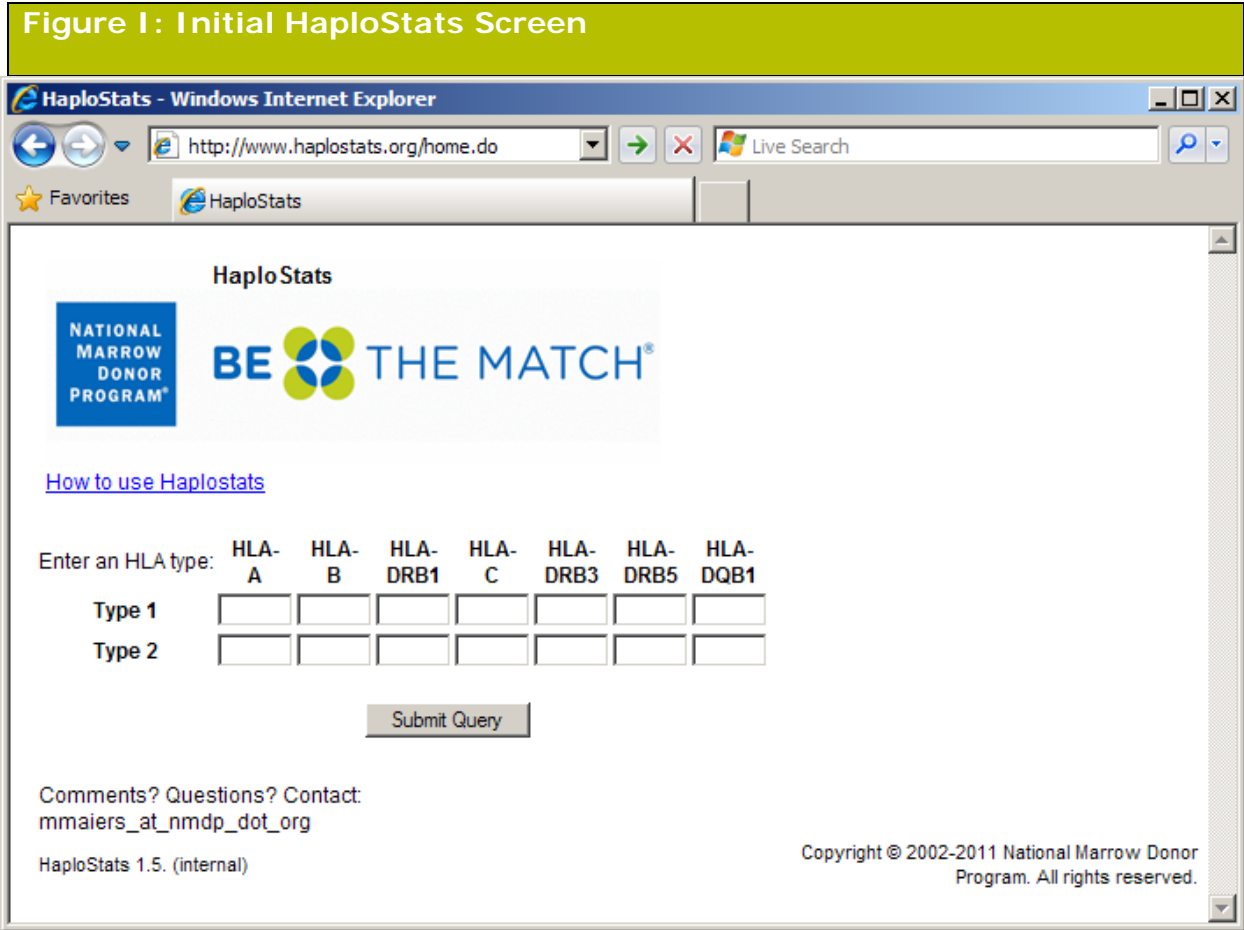


Figure II: Results of the query submitted for figure I



[How to use Haplostats](#)

HLA typing

A	B	DRB1	C	DRB3	DRB5	DQB1
02:06 68:01	40:XX 51:XX	14:06 16:02	08:01 15:06			03:01

▼DNA/Serology Typing Discrepancies

Locus: A

Locus	DNA Srch Dtrm 1	DNA Srch Dtrm 2	Ser Type 1	Ser Type 2	Count	Serology Seen	% Occurrence
A	02	68	2	2	740	33553	2.205%
A	02	68	2	68	572	592	96.622%
A	02	68	28	28	41	1589	2.580%
A	02	68	2	69	6	8	75.000%

Locus: BPR

Locus	DNA Srch Dtrm 1	DNA Srch Dtrm 2	Ser Type 1	Ser Type 2	Count	Serology Seen	% Occurrence
BPR	40	51	40	51	34	36	94.444%
BPR	40	51	52	60	15	211	7.109%
BPR	40	51	53	61	12	121	9.917%
BPR	40	51	53	60	9	203	4.433%
BPR	40	51	52	61	7	344	2.035%

Locus: DRB1

Locus	DNA Srch Dtrm 1	DNA Srch Dtrm 2	Ser Type 1	Ser Type 2	Count	Serology Seen	% Occurrence
DRB1	14	16	14	16	23	23	100.000%

▼(A-B-DRB1) Individual Haplotype Frequencies

Haplotype	CAU		AFA		API		HIS		NAM	
	Freq (%)	Rank	Freq (%)	Rank	Freq (%)	Rank	Freq (%)	Rank	Freq (%)	Rank
A*02:06 B*40:01 DRB1*16:02					0.0140	1159				
A*02:06 B*40:02 DRB1*14:06							0.0630	301		
A*02:06 B*40:02 DRB1*16:02							0.0320	592		
A*02:06 B*40:08 DRB1*14:06							0.0100	1501		
A*02:06 B*40:08 DRB1*16:02							0.0100	1501		
A*02:06 B*51:01 DRB1*14:06					0.0140	1159	0.0110	1394		
A*02:06 B*51:01 DRB1*16:02							0.0300	626		
A*68:01 B*40:01 DRB1*16:02									0.0320	564
A*68:01 B*40:02 DRB1*14:06							0.0230	817		
A*68:01 B*40:02 DRB1*16:02							0.0680	274		
A*68:01 B*40:11 DRB1*14:06							0.0110	1394		
A*68:01 B*51:01 DRB1*16:02	0.0010	4866	0.0050	2917						

▼(A-B-DRB1) Haplotype Pair Frequencies

Race	CAU	AFA	API	HIS	NAM
Haplo- type 1 freq 1 (%) rank 1 total freq	Haplo- type 2 freq 2 (%) rank 2			68:01 02:06 40:02 51:01 16:02 14:06 0.0680 0.0110 274 1394 1.496 x 10⁻⁷	
Haplo- type 1 freq 1 (%) rank 1 total freq	Haplo- type 2 freq 2 (%) rank 2			02:06 68:01 51:01 40:02 16:02 14:06 0.0300 0.0230 626 817 1.38 x 10⁻⁷	
Haplo- type 1 freq 1 (%) rank 1 total freq	Haplo- type 2 freq 2 (%) rank 2			02:06 68:01 51:01 40:11 16:02 14:06 0.0300 0.0110 626 1394 6.600 x 10⁻⁸	

▼(B-C) Individual Haplotype Frequencies

Haplotype	CAU		AFA		API		HIS		NAM	
	Freq (%)	Rank	Freq (%)	Rank	Freq (%)	Rank	Freq (%)	Rank	Freq (%)	Rank
B*40:01 C*08:01					0.0600	134				
B*40:06 C*08:01					1.3190	24			0.0320	118
B*40:27 C*08:01							0.0320	170		
B*51:01 C*08:01					0.0150	218	0.2640	76		
B*51:02 C*08:01							0.4550	56	0.7430	34
B*51:07 C*08:01							0.0050	423		
B*51:01 C*15:06	0.0160	131								
B*51:14 C*15:06							0.0110	262		

▼(B-C) Haplotype Pair Frequencies

Race	CAU	AFA	API	HIS	NAM
Haplo- type 1 freq 1 (%) rank 1 total freq	Haplo- type 2 freq 2 (%) rank 2			4027 5114 08:01 15:06 0.0320 0.0110 170 262 7.04 x 10⁻⁸	

▼(DRB1-DRB3) Individual Haplotype Frequencies

No DRB1-DRB3 Haplotype Frequency Data Available

▼(DRB1-DRB3) Haplotype Pair Frequencies

No DRB1-DRB3 Haplotype Pair Frequency Data Available

▼(DRB1-DRB5) Individual Haplotype Frequencies

No DRB1-DRB5 Haplotype Frequency Data Available

▼(DRB1-DRB5) Haplotype Pair Frequencies

No DRB1-DRB5 Haplotype Pair Frequency Data Available

▼(DRB1-DQB1) Individual Haplotype Frequencies

Haplotype	CAU		AFA		API		HIS		NAM	
	Freq (%)	Rank	Freq (%)	Rank	Freq (%)	Rank	Freq (%)	Rank	Freq (%)	Rank
DRB1*14:06 DQB1*03:01	0.0170	82	0.0120	126	0.2040	48	2.6540	13	0.2130	37
DRB1*16:02 DQB1*03:01	0.0170	82	0.0560	74			1.7800	15	2.3210	16

▼(DRB1-DQB1) Haplotype Pair Frequencies

Race		CAU		AFA		API		HIS		NAM	
Haplo- type 1	Haplo- type 2	14:06 03:01	16:02 03:01	16:02 03:01	14:06 03:01			14:06 03:01	16:02 03:01	16:02 03:01	14:06 03:01
freq 1 (%)	freq 2 (%)	0.0170	0.0170	0.0560	0.0120			2.6540	1.7800	2.3210	0.2130
rank 1	rank 2	82	82	74	126			13	15	16	37
total freq		5.78 x 10⁻⁸		1.344 x 10⁻⁷				9.448 x 10⁻⁴		9.887 x 10⁻⁵	
Haplo- type 1	Haplo- type 2	16:02 03:01	14:06 03:01								
freq 1 (%)	freq 2 (%)	0.0170	0.0170								
rank 1	rank 2	82	82								
total freq		5.78 x 10⁻⁸									

▼Related Designer Search Determinants

Patient search determinants are:

A(02, 68) BPR(40, 51) DRB1(14, 16)

At A locus, the search determinant +02A covers the search determinants: 02, 203, 210, 28, 68, 69.

At BPR locus, the search determinant +05A covers the search determinants: 05, 51, 5102, 5103, 52, 53, 70, 71, 72, 77.

At BPR locus, the search determinant +15A covers the search determinants: 15, 40, 4005, 50, 60, 61, 62, 63, 70, 71, 72, 75, 76, 77 and is a split of 21.

At BPR locus, the search determinant +18A covers the search determinants: 05, 18, 51, 5102, 5103, 52.

At BPR locus, the search determinant +27B covers the search determinants: 27, 40, 60, 61.

At BPR locus, the search determinant +40A covers the search determinants: 40, 4005, 50, 60, 61 and is a split of 21.

At BPR locus, the search determinant +40B covers the search determinants: 40, 48, 60, 61.

At BPR locus, the search determinant +40C covers the search determinants: 48, 60, 61, 70, 71, 72 and is a split of 40.

At BPR locus, the search determinant +40D covers the search determinants: 15, 40, 48, 60, 61, 62, 63, 75, 76, 77.

At BPR locus, the search determinant +40E covers the search determinants: 21, 40, 4005, 49, 50, 60, 61, 70, 71, 72.

At BPR locus, the search determinant +51A covers the search determinants: 51, 5102, 5103, 53 and is a split of 05.

At BPR locus, the search determinant +53A covers the search determinants: 51, 53.

At DRB1 locus, the search determinant +08B covers the search determinants: 08, 14 and is a split of 06.

At DRB1 locus, the search determinant +14A covers the search determinants: 11, 14 and is a split of 05, 06.

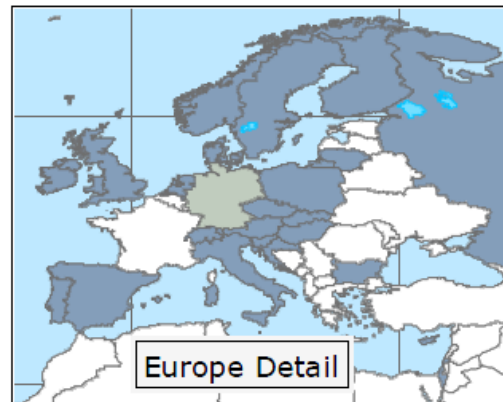
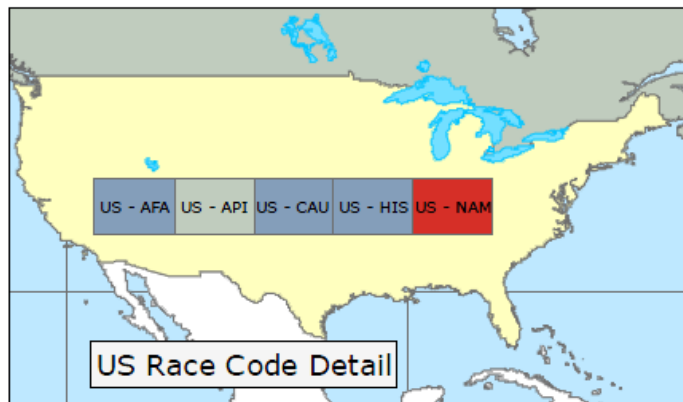
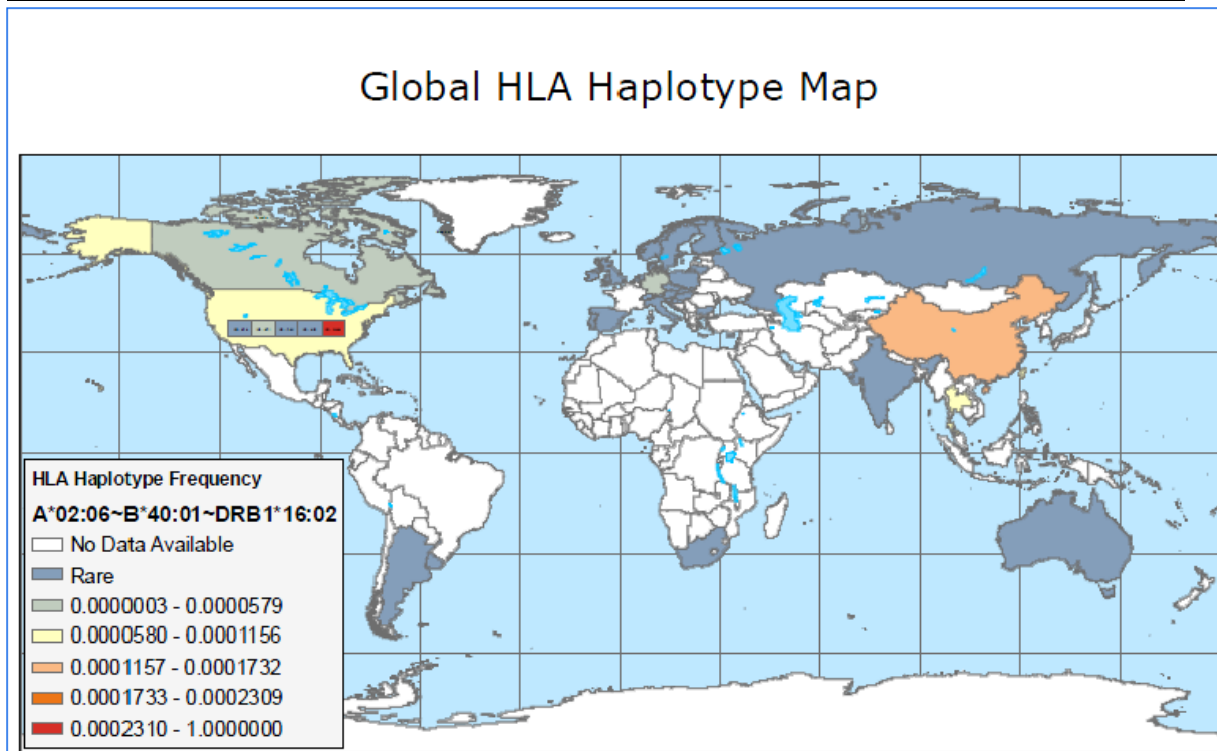
Comments? Questions? Contact:

mmaiars_at_nmdp_dot_org

HaploStats 1.5. (internal)

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Figure III: Global HLA Haplotype Map



HLA A~B~DRB1 haplotype frequencies were estimated by EM algorithm for each country with donors listed in Bone Marrow Donors Worldwide (BMDW) typed by DNA methods as of 2011-01-25. US depicted haplotype frequencies were calculated by broad race categories African American (AFA), Asian or Pacific Islander (API), Caucasian (CAU), Hispanic (HIS) and North American Indian (NAM). The map thematic color is white for countries where no information was available or where associated registries chose not to participate in the study. The thematic color is blue for countries where the haplotype was not observed (Rare).

This map is a research product of the 16th International HLA and Immunogenetics Workshop (IHIWS) Registry Diversity Project http://www.16ihw.org/projects/maiers_diversity.html

Please direct questions regarding Global HLA Haplotype Frequency Maps to <http://bioinformatics.nmdp.org>

Global HLA Haplotype maps can be accessed through <http://haplostats.org>

