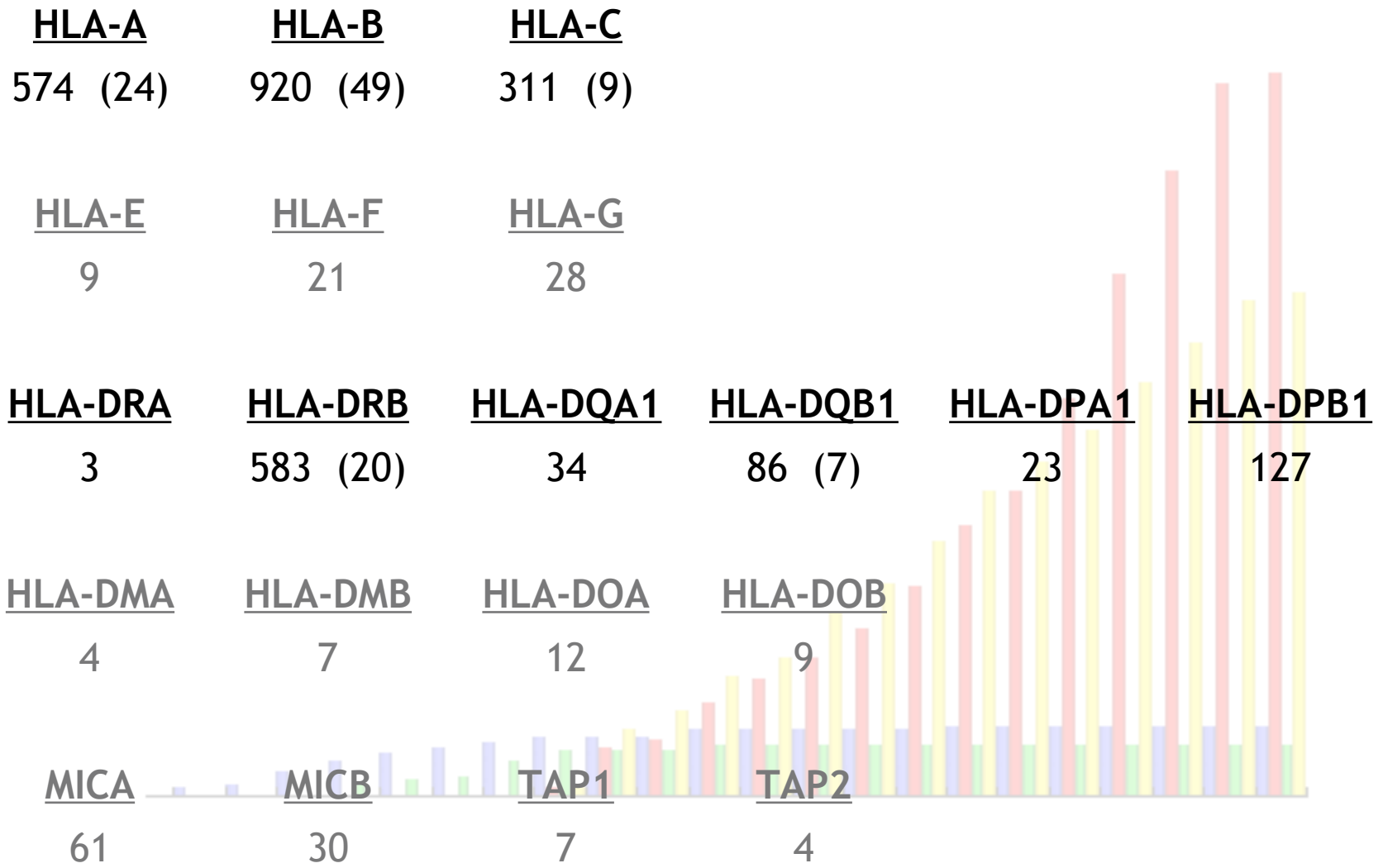




HLA Nomenclature

Steven GE Marsh
Anthony Nolan Research Institute
London

Number of HLA Alleles June 2007



IMGT/HLA Database Statistics



Release 2.17.0, April 2007

- **2,714 HLA alleles**
 - 1,839 Class I alleles
 - 875 Class II alleles
- 102 other alleles (TAP1, TAP2, MICA, MICB)
- 6,139 EMBL component sequences
- 4,325 cells in accompanying cell database
- 4525 Submissions to the database, **~500 new submissions each year**
- Over 240,000 visits to the database each year, download over 840,000 pages

HLA Nomenclature



- WHO Nomenclature Committee for factors of the HLA system was first established in 1968
- The Committee is responsible for naming genes, antigens and alleles
- Nomenclature Committee reports are published in a number of journals

HLA Nomenclature



S.G.E. Marsh
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R.E. Bontrop
B. Dupont
H.A. Erlich
D.E. Geraghty
J.A. Hansen
C.K. Hurley
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J. Trowsdale

Acknowledgments:

The Committee would like to thank James Robinson, Matthew Waller and Sylvie Fail for their work with the IMGT/HLA Sequence database and their help in the preparation of tables for this report. Also thanked are Dr Peter Stoehr and the staff at the European Bioinformatics Institute for their continued support of the IMGT/HLA Database. We would also like to thank the many organizations who provide financial support for the IMGT/HLA database

Report

Nomenclature for factors of the HLA system, 2004

Tissue Antigens (2005) **65** 301-369

International Journal of Immunogenetics (2005) **32** 107-159

Human Immunology (2005) **66** 571-636

Following the decision to hold their next full meeting after the 14th International Histocompatibility Workshop in 2005, the WHO Nomenclature Committee for Factors of the HLA System has decided to publish an interim report listing updated tables of alleles including those assigned since the publication of the last full report in 2002 (1). The alleles named during the period follow the principles established in previous reports (1–17).

1 Naming of additional alleles

A. Conditions for acceptance of new allele sequences

As emphasized in previous reports, there are required conditions for acceptance of new sequences for official names.

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HLA Workshops



Workshop	Year	Chairman	Venue	Advances
1st	1964	DB Amos	Durham, North Carolina, USA	Definition of “Hu-1”, “LA” and “Four” antigen specificities
2nd	1965	JJ van Rood	Leiden, The Netherlands	Mixed lymphocyte culture testing
3rd	1967	R Ceppellini	Torino, Italy	Family studies. HLA in renal transplantation
4th	1970	PI Terasaki	Los Angeles, California, USA	Definition of 27 HLA-A, B, C specificities
5th	1972	J Dausset	Evian, France	Worldwide typing of 49 populations
6th	1975	F Kissmeyer-Nielsen	Aarhus, Denmark	Description of Dw specificities
7th	1977	WF Bodmer	Oxford, UK	Definition of DR1-7 specificities. HTC testing
8th	1980	PI Terasaki	Los Angeles, California, USA	Definition of MB (DQ) and MT (DR52/53). HLA in transplantation and disease
9th	1984	EA Albert/W Mayr	Munich, Germany Vienna, Austria	New class I and II specificities. HLA class II in renal transplantation
10th	1987	B Dupont	Princeton, New Jersey New York, NY, USA	Establishment of RFLP, T cell clones, biochemical and HTC methods, created a panel of cell lines, gene and allele nomenclature
11th	1991	T Sasazuki/K Tsuji/M Aizawa	Yokohama, Japan	HLA class II typing by PCR methods
12th	1996	D Charron	St Malo/Paris, France	Sequencing, HLA class I typing by PCR
13th	2002	J Hansen	Victoria, BC, Canada Seattle, Washington, USA	Virtual DNA analysis, SNP markers, HLA in HSCT
14th	2005	J McCluskey	Melbourne, Australia	MHC and anthropology, HLA and disease
15th	2008	M Gerbase de Lima/ME Moraes	Rio de Janeiro, Brazil	

HLA Nomenclature 1965



The first mention of nomenclature came during the 2nd Workshop in 1965.

J. W. BRUNING, A. VAN LEEUWEN AND J. J. VAN ROOD

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should in most instances not be considered as final.

Because the statistical analysis was used as a guide and not as a final proof, the χ^2

sera for the typing of all future kidney homografts. For this reason, it is extremely gratifying that as a result of the Workshop the number of centers which can recognize these

“The question of nomenclature of the leukocyte antigens has been raised during the workshop. An advice on this matter will be formulated by a committee on nomenclature, which has been formed during this Workshop.”

homograft survivors are more compatible as far as leukocyte groups are concerned than a random control group (24). It is impossible for any one group of investigators to provide

Many other points of interest resulting from this study, as for instance the relative antigenicity of the antigens are still very much under discussion and cannot be included in this brief summary of results.

HLA Nomenclature 1967



After the 3rd Workshop in 1967 a one page report was issued:

“Nomenclature: HL-A

As an interim measure, while awaiting the formation of the Nomenclature Committee, the investigators listed below have agreed to use the term HL-A for indicating the major system of leucocyte antigens (previous names: Du-1, Four, Hu-1, LA etc).”

Hu1 (Dausset) + LA (Payne/Bodmer) = HL-A

HLA Nomenclature 1968



The first true report was published in 1968 and listed the following as officially recognised antigens, with their previous equivalents. Correlation of antigen specificity between the different groups is achieved using a common panel of antibodies.

NEW HL-A NOMENCLATURE AND PREVIOUS DESIGNATIONS ^a										
New HL-A nomenclature ^b	Amos	Batchelor	Ceppellini	Dausset	Kissmeyer-Nielsen	Payne/Bodmer	van Rood	Shulman	Terasaki	Walford
HL-A1	19	1	To-8	11	LA1	LA1	LA1	—	1	Lc-1
HL-A2, or HL-AMac	1	5	To-9	1 or Mac	LA2	LA2	8a	PIGrLyB ¹	2	Lc-2
HL-A3	4	—	To-10	12	LA3	LA3	LA3	Hill	8	Lc-3
HL-A4										
HL-A5	45	25	To-5	5	—	—	Da5	—	6	—
HL-A6										
HL-A7	2	—	To-20	10	—	4d	7c	—	5	Lc-8
HL-A8	41	2	To-7	8	—	7d	7d	—	11	Lc-7

^a A dash (—) indicates that no symbol has been allocated within the nomenclature concerned.

^b HL-A4 will be reserved for one of the higher frequency 4^a factors, and HL-A6 for 4^b. Before assigning these specificities, an exchange of serum among collaborating laboratories will be necessary.

HLA Nomenclature Milestones



- 1970 Preliminary designations identified by the use of a 'w' (workshop status).
- 1975 HL-A becomes HLA-A, -B and HLA-C and HLA-D defined
The concept of split antigens is introduced (A9 is split into Aw23 and Aw24)
- 1977 First HLA-DR antigens named 'D' related
- 1987 A comprehensive list of HLA genes are named, Alleles named using four digit name
- 1990 Fifth digit to allele names indicates a silent (non-coding) polymorphism.
- 1994 The first null allele is named (DRB4*01012N)
- 1995 Extra digits added to code for polymorphism in the non-coding regions of alleles
- 1996 L suffix added (low level of expression)
- 2002 C, S, A suffices added. Allele names extended to eight digits
- 2005 Q suffix added



Q Expression of an allele is questionable given that the mutation seen in the allele has previously been shown to affect normal expression levels

S Allele specifying a protein that is expressed as a soluble secreted molecule but is not present on the cell surface

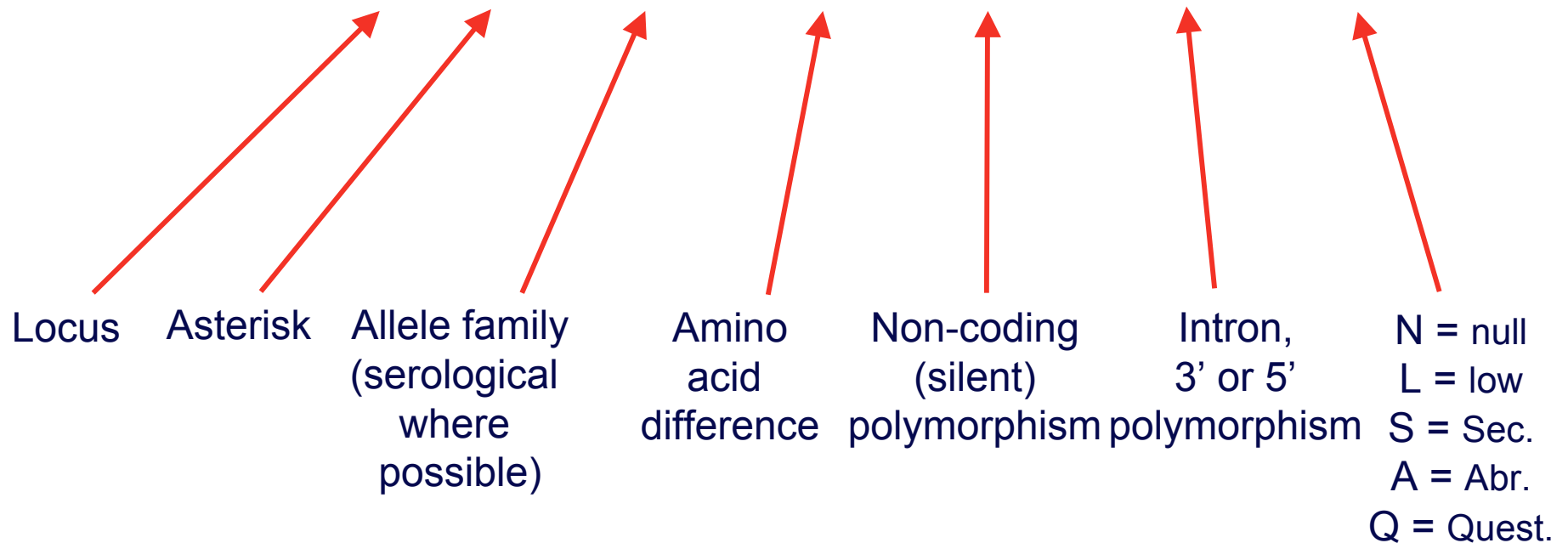
A Aberrant; some doubt as to expression

C Allele product remains in the cytoplasm and is not expressed on the cell surface

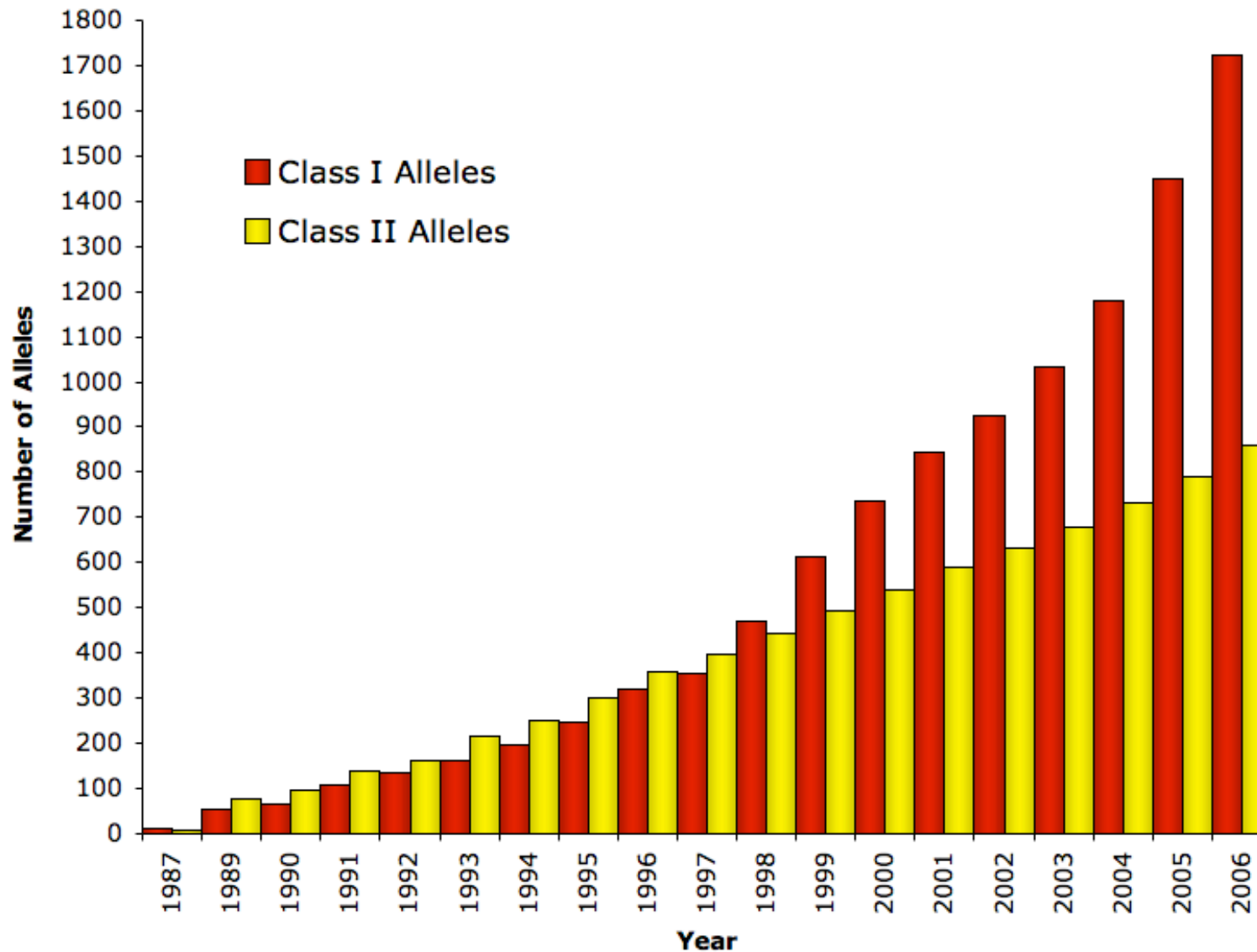
HLA Allele Nomenclature



HLA - A * 24 02 01 01
HLA - A * 24 02 01 02 L



Numbers of HLA alleles 1987 - 2006





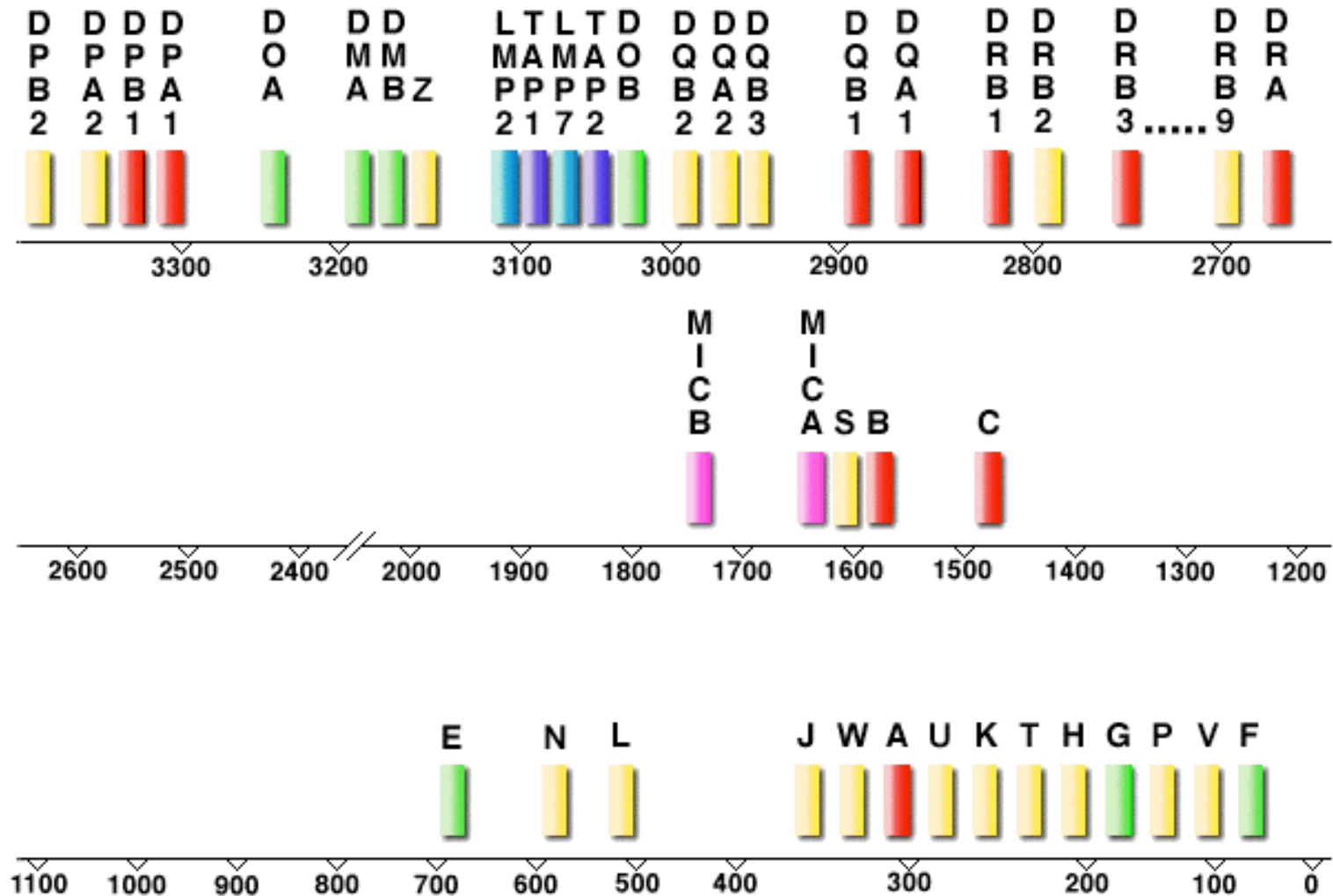
- Sequence database specialising in genes of the human major histocompatibility complex
- Official database of the WHO Nomenclature Committee for Factors of the HLA System
- Initially funded as part of the International ImMunoGeneTics (IMGT) database project
- IMGT/HLA Database on-line since 1998
- Database housed by the EBI, maintained at the ANRI in London.

Why do we need a database?

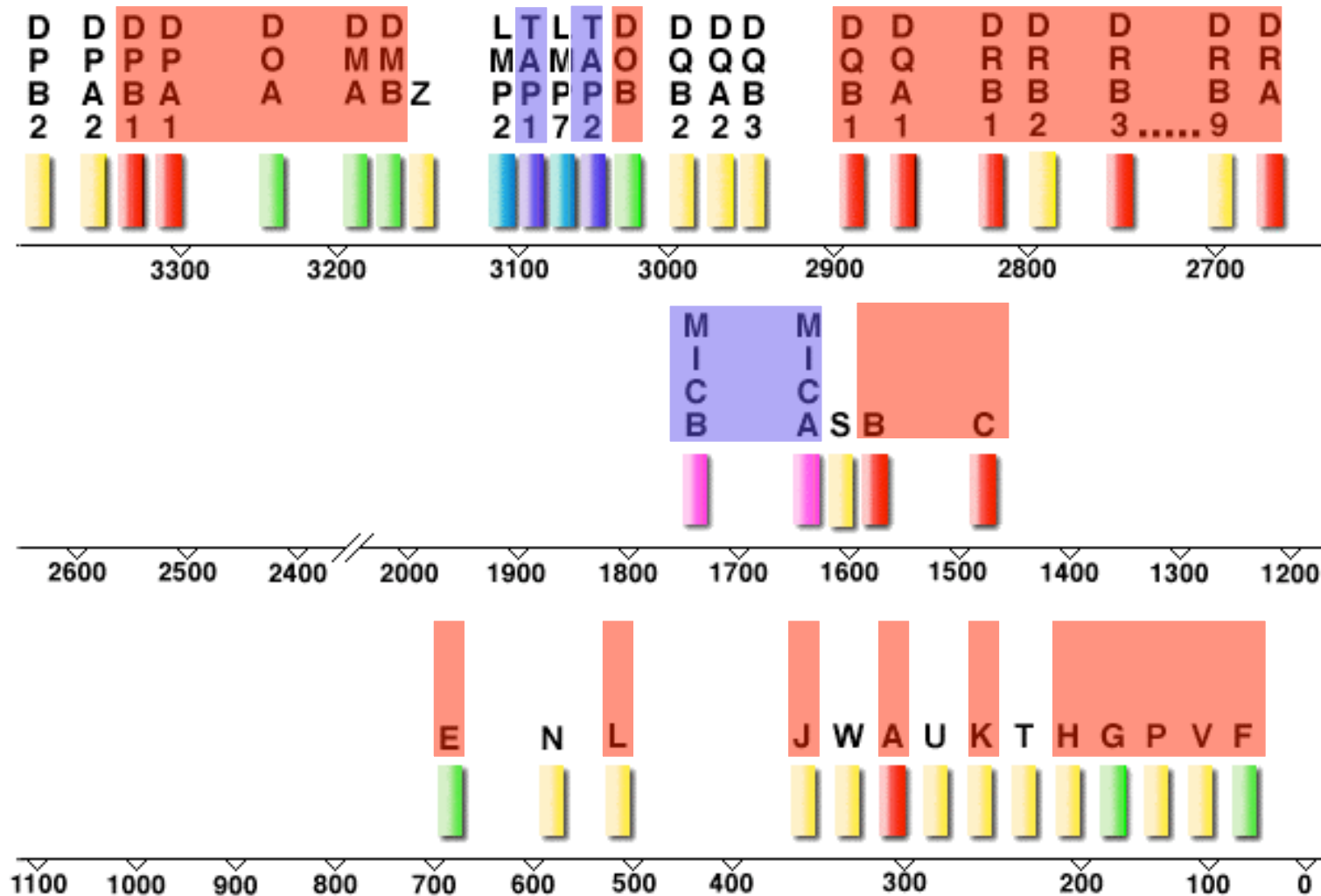


- HLA genes are highly polymorphic
- Allele sequence differ by as little as a single nucleotide
- Functional variants defined by polymorphisms within exon, intron and promoter sequences
- Early sequence publications contained many errors
- Important for accurate reagent design - primers, probes or sequence-based typing strategies
- Over 11,000,000 prospective haematopoietic stem cell donors have been HLA typed

Map of the HLA region



Map of the HLA region



Genes included in the IMGT/HLA Database

■ [IMGT/HLA Home](#)■ [Access](#)[Alignments](#)[Alleles](#)[Ambiguous Typings](#)[BLAST Searches](#)[Cells](#)[FTP Directory](#)[HLA Dictionary](#)[More Tools](#)[Search](#)[Determinants](#)[Statistics](#)■ [FAQ](#)■ [Links](#)■ [Publications](#)■ [Nomenclature](#)■ [Release Information](#)■ [Submissions](#)

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IMGT/HLA Database

Release 2.17.0, 12 April 2007

The IMGT/HLA Database provides a specialist databases for sequences of the human major histocompatibility complex (HLA) and includes the official sequences for the WHO Nomenclature Committee For Factors of the HLA System. The IMGT/HLA Database is part of the international ImMunoGeneTics project ([IMGT](#)).



- [Introduction to the IMGT/HLA Database](#)
- [Database Statistics](#)
- [Publications and citing the database](#)
- [What's new in the latest release](#)

Latest Developments

- [Allele Ethnicity Tool](#)
- [Representation of Splice Site Variants](#)
- [What does the 'Q' mean? - Suffixes in the HLA Nomenclature](#)
- [Registry Search Determinants](#)
- [Other recent updates to the site](#)

For more information about the database, queries (including website) or to subscribe to the IMGT/HLA mailing list please contact [IMGT/HLA Support](#).

The IMGT/HLA Database is sponsored by the institutes and companies shown. For more details please see the [funding page](#).

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Related Links

IPD - The Immuno Polymorphism Database provides specialist databases for the study of polymorphism in genes of the immune system. [more](#)

EBI > Databases > Nucleotide Databases > IMGT/HLA

IMGT/HLA Database

Sequence Alignment Tool

The latest version of the alignment tool now includes genomic sequences as well alignments of commonly sequenced regions. Where discrepancies have arisen between reported sequences and those stored in the database, the original authors have been contacted where possible, and necessary amendments to published sequences have been incorporated into this alignment. Future sequencing may identify errors in this list and the WHO Nomenclature Committee would welcome any evidence that helps to maintain the accuracy of these sequence alignments.

IMGT/HLA Alignment Tool		
Select Locus :	<input type="text" value="A"/>	Help
Select the feature to align :	<input type="text" value="Nucleotide - CDS"/>	Help
Enter any specific sequences required :	<input type="text"/>	Help
Enter the reference sequence :	<input type="text" value="01010101"/>	Help
Select how you wish to view any mismatches :	<input type="text" value="Show mismatches between sequences"/>	Help
Select how the alignment will be numbered :	<input type="text" value="In Codons - nucleotide sequence displayed in codons"/>	Help
Omit alleles unsequenced for this region :	<input type="text" value="Show all alleles"/>	Help
Select type of output :	<input type="text" value="Plain text, ideal for cut & paste"/>	Help
Proceed with the alignment :	<input type="button" value="Align Sequences Now"/> <input type="button" value="Reset Form"/>	

Help with the Sequence Alignment Tool

- Genomic alignments can contain over 1.5 million bases if all sequences are selected and displaying this many characters is time consuming, please be patient. Where possible select only the sequences needed, this will reduce time and make the alignments easier to view.
- Specific Sequences are optional, to align specific sequences either enter the common nomenclature or list the allele names separated by a comma. Do not include the locus in the name.
- Specific sequences cannot be selected in multi-locus alignments like DRB1,3,4,5, DRB2,6,7,8,9 and DRB1-9.
- The default reference sequence for all genes is automatically provided. An alternative reference sequence may be defined by entering the numerical part of the allele name into the text box. The full numerical code is required, so for A*01010101, this would be 01010101 and not 0101.
- Splice site variations have previously not been marked for alternatively spliced alleles like A*0111N,



IMGT/HLA Database

Sequence Alignments based on Release 2.17.0 (12-April-2007)

To Change The Font Size

- In Firefox, Internet Explorer and Netscape hold 'Ctrl' and press '+' or '-' to change the size of the text. [Further instructions](#) are available for Internet Explorer.
- In Safari users need to hold the 'Apple' key and press '+' or '-' in order to change the size of the text.
- In Opera press '+' or '-' to change the size of the text.

```

                                     -20          -15          -10          -5          1
A* 01010101    ATG GCC GTC ATG GCG CCC CGA ACC CTC CTC CTG CTA CTC TCG GGG GCC CTG GCC CTG ACC CAG ACC TGG GCG G|GC
A* 02010101    --- --- --- --- --- --- --- --- --- G-- --- --- --- --- --- --- --- --- --- --- --- |---
A* 03010101    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- |---
A* 24020101    --- --- --- --- --- --- --- --- --- G-- --- --- --- --- --- --- --- --- --- --- --- |---
A* 250101      --- --- --- --- --- --- --- --- --- G-- --- --- --- --- --- --- --- --- --- --- --- |---
A* 250102      *** *** *** *** *** *** *** *** *** *** *** *** *** *** *** *** *** *** *** *** *** *** *|---
A* 260101      --- --- --- --- --- --- --- --- --- G-- --- --- --- --- --- --- --- --- --- --- --- |---
A* 29010101    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- |---
A* 29010102N   --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- |---
A* 300101      --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- |---
A* 300102      --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- |---

                                     5          10          15          20          25
A* 01010101    TCC CAC TCC ATG AGG TAT TTC TTC ACA TCC GTG TCC CGG CCC GGC CGC GGG GAG CCC CGC TTC ATC GCC GTG GGC
A* 02010101    --T --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- |---
A* 03010101    --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- --- |---
A* 24020101    --- --- --- --- --- --- --- --- --- -C- --- --- --- --- --- --- --- --- --- --- --- |---
A* 250101      --- --- --- --- --- --- --- --- --- -A- --C --- --- --- --- --- --- --- --- --- --- --- |---
A* 250102      --- --- --- --- --- --- --- --- --- -A- --C --- --- --- --- --- --- --- --- --- --- --- |---
A* 260101      --- --- --- --- --- --- --- --- --- -A- --C --- --- --- --- --- --- --- --- --- --- --- |---
A* 29010101    --- --- --- --- --- --- --- --- --- AC- --- --- --- --- --- --- --- --- --- --- --- |---
A* 29010102N   --- --- --- --- --- --- --- --- --- AC- --- --- --- --- --- --- --- --- --- --- --- |---
A* 300101      --- --- --- --- --- --- --- --- --- -C- --- --- --- --- --- --- --- --- --- --- --- |---
A* 300102      --- --- --- --- --- --- --- --- --- -C- --- --- --- --- --- --- --- --- --- --- --- |---

```

IMGT/HLA Database

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- In Opera press '+' or '-' to change the size of the text.

```

                -291      -281      -271      -261      -251      -241      -231      -221      -211      -201
A* 01010101  CAGGAGCAGA GGGGTCAGGG CGAAGTCCCA GGGCCCCAGG CGTGGCTCTC AGGGTCTCAG GCCCCGAAGG CCGTGTATGG ATTGGGGAGT CCCAGCCTTG
A* 02010101  ---A-----
A* 03010101  -----
A* 24020101  ---A-----
A* 260101    -----
A* 29010101  -----

                -191      -181      -171      -161      -151      -141      -131      -121      -111      -101
A* 01010101  GGGATPCCCC AACTCCGCAG TTTCPTTCTT CCCTCTCCCA ACCTACGTAG GGTCTTCAT  CCTGGATACT CACGACGCGG ACCCAGTCTT CACTCCCATT
A* 02010101  -----
A* 03010101  -----
A* 24020101  -----
A* 260101    -----
A* 29010101  -----G-----T-----T-----

                -91       -81       -71       -61       -51       -41       -31       -21       -11       -1
A* 01010101  GGGTGTCCGG TTTCAGAGAG AGCCAATCAG TGTCGTCGCG GTCGCTGTTT TAAAGTCCGC ACGCACCCAC CGGGACTCAG ATTCTCCCA  GACGCCGAGG
A* 02010101  -----
A* 03010101  -----
A* 24020101  -----
A* 260101    -----
A* 29010101  -----G-----

                10       20       30       40       50       60       70       80       90      100
A* 01010101  |ATGGCCGTC TGGCGCCCG AACCTCCTC CTGCTACTCT CGGGGCCCTT GGCCTGACC CAGACCTGGG CGG|GTGAGTG CGGGTCCGG AGGGAACCG
A* 02010101  |-----G-----T-----G-----
A* 03010101  |-----
A* 24020101  |-----G-----A-----G-----
A* 260101    |-----G-----
A* 29010101  |-----T-----T-----

```



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IMGT/HLA Database

Sequence Alignments based on Release 2.17.0 (12-April-2007)

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- In Opera press '+' or '-' to change the size of the text.

	10	20	30	40	50	60	70	80	90	100
A* 01010101	GSHSMRYFFT	SVSRPGRGEP	RFIAVGVYDD	TQFVRFDSDA	ASQKMEPRAP	WIEQEGPEYW	DQETRNMKAH	SQTPDRANLGT	LRGYYNQSED	GSHTIQIMYG
A* 02010101	-----	-----	-----	-----	---R---	-----	-G---KV---	---H-VD---	-----A	----V-R---
A* 03010101	-----	-----	-----	-----	---R---	-----	-----V-Q	-----VD---	-----A	-----
A* 24020101	-----S-	-----	-----	-----	---R---	-----	-E--GKV---	---E--RI	ALR-----A	----L-M-F-
A* 250101	-----Y-	-----	-----	-----	---R---	-----	---RN---V---	---ES-RI	ALR-----	-----R---
A* 250102	*-----Y-	-----	-----	-----	---R---	-----	---RN---V---	---ES-RI	ALR-----	-----R---
A* 260101	-----Y-	-----	-----	-----	---R---	-----	---RN---V---	-----	-----	-----R---
A* 29010101	-----T-	-----	-----	-----	---R---	-----	-LQ---V-Q	-----	-----A	----M---
A* 300101	-----S-	-----S-	-----	-----	---R---	---R---	-----V-Q	---VD---	-----A	-----
A* 300102	-----S-	-----S-	-----	-----	---R---	---R---	-----V-Q	---VD---	-----A	-----
	110	120	130	140	150	160	170	180	190	200
A* 01010101	CDVGPDGRFL	RGYRQDAYDG	KDYIALNEDL	RSWTAADMAA	QITKRKWEAV	HAAEQRRVYL	EGRCVDGLRR	YLENGKETLQ	RTDPPKTHMT	HHPIDSHHEAT
A* 02010101	---S-W---	---H-Y---	---K---	-----	-T--H---A	-V---L-A-	--T--EW---	-----	---A---	--AV-----
A* 03010101	---S---	-----	-----	-----	-----A	-E---L-A-	D-T--EW---	-----	-----	-----
A* 24020101	---S---	---H-Y---	---K---	-----	-----A	-V---Q-A-	--T--EW---	-----	-----	-----
A* 250101	-----	---Q---	-----	-----	---Q---TA	-E---W-A-	---EW---	-----	---A---	--AV-----
A* 250102	-----	---Q---	-----	-----	---Q---TA	-E---W-A-	---EW---	-----	*****	*****
A* 260101	-----	---Q---	-----	-----	---Q---TA	-E---W-A-	---EW---	-----	---A---	--AV-----
A* 29010101	-H--S---	-----	-----	-----	---Q---A	RV---L-A-	--T--EW---	-----	---A---	--AV-----
A* 300101	---S---	---E-H---	-----	-----	---Q---A	RW---L-A-	--T--EW---	-----	-----	-----
A* 300102	---S---	---E-H---	-----	-----	---Q---A	RW---L-A-	--T--EW---	-----	-----	-----
	210	220	230	240	250	260	270	280	290	300
A* 01010101	LRCWALGFYP	AEITLTWQRD	GEDQTQDTEL	VETRPAGDGT	FOKWAAVVVP	SGEEQRYTCH	VQHEGLPKPL	TLRWELSSQP	TPIVGGIAG	LVLGAVITG
A* 02010101	-----S---	-----	-----	-----	-----	---Q---	-----	---P---	-----	---F-----
A* 03010101	-----	-----	-----	-----	-----	-----	-----	-----	-----	-----
A* 24020101	-----	-----	-----	-----	-----	-----	-----	---P---	---V---	-----
A* 250101	-----S---	-----	-----	-----	---S---	---Q---	-----	---P---	-----	---F---A-

HLA Nomenclature Requirements



The nomenclature system needs:

- To be expandable
- To encode relatedness
- To encode ambiguity
- To be usable

Level of resolution



Low level of resolution A*02

Medium level A*0201/0205/0209/0240

High level A*02010101

Ambiguity



Using medium level resolution typing it is possible to exclude some but not all alleles from a group, hence the National Marrow Donor Program (NMDP) codes.

B*1501 or B*1502 = B*15AB

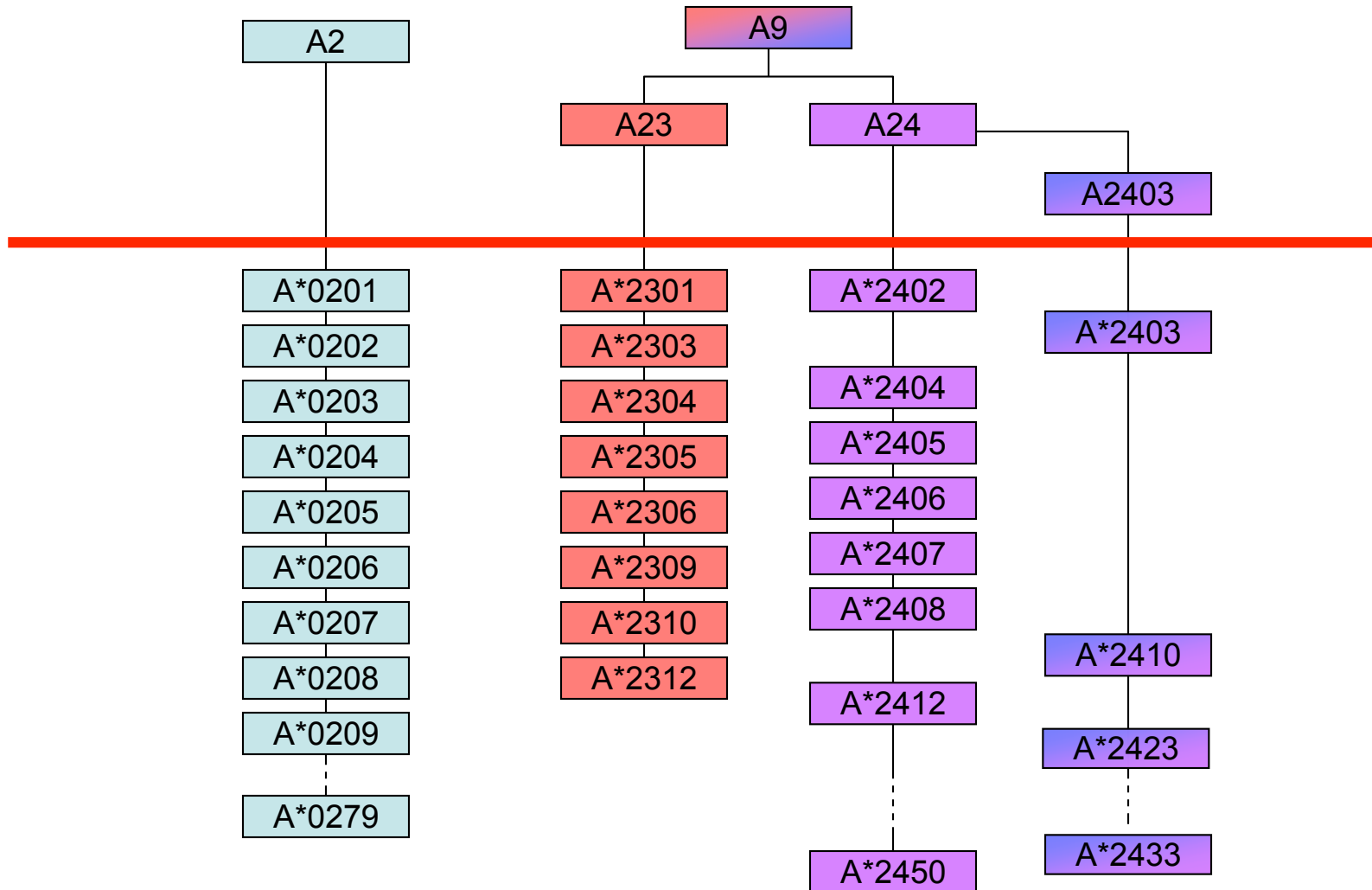
B*1501/1502/1505/1515/1521/1545/1556/1570 = B*15FGR

HLA Nomenclature

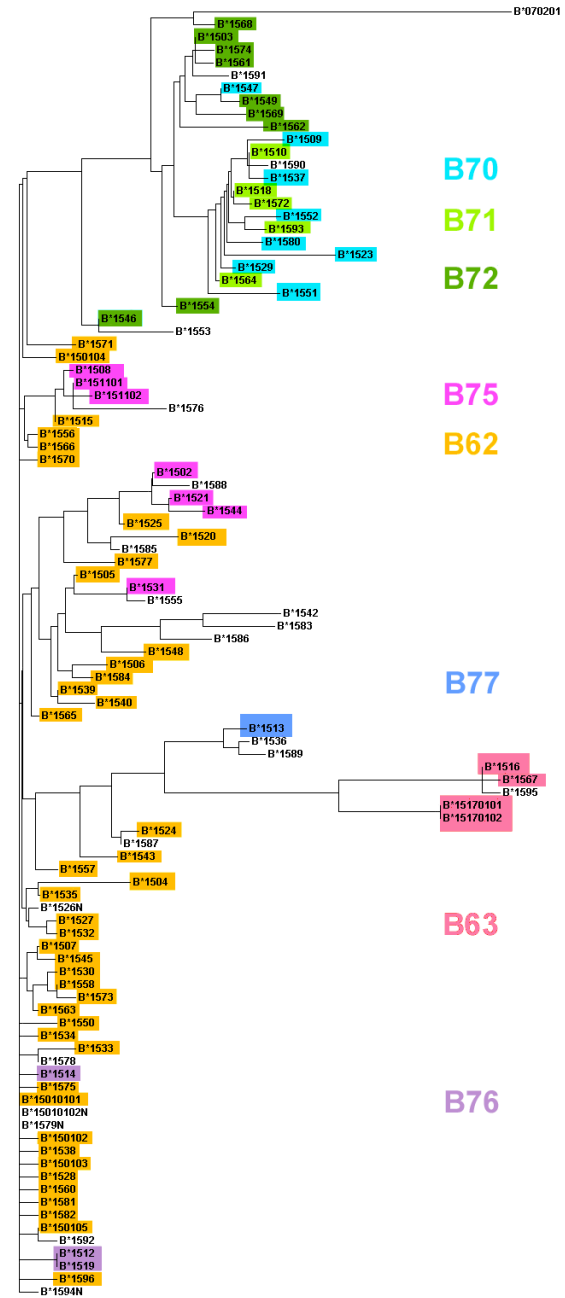


- Gene names
HLA-A or HLA-DRB1
- Antigen names
A2 or DR1
- Allele names
A*020101 or DRB1*01010101

Alleles versus Serology - ideal



B*15 Reality





- Samples typed historically used serology or cellular methods for class II.
- Samples typed in DNA era: low, intermediate, high resolution.
- Different HLA loci in a given sample may be typed using different technology and at different resolution:

HLA-A*0101, 03; B*07, 1501; DRB1*0301, 1501

HLA-A1, 3; B7, 62(15); DRB1*0301, 1501



Not all alleles have been defined by serology



HLA-A*2402-2436

Most type by serology
as A24(9)

HLA-A*2436-2466

Exact serological
equivalent or typing
pattern is unknown

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IPD - The Immuno Polymorphism Database provides specialist databases for the study of polymorphism in genes of the immune system.

[more](#)



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IMGT/HLA Database

The HLA Dictionary 2004

The IMGT/HLA Database allows you to retrieve information from the HLA Dictionary.

- Schreuder GMTh, Hurley CK, Marsh SGE, Lau M, Fernandez-Vina MA, Noreen HJ, Setterholm M, Maier M:
The HLA Dictionary 2004: a summary of HLA-A, -B, -C, -DRB1/3/4/5, -DQB1 alleles and their association with serologically defined HLA-A, -B, -C, -DR and -DQ antigens
Tissue Antigens (2005) 65:1-55
Human Immunology (2005) 66:170-210
International Journal of Immunogenetics (2005) 32:19-69

The [Full Text](#)  of the Tissue Antigens article is available from Blackwell Synergy or you can download the [PDF File](#). 

This dictionary presents the serological equivalents of HLA-A, -B, -C, -DRB1, -DRB3, -DRB4, -DRB5 and -DQB1 alleles and is an update of the one published in 2001. The data summarises equivalents obtained by the WHO Nomenclature Committee for Factors of the HLA System, the International Cell Exchange (UCLA), the National Marrow Donor Program (NMDP), the 13th International Histocompatibility Workshop, recent publications and individual laboratories.

How To Search the Dictionary

The search tool can be used to search for an allele, an expert assigned type of a WHO assigned type.

- To search for an entry for an allele name enter either the locus or the locus and up to four digits. (i.e.: A, A*01, A*0101)
- To search for an expert or WHO assigned type enter the serological type (i.e. A1, A2, A32), broad classifications will automatically be expanded (i.e. A28 will retrieve A68 and A69).

The search tool will then retrieve all relevant hits.

HLA Dictionary Search Tool

Search for:	<input type="text" value="HLA Allele"/>	<input type="button" value="Search the HLA Dictionary"/>
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For a further explanation of the output form, [click here](#).

Information

Useful Web sites

Anthony Nolan Trust

For HLA Nomenclature Information

www.anthonynolan.org.uk/hig/

IMGT/HLA Sequence Database

For HLA Sequences

www.ebi.ac.uk/imgt/hla