

mAb specificity and immunogenicity: what do we learn from IMGT Collier de Perles?

<http://www.imgt.org>

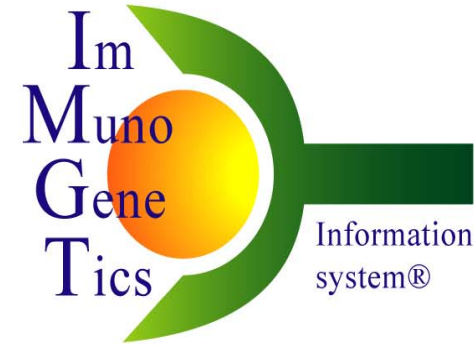
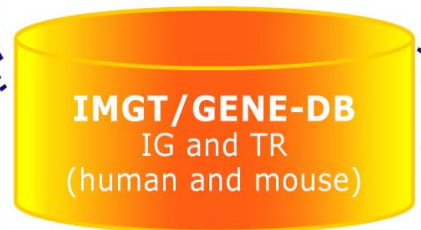
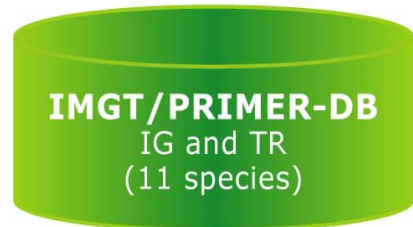
Marie-Paule Lefranc

IMGT Founder and Director

Professor University Montpellier 2, CNRS, Montpellier, France

Advances in Antibody and Peptide Therapeutics
Berlin, Germany, June 8-9, 2010

Sequences



<http://www.imgt.org>
created in 1989

Genome

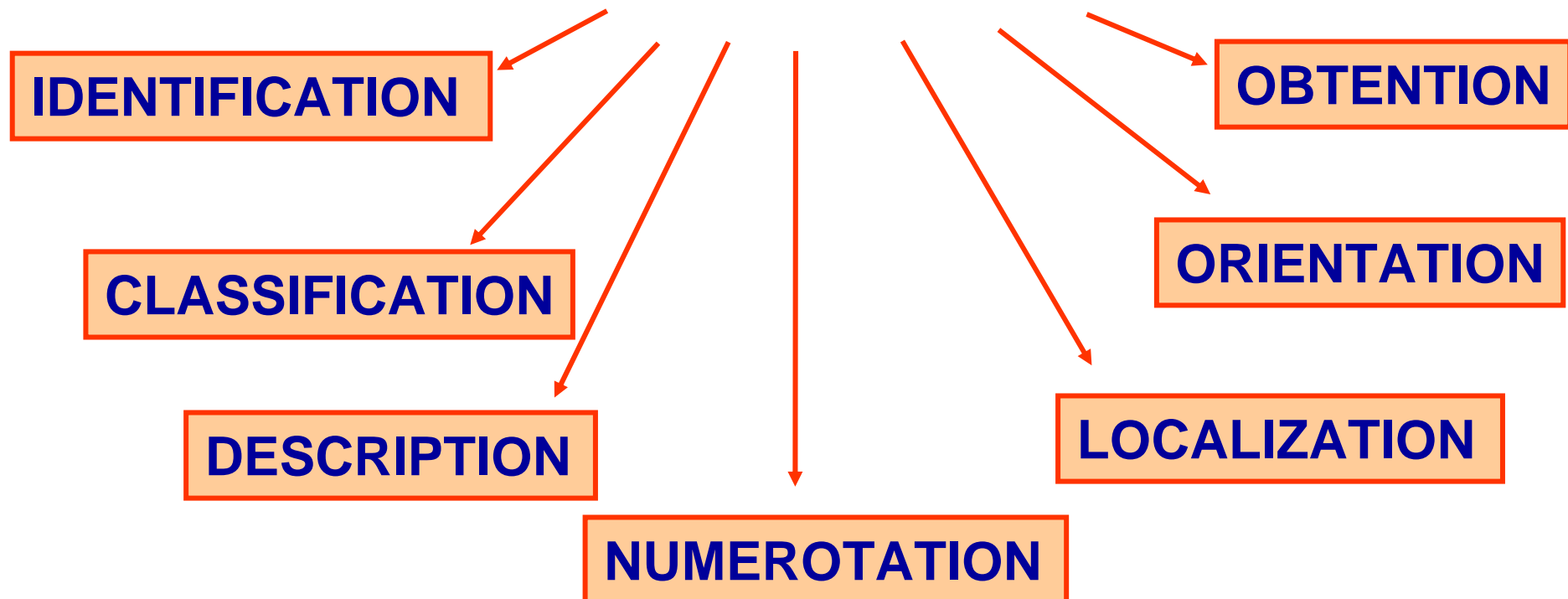


2D and 3D structures

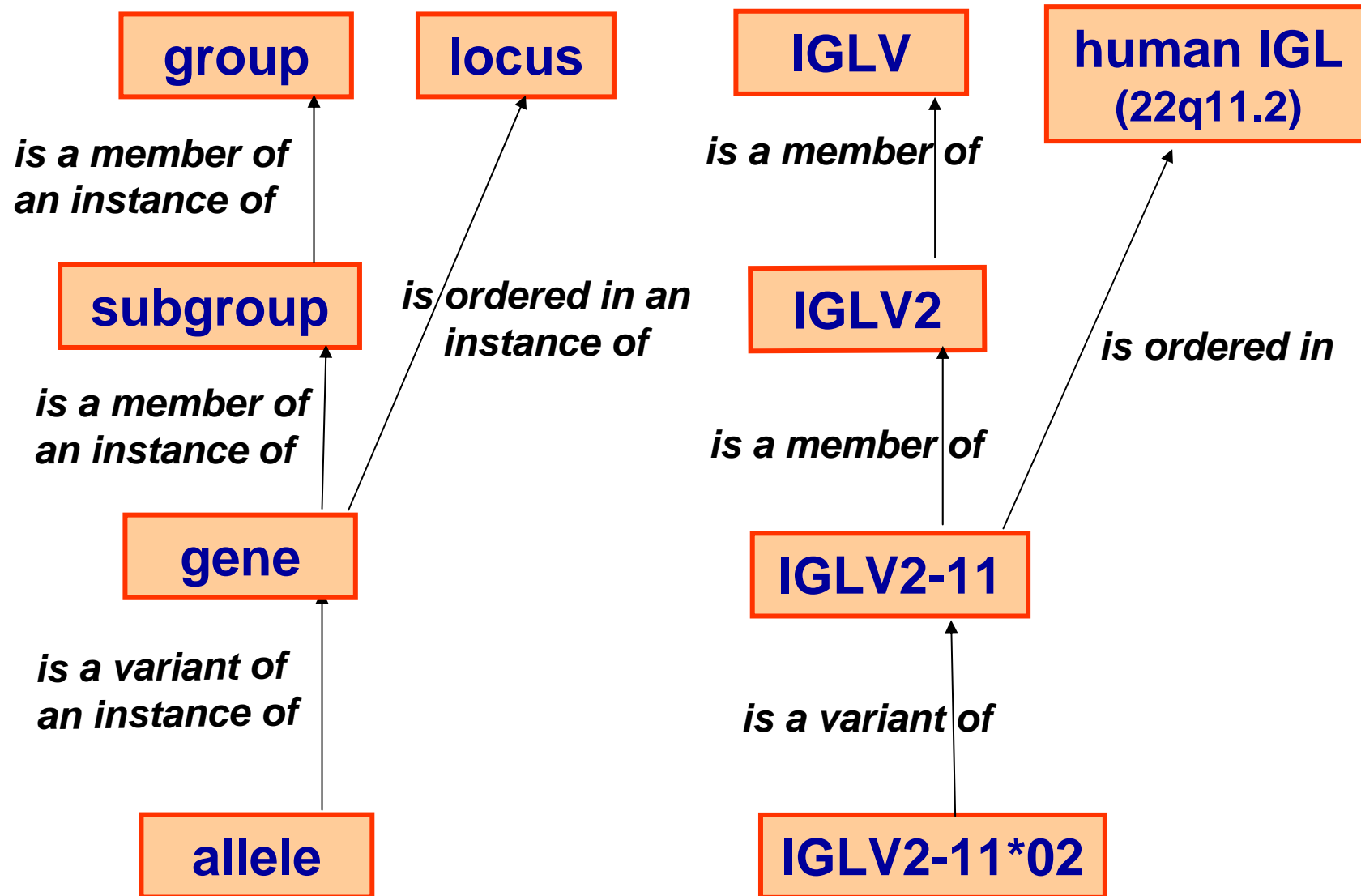
IMGT standards based on IMGT-ONTOLOGY

IMGT-ONTOLOGY seven axioms:

To share, reuse and represent knowledge
in Immunogenetics and Life Sciences



CLASSIFICATION axiom



« Concepts »

« Instances »

Concepts of CLASSIFICATION



<http://www.imgt.org>

1. The IMGT-ONTOLOGY main concepts of classification
 - include 'group', 'subgroup', 'gene', 'allele'.
 - have allowed to set up the **nomenclature** of the immunoglobulin (IG) and T cell receptor (TR) genes (V, D, J, C genes).
2. **IMGT gene names** have been approved by the **HUGO Nomenclature Committee (HGNC)** in 1999.
3. **New alleles** are validated by the **WHO-IUIS/IMGT nomenclature committee** and entered in **IMGT/GENE-DB**.
4. **IMGT/GENE-DB** is the **international reference database** for IG and TR genes (**direct links from NCBI Entrez Gene**) and alleles.

Concepts of CLASSIFICATION

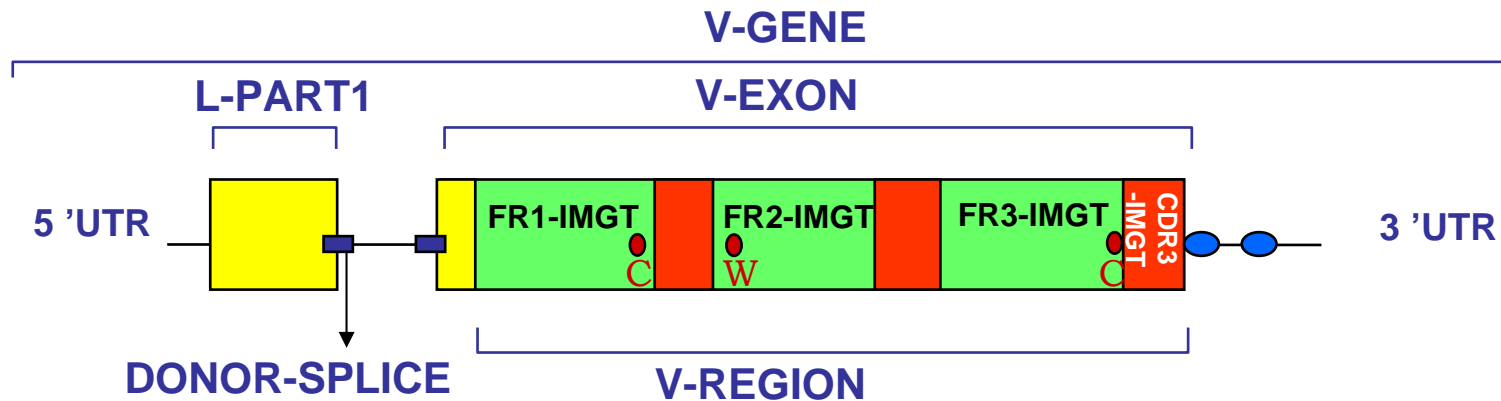


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DESCRIPTION axiom

PROTOTYPE for a V-GENE



Label 1

Label 2

Relations entre Labels

V-GENE

V-EXON



FR3-IMGT

CDR3-IMGT



L-PART1

DONOR-SPLICE



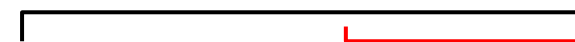
V-REGION

FR1-IMGT



V-REGION

CDR3-IMGT



Concepts of DESCRIPTION



<http://www.imgt.org>

1. The IMGT-ONTOLOGY concepts of description:
 - comprise the **standardized IMGT labels** and their **relations**.
 - have allowed **to describe** the IG (or antibody) and TR sequences and structures, **whatever the receptor type, the chain type or the species**.
2. **IMGT labels** are used in all IMGT® databases and tools for the description of:
 - **nucleotide and amino acid sequences (IMGT/LIGM-DB...)**
 - **2D and 3D structures (IMGT/3Dstructure-DB...)**.
3. Sequence Ontology (**SO**) includes **IMGT labels**.
4. **IMGT® databases** can be queried **using labels** (a big 'plus' compared to generalist databases).

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DESCRIPTION

```

IMGT/LIGM-DB Consultation module v3 - Mozilla Firefox
File Edit View Go Bookmarks Tools Help
FH Key Location/Qualifiers
FH
FT L-V-D-J-C-SEQUENCE <1..375>
FT /partial
FT /db_xref="taxon:9606"
FT /cell_type="B-cell hybridoma 2F7"
FT /IMGT_note="automatically annotated with IMGT tools"
FT /organism="Homo sapiens"
FT V-D-J-REGION 1..375
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FT AKGLEWVAVIWIYDGSNKYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC
FT AKHVTIAAAGRAGMDVWGQGT TTVTVSS"
FT V-REGION 1..296
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FT /gene="IGHV3-33"
FT /CDR_length="[8.8.18]"
FT /putative_limit="3' side"
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FT AKGLEWVAVIWIYDGSNKYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC
FT AK"
FT FR1-IMGT 1..75
FT /AA_IMGT="1 to 26, AA 10 is missing"
FT /translation="QVHLVESGGAVFHPGRSLRLSRAAS"
FT CDR1-IMGT 76..99
FT /AA_IMGT="27 to 34"
FT /translation="GFTFSSYG"
FT FR2-IMGT 100..150
FT /AA_IMGT="39 to 55"
FT /translation="MHWVRQAPAKGLEWVAV"
FT CONSERVED-TRP 106..108
FT CDR2-IMGT 151..174
FT /AA_IMGT="56 to 63"
FT /translation="IWIYDGSNK"
FT FR3-IMGT 175..288
FT /AA_IMGT="66 to 104, AA 73 is missing"
FT /translation="YYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYC"
Done
    
```

145 795 sequences from 251 species

IMGT-ONTOLOGY:

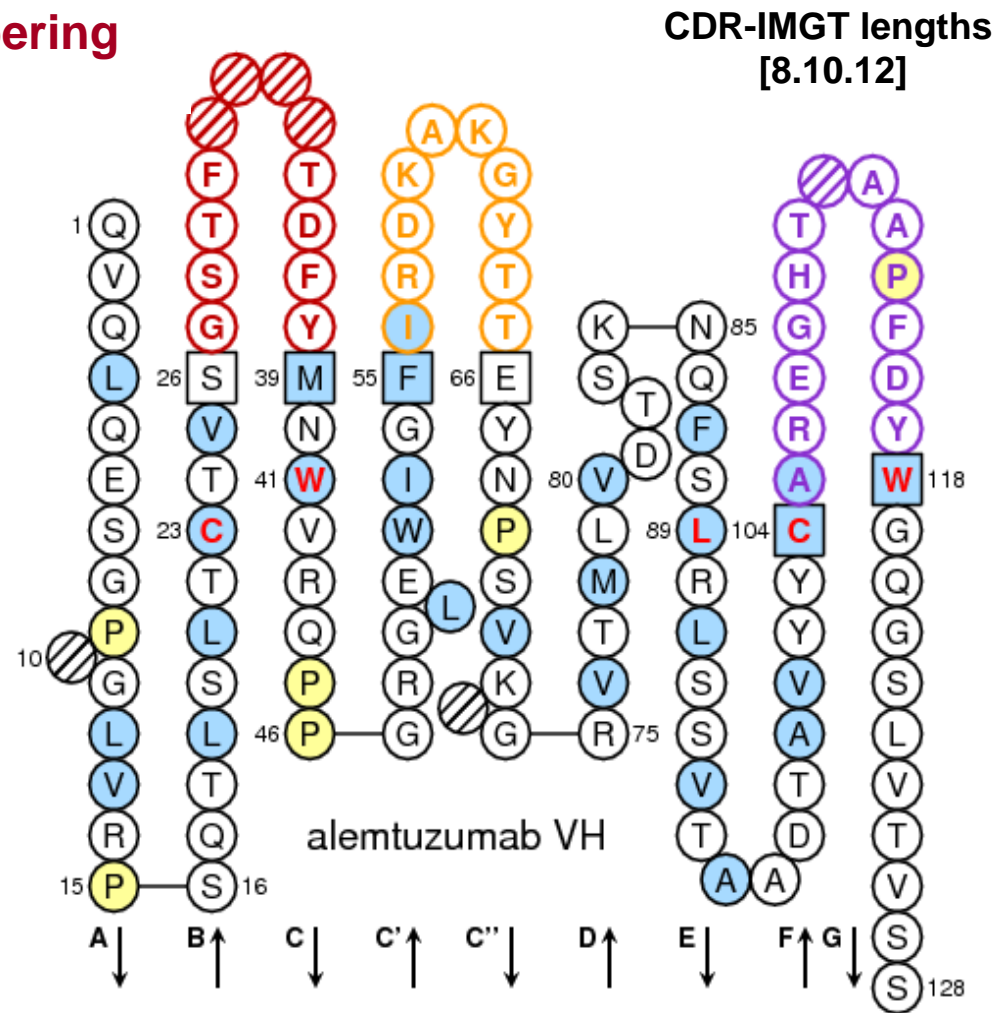
277 IMGT labels for sequences

285 IMGT labels for 3D structures

NUMEROTATION axiom

IMGT Collier de Perles

Based on the **IMGT unique numbering**
(first one in **1997**)



NUMEROTATION axiom

IMGT Collier de Perles

Based on the **IMGT unique numbering**
(first one in **1997**)

- conserved AA (and codons)
are always at the **same positions**:

23 1st-CYS

41 CONSERVED-TRP

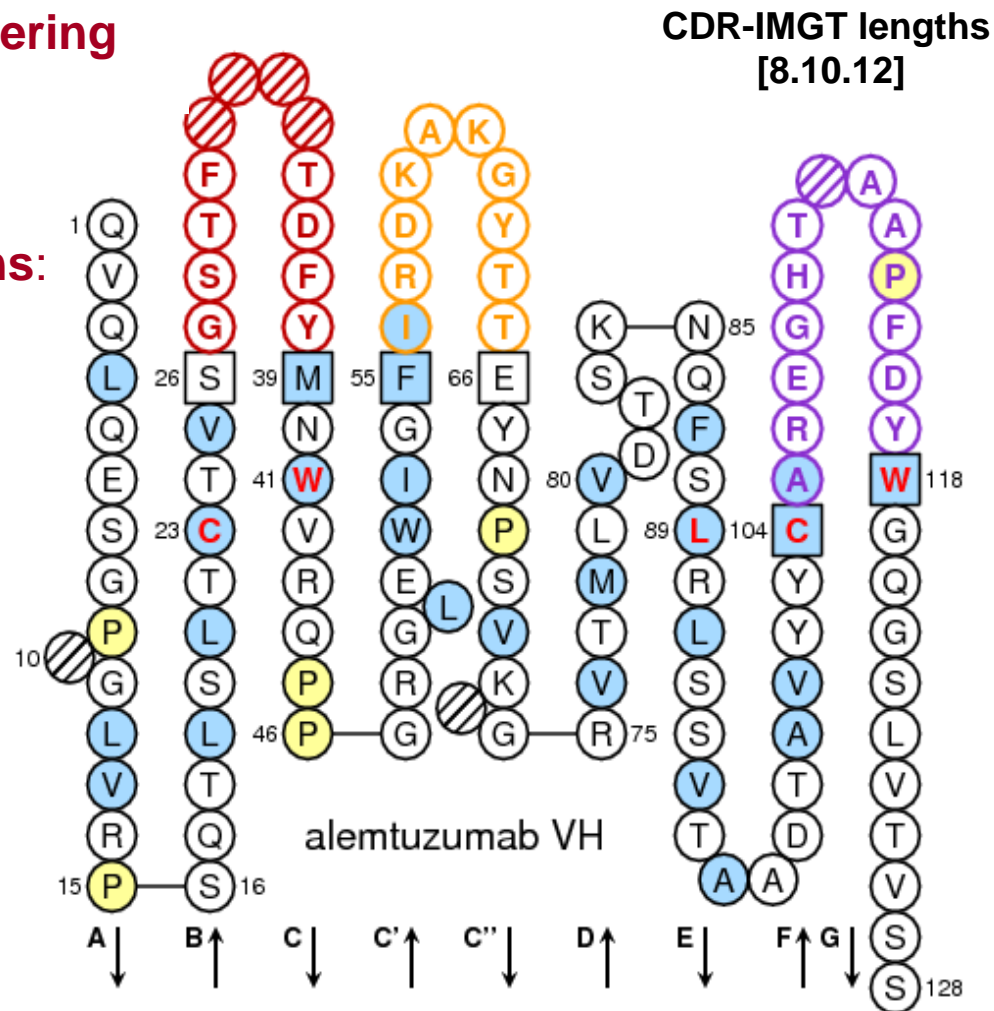
89 hydrophobic

104 2nd-CYS

118 J-PHE, J-TRP

- delimitation of the **FR-IMGT**
and **CDR-IMGT** is standardized

- **CDR-IMGT lengths** are crucial
information



Concepts of NUMEROTATION



<http://www.imgt.org>

1. The IMGT-ONTOLOGY concepts of numerotation include:
 - IMGT unique numbering
 - IMGT Collier de Perles.
2. The concepts bridge the gap between sequences and 3D structures, at the amino acid (and codon) level, for:
 - the variable domains (V-DOMAIN)
 - the constant domains (C-DOMAIN).
4. The concepts are used for:
 - mutations, polymorphisms
 - CDR-IMGT lengths
 - contact analysis, paratope definition.
5. WHO-INN programme requires the CDR-IMGT lengths for antibody.

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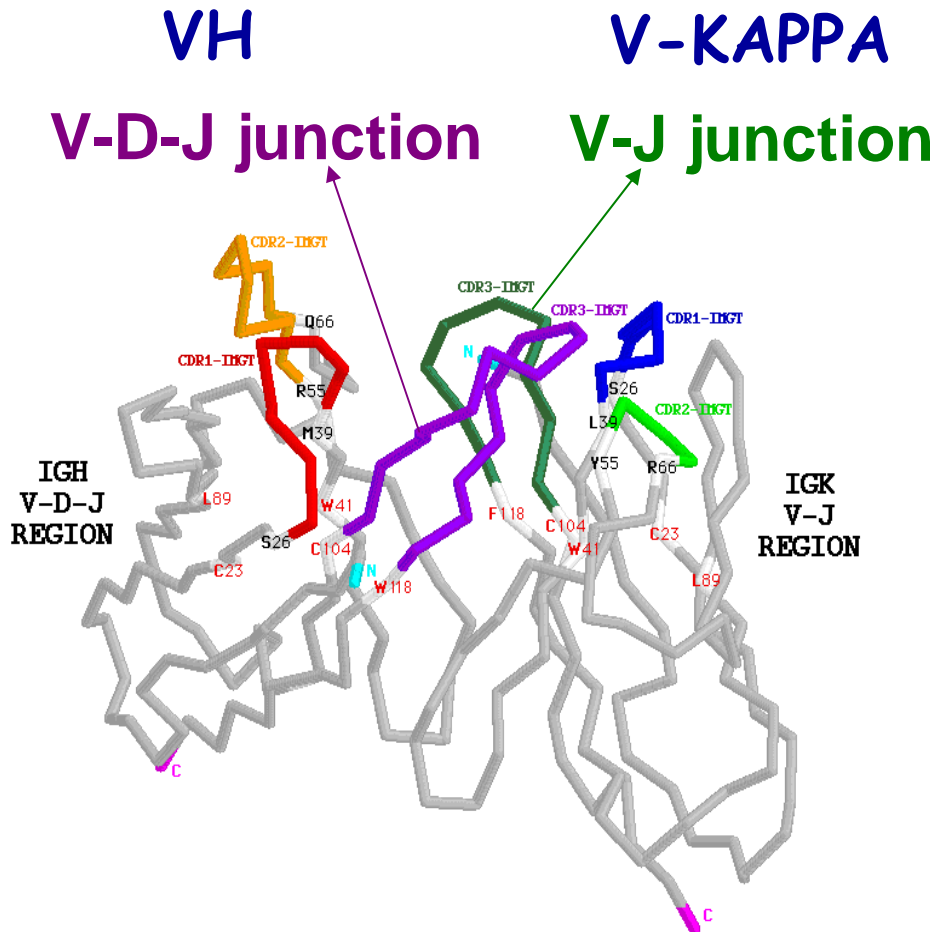
- the variable domains (V-DOMAIN)
- the constant domains (C-DOMAIN).

4. The concepts are used for:

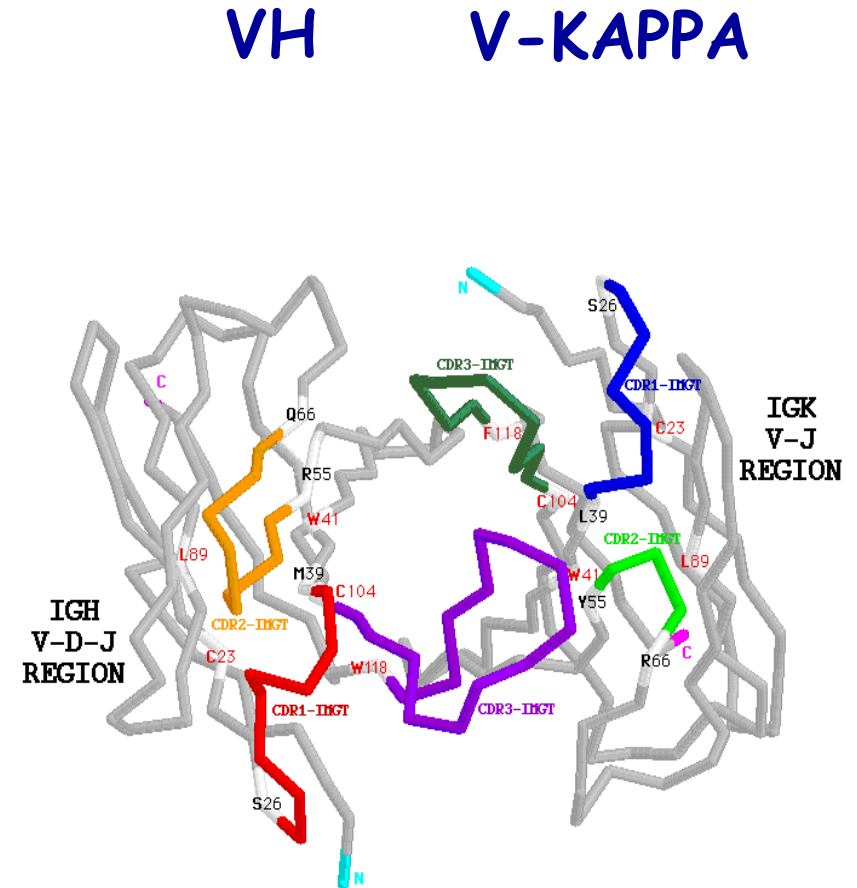
- Mutations, polymorphisms
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- contact analysis, paratope definition.

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V-DOMAIN: VH and V-KAPPA



Side view of the V-DOMAIN



View from above the CDR-IMGT

CDR: complementarity determining region
 CDR3-IMGT (105-117)
 V-D-J junction (104-118), V-J junction (104-118)

The 11 IMGT physicochemical AA classes

'Volume' classes		'Hydropathy' classes							
	in Å ³	Hydrophobic		Neutral			Hydrophilic		
Very large	189-228	F		W		Y			
Large	162-174	I	L	M			H	K R	
Medium	138-154	V						E Q	
Small	108-117			C	P	T		D N	
Very small	60-90	A			G	S			
		Aliphatic		Sulfur	Hydroxyl		Basic	Acidic	Amide
		Nonpolar			Uncharged	Charged		Uncharged	
					Polar				

IMGT/JunctionAnalysis

Analysis of the IG and TR junctions



<http://www.imgt.org>

JUNCTION alignments with translation and IMGT AA classes

Click on mutated (underlined) amino acid to see the original one:

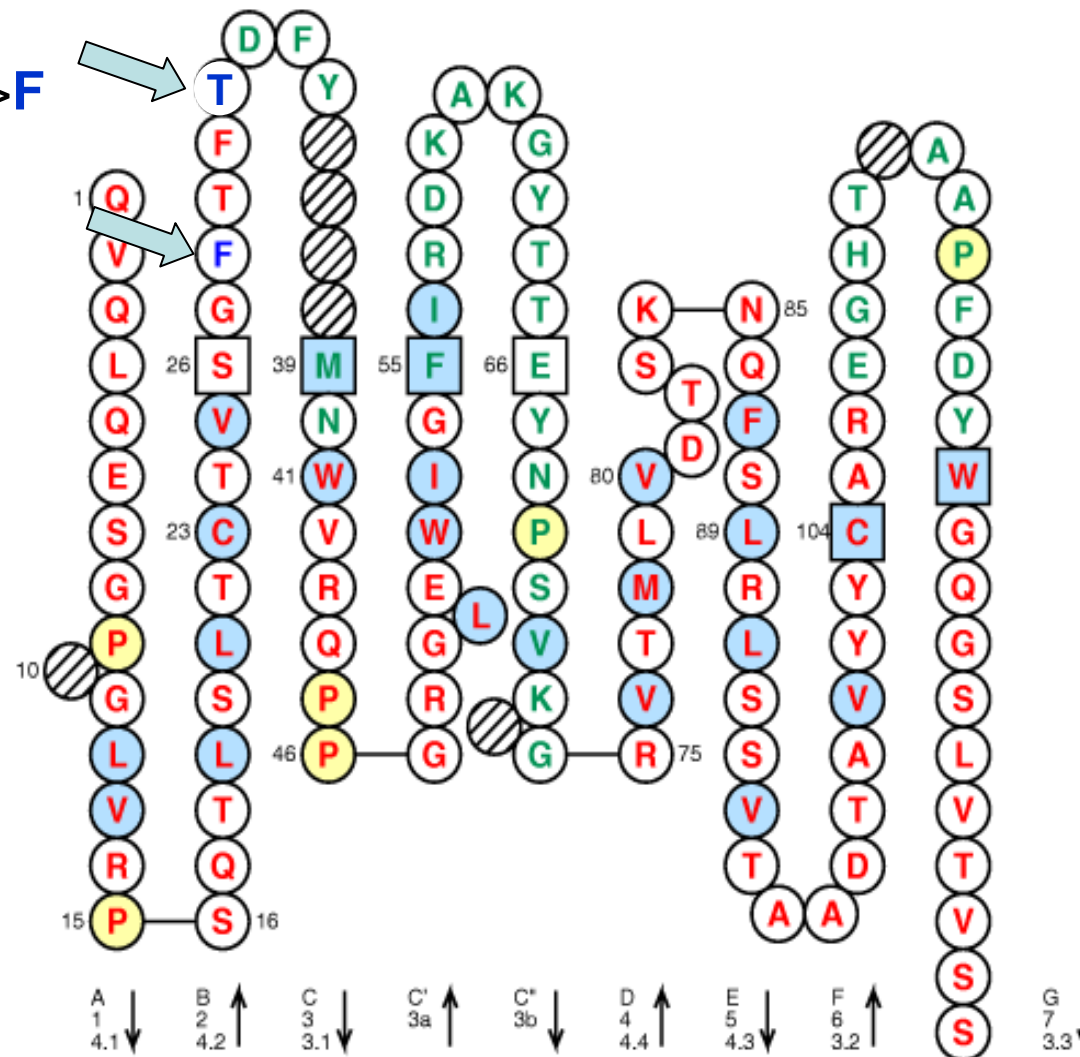
	104	105	106	107	108	109	110	111	111.1	111.2	111.3	112.3	112.2	112.1	112	113	114	115	116	117	118
	C	S	P	G	G	S	<u>A</u>	Y						Y	<u>H</u>	E	<u>H</u>	F	Q	<u>Q</u>	W
#1 AY393054	tgt	agt	ccc	ggg	ggt	agt	gct	tat	tac	<u>cac</u>	gaa	<u>cac</u>	ttc	cag	cag	tgg
	C	<u>V</u>	K	P	T	D	D	D	G				<u>H</u>	R	A	E	Y	F	Q	<u>Y</u>	W
#2 AY393055	tgt	gtg	aaa	ccc	acg	gat	gat	gat	ggc	<u>cac</u>	cgg	gct	gaa	tac	ttc	cag	<u>tac</u>	tgg
	C	S	P	G	G	S	<u>A</u>	Y						Y	<u>H</u>	E	<u>D</u>	F	Q	<u>Q</u>	W
#3 AY393058	tgt	agt	ccc	ggg	ggt	agc	gct	tat	tac	<u>cac</u>	gaa	<u>gac</u>	ttc	cag	cag	tgg
	C	S	P	G	G	S	<u>A</u>	Y						Y	<u>H</u>	E	<u>H</u>	F	Q	<u>Q</u>	W
#4 AY393072	tgt	agt	ccc	ggg	ggt	agt	gct	tat	tac	<u>cac</u>	gaa	<u>cac</u>	ttc	cag	cag	tgg
	C	A	R	Q	N	P	P	E	Y	S	G	A	Y	<u>H</u>	<u>D</u>	G	W	F	D	P	W
#5 AY393088	tgt	gcg	aga	caa	aac	ccc	ccc	gag	tat	agt	ggc	gca	tat	<u>cat</u>	<u>gat</u>	ggg	tgg	ttc	gac	ccc	tgg
	C	A	R	E	M	L	Y	G	S	G	<u>G</u>	Y	Y	P	P	D	A	F	<u>E</u>	<u>L</u>	W
#6 AY393089	tgt	gcg	aga	gag	atg	ctc	tat	ggt	tcg	ggg	<u>ggt</u>	tat	tac	ccc	cct	gat	gca	ttt	gag	<u>ctc</u>	tgg
	C	A	R	Q	N	P	P	E	Y	S	G	A	Y	<u>H</u>	<u>D</u>	G	W	F	D	P	W
#7 AY393091	tgt	gcg	aga	cag	aat	ccc	ccc	gag	tat	agt	ggc	gca	tat	<u>cat</u>	<u>gat</u>	ggg	tgg	ttc	gac	ccc	tgg
	C	A	R	E	M	L	Y	G	S	G	<u>G</u>	Y	Y	P	P	D	A	F	<u>E</u>	V	W
#8 AY393092	tgt	gcg	aga	gag	atg	ctc	tat	ggt	tcg	ggg	<u>ggt</u>	tat	tac	ccc	cct	gat	<u>gca</u>	ttt	gag	gtc	tgg
	C	A	R	Q	N	P	P	E	Y	S	G	A	Y	<u>H</u>	<u>D</u>	G	W	F	D	P	W
#9 AY393094	tgt	gcg	aga	cag	aac	ccc	ccc	gag	tat	agt	ggc	gca	tat	<u>cat</u>	<u>gat</u>	ggg	tgg	ttc	gac	ccc	tgg

Yousfi Monod et al. Bioinformatics 20, i379-385 (2004)
Pommié et al. J. Mol Recognit. 17, 17-32 (2004)

Antibody humanization and engineering

Alemtuzumab (CAMPATH®)

2 mutations:
S31>T, **S28>F**



VH domain
 [8.10.12]

■ human
 ■ rat

Towards «Potential immunogenicity evaluation»



<http://www.imgt.org>

- Comparison with the closest human germline genes and alleles
- Number of different AA in FR-IMGT

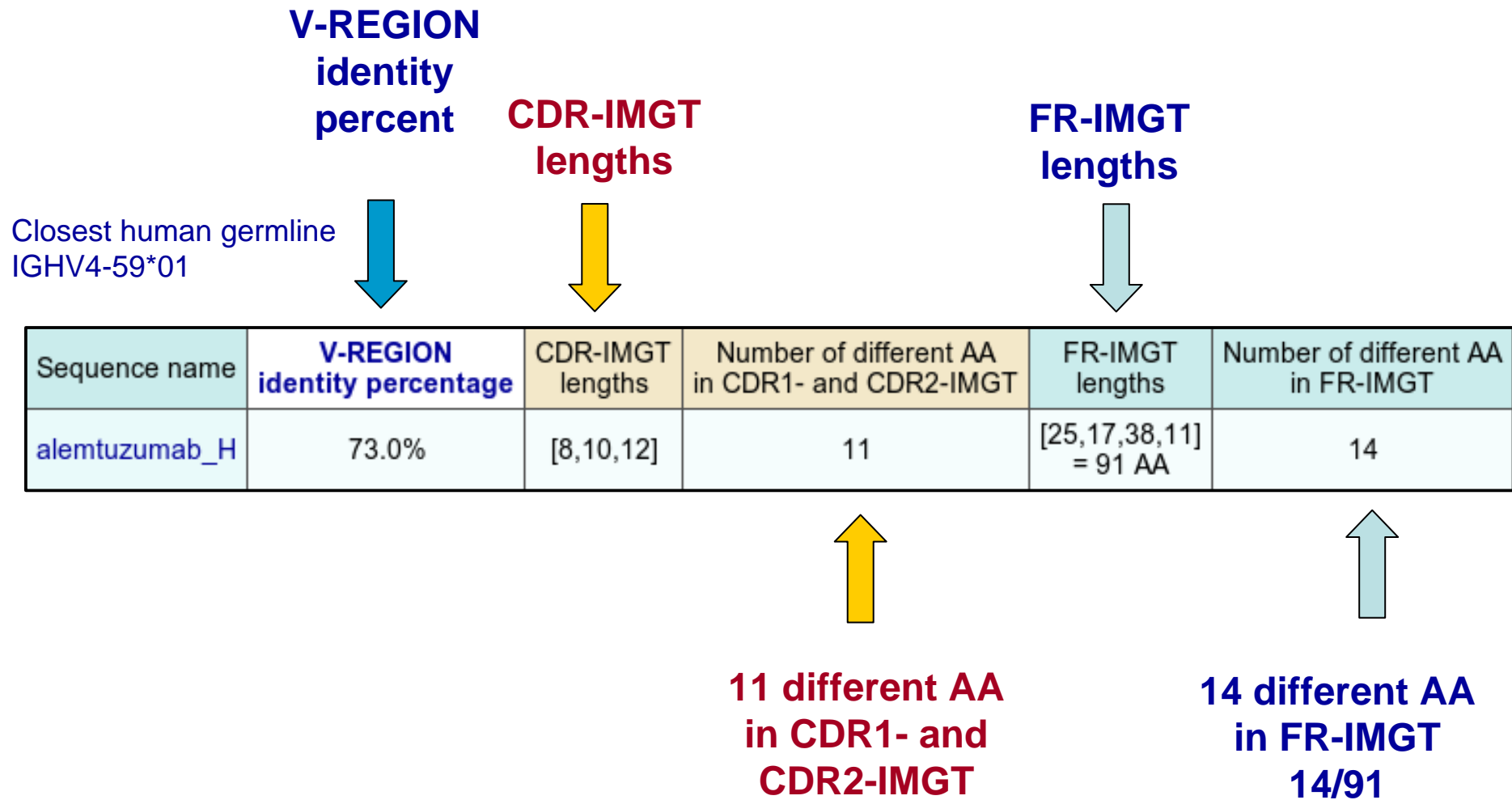
		V-REGION identity percent	FR-IMGT AA differences
VH	alemtuzumab	73 %	14 /91
	bevacizumab	72.40 %	23
	trastuzumab	81.63 %	9
V-KAPPA	alemtuzumab	86.32 %	2 /89
	bevacizumab	87.40 %	7
	trastuzumab	86.32 %	6

IMG/DomainGapAlign



<http://www.imgt.org>

Towards «Potential immunogenicity evaluation»



IMGT/DomainGapAlign



<http://www.imgt.org>

Towards «Potential immunogenicity evaluation»

Characteristics of the AA class changes:

CDR-IMGT	Number of different AA	Different AA with class changes
CDR1-IMGT (27-38)	6	G28>F (- - -) very dissimilar S29>T (+ - +) similar I30>F (+ - -) dissimilar S35>T (+ - +) similar S36>D (- - -) very dissimilar Y37>F (- + -) dissimilar
CDR2-IMGT (56-65)	5	Y57>R (- - -) very dissimilar Y58>D (- - -) very dissimilar S59>K (- - -) very dissimilar G63>Y (+ - -) dissimilar S64>T (+ - +) similar

FR-IMGT	Number of different AA	Different AA with class changes
FR1-IMGT (1-26)	2	K14>R (+ + +) very similar E17>Q (+ + -) similar
FR2-IMGT (39-55)	5	W39>M (+ - -) dissimilar S40>N (- - -) very dissimilar I42>V (+ - +) similar K48>R (+ + +) very similar Y55>F (- + -) dissimilar
FR3-IMGT (66-104)	6	N66>E (+ - -) dissimilar L71>V (+ - +) similar S74>G (+ + -) similar I78>M (+ + -) similar S79>L (- - -) very dissimilar K90>R (+ + +) very similar
FR4-IMGT (118-129)	1	T122>S (+ - +) similar

(Hydropathy Volume Physicochemical)

+ : conserved classes

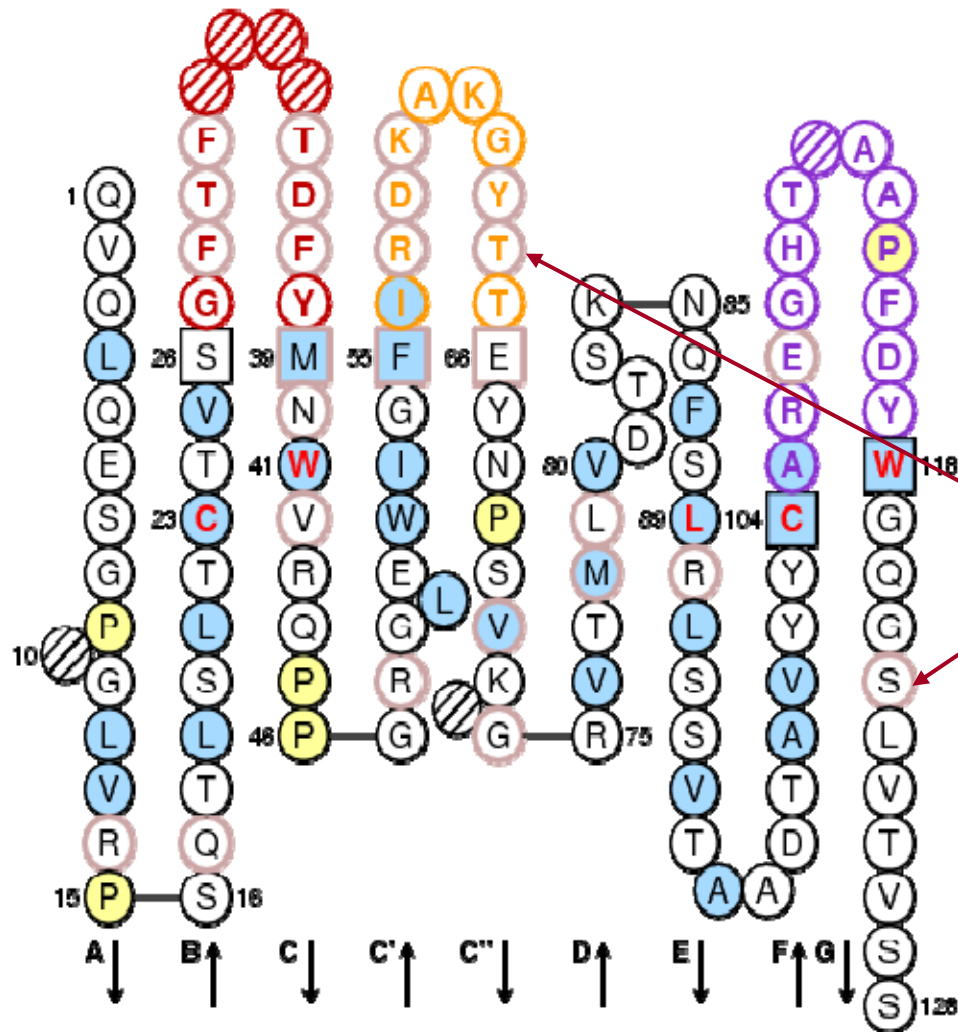
- : different classes

- **very similar (+ + +)**
- **similar (+ - +), (+ + -)**
- **dissimilar (+ - -), (- + -), (- - +)**
- **very dissimilar (- - -)**

IMGT/DomainGapAlign:

Towards «Potential immunogenicity evaluation»

IMGT Collier de Perles



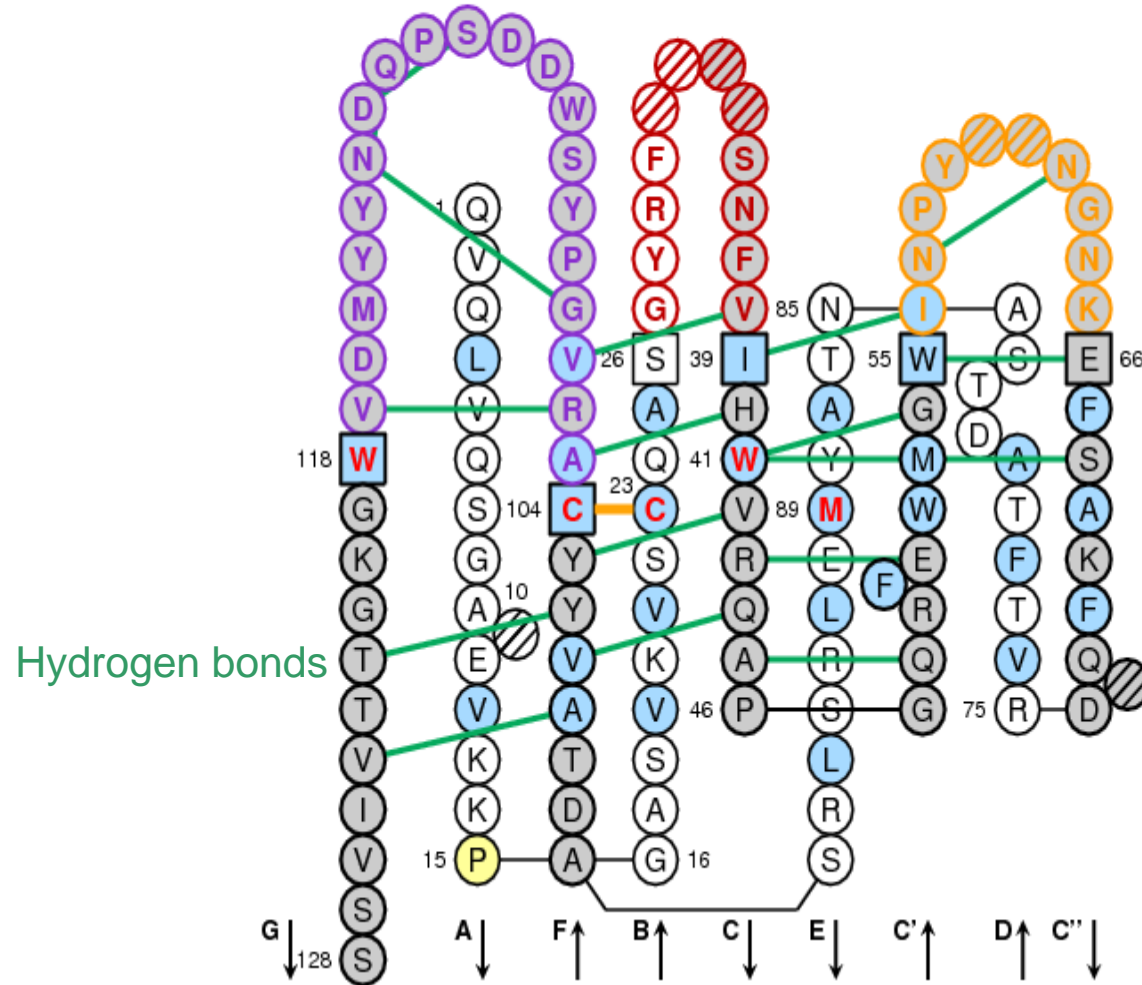
AA that are different compared to the closest germline V and J genes and alleles

(e.g. for alemtuzumab: 11 AA in CDR1- and CDR2-IMGT and 14 AA in the FR-IMGT, compared to *Homo sapiens* IGHV4-59*01)

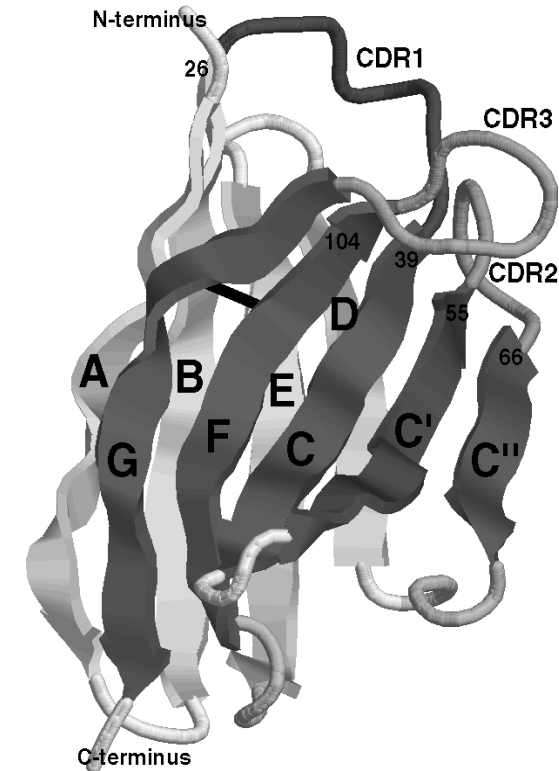
IMGT/3Dstructure-DB

IMGT Collier de Perles : *Homo sapiens* (Human) IGHV V-DOMAIN from **b12** (1hzh_H)

CDR-IMGT lengths [8.8.20]



V-DOMAIN



Contacts VH-(Ligand), V-KAPPA-(Ligand)

IMGT molecule name	IMGT description	Chain ID	IMGT chain description	Domain number	IMGT domain description
CAMPATH-1H, alemtuzumab , MABCAMPATH®	FAB-GAMMA-1_KAPPA	1ce1_H	VH-CH1	[D1]	VH
				[D2]	CH1
		1ce1_L	L-KAPPA	[D1]	V-KAPPA
				[D2]	C-KAPPA
CD52 (synthetic peptide)	Peptide	1ce1_P	Peptide		

	Unit 1		Unit 2		Residue contacts	Number of residues			Atom contact types		
	Domain	Chain	Domain	Chain		Total	From 1	From 2	Total	Polar	Hydrogen
DomPair	VH	1ce1_H	CH1	1ce1_H	19	17	8	9	125	9	1
DomPair			V-KAPPA	1ce1_L	63	45	24	21	532	61	6
DomPair			(Ligand)	1ce1_P	25	19	12	7	216	40	9
DomPair	CH1	1ce1_H	VH	1ce1_H	19	17	9	8	125	9	1
DomPair			C-KAPPA	1ce1_L	68	58	28	30	498	40	6
DomPair	V-KAPPA	1ce1_L	VH	1ce1_H	63	45	21	24	532	61	6
DomPair			C-KAPPA	1ce1_L	18	18	8	10	137	19	2
DomPair			(Ligand)	1ce1_P	16	14	7	7	171	37	5
DomPair	C-KAPPA	1ce1_L	CH1	1ce1_H	68	58	30	28	498	40	6
DomPair			V-KAPPA	1ce1_L	18	18	10	8	137	19	2

Contacts V-KAPPA-(Ligand)

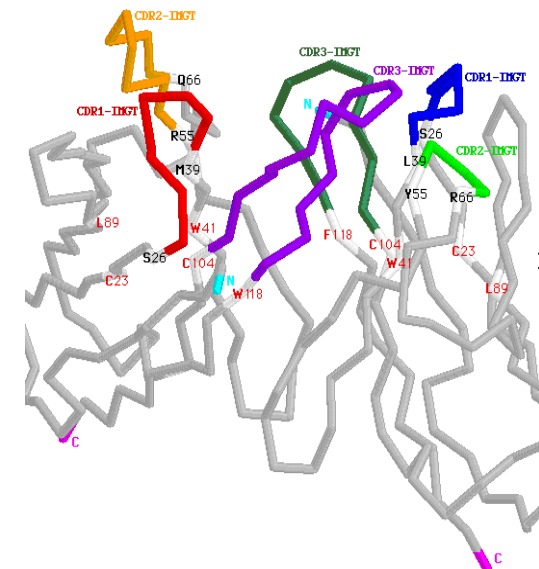
Summary:

Residue contacts	Number of residues			Atom contact types		
	Total	From 1	From 2	Total	Polar	Hydrogen
16	14	7	7	171	37	5

List of the Residue@Position pair contacts:

Click 'R@P' for IMGT Residue@Position cards

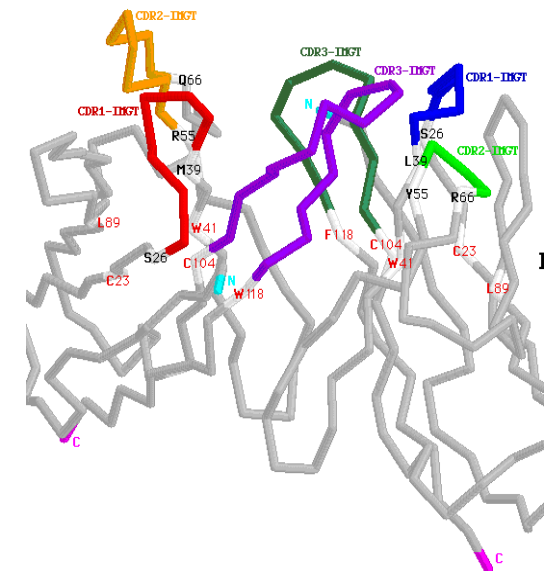
Order					Order				Atom contacts		
IMGT Num	Residue	Domain	Chain		IMGT Num	Residue	Domain	Chain	Total	Polar	Hydrogen
R@P 38	TYR	Y	V-KAPPA	Ice1_L	R@P 3	SER	S	Ice1_P	1	0	0
R@P 38	TYR	Y	V-KAPPA	Ice1_L	R@P 5	PRO	P	Ice1_P	21	0	0
R@P 56	ASN	N	V-KAPPA	Ice1_L	R@P 3	SER	S	Ice1_P	3	2	0
R@P 107	HIS	H	V-KAPPA	Ice1_L	R@P 4	SER	S	Ice1_P	20	4	1
R@P 107	HIS	H	V-KAPPA	Ice1_L	R@P 5	PRO	P	Ice1_P	12	2	0
R@P 107	HIS	H	V-KAPPA	Ice1_L	R@P 6	SER	S	Ice1_P	14	3	1
R@P 108	ILE	I	V-KAPPA	Ice1_L	R@P 5	PRO	P	Ice1_P	12	1	0
R@P 108	ILE	I	V-KAPPA	Ice1_L	R@P 6	SER	S	Ice1_P	12	3	0
R@P 109	SER	S	V-KAPPA	Ice1_L	R@P 6	SER	S	Ice1_P	11	2	0
R@P 114	ARG	R	V-KAPPA	Ice1_L	R@P 6	SER	S	Ice1_P	18	3	1
R@P 114	ARG	R	V-KAPPA	Ice1_L	R@P 7	ALA	A	Ice1_P	4	2	0
R@P 114	ARG	R	V-KAPPA	Ice1_L	R@P 8	ASP	D	Ice1_P	6	2	0
R@P 116	ARG	R	V-KAPPA	Ice1_L	R@P 2	THR	T	Ice1_P	1	1	0
R@P 116	ARG	R	V-KAPPA	Ice1_L	R@P 4	SER	S	Ice1_P	9	4	1
R@P 116	ARG	R	V-KAPPA	Ice1_L	R@P 6	SER	S	Ice1_P	20	6	1
R@P 116	ARG	R	V-KAPPA	Ice1_L	R@P 7	ALA	A	Ice1_P	7	2	0



Kaas Q. et al.
Nucl. Acids Res. (2004)

Contacts VH-(Ligand)

	IMGT Num	Residue	Domain	Chain		IMGT Num	Residue	Domain	Chain	Total	Polar	Hydrogen	
R@P	38	TYR	Y	VH	1ce1_H	R@P	2	THR	T	1ce1_P	4	0	0
R@P	38	TYR	Y	VH	1ce1_H	R@P	7	ALA	A	1ce1_P	13	1	0
R@P	38	TYR	Y	VH	1ce1_H	R@P	8	ASP	D	1ce1_P	14	2	2
R@P	55	PHE	F	VH	1ce1_H	R@P	6	SER	S	1ce1_P	5	0	0
R@P	55	PHE	F	VH	1ce1_H	R@P	7	ALA	A	1ce1_P	16	0	0
R@P	55	PHE	F	VH	1ce1_H	R@P	8	ASP	D	1ce1_P	1	0	0
R@P	57	ARG	R	VH	1ce1_H	R@P	7	ALA	A	1ce1_P	9	3	2
R@P	57	ARG	R	VH	1ce1_H	R@P	8	ASP	D	1ce1_P	20	6	1
R@P	61	LYS	K	VH	1ce1_H	R@P	8	ASP	D	1ce1_P	11	2	1
R@P	66	GLU	E	VH	1ce1_H	R@P	7	ALA	A	1ce1_P	1	0	0
R@P	107	GLU	E	VH	1ce1_H	R@P	2	THR	T	1ce1_P	13	2	1
R@P	107	GLU	E	VH	1ce1_H	R@P	4	SER	S	1ce1_P	5	2	0
R@P	107	GLU	E	VH	1ce1_H	R@P	7	ALA	A	1ce1_P	5	0	0
R@P	108	GLY	G	VH	1ce1_H	R@P	1	GLY	G	1ce1_P	2	1	0
R@P	108	GLY	G	VH	1ce1_H	R@P	2	THR	T	1ce1_P	9	2	0
R@P	109	HIS	H	VH	1ce1_H	R@P	1	GLY	G	1ce1_P	24	4	0
R@P	109	HIS	H	VH	1ce1_H	R@P	2	THR	T	1ce1_P	21	5	0
R@P	109	HIS	H	VH	1ce1_H	R@P	3	SER	S	1ce1_P	9	2	1
R@P	110	THR	T	VH	1ce1_H	R@P	1	GLY	G	1ce1_P	1	1	0
R@P	110	THR	T	VH	1ce1_H	R@P	3	SER	S	1ce1_P	11	4	1
R@P	112	ALA	A	VH	1ce1_H	R@P	3	SER	S	1ce1_P	3	1	0
R@P	113	ALA	A	VH	1ce1_H	R@P	2	THR	T	1ce1_P	3	0	0
R@P	113	ALA	A	VH	1ce1_H	R@P	3	SER	S	1ce1_P	7	2	0
R@P	113	ALA	A	VH	1ce1_H	R@P	4	SER	S	1ce1_P	4	0	0
R@P	114	PRO	P	VH	1ce1_H	R@P	4	SER	S	1ce1_P	5	0	0



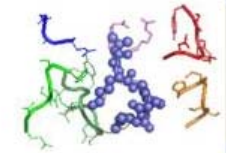
Kaas Q. et al.
Nucl. Acids Res. (2004)

IMGT/2Dstructure-DB

Overview

Your query: INN entries.

International Nonproprietary Name (INN)



Number of results: **53**

Click on **IMGT entry ID** (2nd column) for entry card

	IMGT entry ID	IMGT molecule name	IMGT entry type	IMGT receptor description	Species	Proposed list	Recommended list	CAS number
1	7637	trastuzumab, 4D5V8, HERCEPTIN®	INN	IG-GAMMA-1_KAPPA	Humanized	L78 (1997)	R40 (1998)	180288-69-1
2	7906	cetuximab, Fab C225, IMC-225, ERBITUX™	INN	IG-GAMMA-1_KAPPA	Chimeric	L82 (1999)	R44 (2000)	205923-56-4
3	8005	alemtuzumab, Campath-1H, LDP-03, CAMPATH®/MABCAMPATH®	INN	IG-GAMMA-1_KAPPA	Humanized	L83 (2000)	R45 (2001)	216503-57-0
4	8017	bevacizumab, 12-IgG1, F(ab)-12 IgG1, Fab-12 IgG1, rhuMab-VEGF, AVASTIN®	INN	FAB-GAMMA-1_KAPPA	Humanized	L83 (2000)	R45 (2001)	216974-75-3
5	8313	ranibizumab, Fab-12 variant Y0317, RhuFab, LUCENTIS®	INN	FAB-GAMMA-1_KAPPA	Humanized	L90 (2004)	R52 (2004)	347396-82-1
6	8380	pertuzumab, rhuMAB 2C4	INN	FAB-GAMMA-1_KAPPA	Humanized	L89 (2003)	R51 (2004)	380610-27-5
7	8598	napatumomab estafenatox	INN	FAB-GAMMA-1-SAG_KAPPA	Mus musculus	L96 (2006)	R58 (2007)	676258-98-3
8	8651	tadocizumab	INN	FAB-GAMMA-1_KAPPA	Humanized	L94 (2005)	R56 (2006)	339086-80-5
9	8658	efungumab	INN	SCFV-HEAVY-KAPPA	Homo sapiens	L95 (2006)	R57 (2007)	762260-74-2
10	8659	abagovomab	INN	IG-GAMMA-1_KAPPA	Mus musculus	L95 (2006)	R57 (2007)	792921-10-9
11	8669	atacicept	INN	FUSION-TNFRSF13B-FC-GAMMA-1	Homo sapiens	L95 (2006)	R57 (2007)	845264-92-8
12	8693	motavizumab	INN	IG-GAMMA-1_KAPPA	Humanized	L95 (2006)	R57 (2007)	677010-34-3
13	8734	bavituximab	INN	IG-GAMMA-1_KAPPA	Chimeric	L95 (2006)	R57 (2007)	648904-28-3
14	8739	afibercept	INN	FUSION-FLT1-KDR-FC-GAMMA-1	Homo sapiens	L95 (2006)	R57 (2007)	862111-32-8
15	8750	riloncept, ARCALYST™	INN	FUSION-IL1RAP-IL1R1-FC-GAMMA-1	Homo sapiens	L95 (2006)	R57 (2007)	501081-76-1
16	8753	lexatumumab	INN	IG-GAMMA-1_LAMBDA	Homo sapiens	L95 (2006)	R57 (2007)	845816-02-6
17	8818	ibalizumab	INN	IG-GAMMA-4_KAPPA	Humanized	L97 (2007)	R59 (2008)	680188-33-4
18	8832	tenatumomab, ST2146	INN	IG-GAMMA-2B_KAPPA	Mus musculus	L98 (2007)	R60 (2008)	592557-43-2 592557-41-0
19	8836	canakinumab	INN	IG-GAMMA-1_KAPPA	Homo sapiens	L97 (2007)	R59 (2008)	402710-27-4 402710-25-2
20	8862	etaracizumab, MEDI-522, hLM609	INN	IG-GAMMA-1_KAPPA	Humanized	L99 (2008)	R61 (2009)	892553-42-3
21	8864	otelixizumab	INN	IG-GAMMA-1_LAMBDA	Humanized	L98 (2007)	R60 (2008)	881191-44-2
22	8869	teplizumab	INN	IG-GAMMA-1_KAPPA	Humanized	L97 (2007)	R59 (2008)	876387-05-2
23	8887	lucatumumab	INN	IG-GAMMA-1_KAPPA	Homo sapiens	L98 (2007)	R60 (2008)	903512-50-5
24	8888	panobacumab, Aerumab 11	INN	IG-MU_KAPPA_J-CHAIN	Homo sapiens Mus musculus	L100 (2008)	Unpublished	885053-97-4
25	8894	gantenerumab	INN	IG-GAMMA-1_KAPPA	Homo sapiens	L97 (2007)	R59 (2008)	89957-37-9
26	8922	milatuzumab	INN	IG-GAMMA-1_KAPPA	Humanized	L98 (2007)	R60 (2008)	899796-83-9
27	8932	veltuzumab	INN	IG-GAMMA-1_KAPPA	Humanized	L98 (2007)	R60 (2008)	728917-18-8
28	8941	tanezumab, RN624	INN	IG-GAMMA-2_KAPPA	Humanized	L99 (2008)	R61 (2009)	880266-57-9
29	8947	anikinzumab	INN	IG-GAMMA-1_KAPPA	Humanized	L98 (2007)	R60 (2008)	910649-32-0

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IMGT/2Dstructure-DB

IMGT/2Dstructure-DB card for INN: **7637**



IMGT molecule name	IMGT receptor type	IMGT receptor description	Ligand(s)	Species	CC	Chain ID
INN name trastuzumab	IG	IG-GAMMA-1_KAPPA		Humanized	1	[7637_H,7637_L]
Common name 4D5V8						
Commercial name HERCEPTIN®						

Proposed list **L78 (1997)** Recommended list **R40 (1998)**

IMGT note
 Trastuzumab has been engineered with two amino acid changes IGHG1 CH3 D12>E, L14>M to convert the G1m1 allotype to the iso-allotype nG1m1, the resulting gamma1 chain being Gm17, nG1m1, in an attempt to reduce the risk of anti-G1m1 antibodies interfering with therapy.
 Carter P. et al. Proc. Natl Acad. Sci. USA, 89, 4285-4289 (1992) PMID: 1350088
 Trastuzumab constant genes and alleles, and allotypes, based on sequence analysis are:
 IGHG1*01, CH3 D12>E, L14>M Allotype G1m17nG1m1
 IGKC*01 (100%) Allotype Km3
 The allotypes have been confirmed serologically.

- INN definitions
- Chain details
- Contact analysis
- 3D visualization
Jmol or QuickPDB
- Renumbered
IMGT file
- References and links
- Printable card

Chain details

Differences with the closest IMGT allele sequence are in orange.

Chain details of [trastuzumab](#), 4D5V8, **IG**, IG-GAMMA-1_KAPPA Humanized [\[7637_H,7637_L\]](#)

Chain ID	INN 7637_H
Chain length	450
IMGT chain description	H-GAMMA-1 = VH(1-120) + CH1(121-218) + HINGE-REGION(219-233) + CH2(234-343) + CH3(344-450)
	<pre> [V-REGION EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKLEWVARIYPTNGYTRVADSVKGRFTISADTSKNTAYLQMNSLRAED]N-AND[J-REGION] [CH1 TAVYYCSRWGGDGFYAMDYWGQGLLVIVSSASTKGPSVFLPAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS] [HINGE-REGION] [</pre>

IMGT/2Dstructure-DB

Chain details of **trastuzumab**, 4D5V8, **IG**, IG-GAMMA-1_KAPPA Humanized [7637_H,7637_L]

Chain ID	INN 7637_H	DESCRIPTION	
Chain length	450		
IMGT chain description	H-GAMMA-1 = VH(1-120) + CH1(121-218) + HINGE-REGION(219-233) + CH2(234-343) + CH3(344-450)		
Chain sequence	<p>[V-REGION EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAED]N-AND[J-REGION] [CH1 TAVYYCSRWGGDGFYAMDYWGQGLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTISWNSGALTSGVHTFPAVLQSS] [HINGE-REGION] [CH2 GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDTPPPCPRCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVVS] [CH3 HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE] [CH3 LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK</p> <p>Sequence in FASTA format Sequence in IMGT format</p>		
V-DOMAIN	IMGT domain description	VH	CLASSIFICATION
	IMGT gene and allele name	IGHV3-66*01 (81.60%)(Human) , IGHV3-66*02 (81.60%)(Human) , IGHV3-66*04 (81.60%)(Human) Alignment details	
	IMGT gene and allele name	IGHJ6*01 (76.50%)(Human) , IGHJ6*02 (76.50%)(Human) Alignment details	
	2D representation	IMGT Collier de Perles or IMGT Collier de Perles on 2 layers	
	Contact analysis	Not available	
	CDR-IMGT lengths	[8.8.13]	
	Sheet composition	Not available	NUMEROTATION
	<p>[CDR1] [CDR2] EVQLVESGG. GLVQPGGSLRLSCAASGFNI...KDTYIHWVRQAPGKGLEWVARIYPT...NGYTRYADSVK. GRFTISADTSKNTAYLQ [CDR3] MNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGLVTVSS</p> <p>IMGT/DomainGapAlign results</p>		

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WELCOME ! to IMGT/mAb-DB

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IMGT/mAb-DB Query page



Today is Monday, Nov 02 2009
345 entries
156 -mab
14 -cept

Search by:

INN (International Nonproprietary Name) <input type="text"/> - <input type="text"/>		INN proposed list	- <input type="text"/>	<input type="radio"/> and before <input type="radio"/> and after
INN number <input type="text"/>		INN recommended list	- <input type="text"/>	<input type="radio"/> and before <input type="radio"/> and after
IMGT/mAb-DB section	- <input type="text"/>	Radiolabelled/ Conjugated	- <input type="text"/>	
Common name	<input type="text"/>	Entries with sequences	- <input type="text"/>	
Proprietary name	- <input type="text"/>	Entries with 3Dstructure	- <input type="text"/>	
Isotype and format	<input type="text"/>	OR	Fusion protein format	- <input type="text"/>
Origin clone species	- <input type="text"/>		Origin clone name	<input type="text"/>
Specificity (target)	- <input type="text"/>		Specificity origin	- <input type="text"/>
Company	<input type="text"/>	Development status	- <input type="text"/>	
Clinical indication	<input type="text"/>	Regulatory agency	- <input type="text"/>	
Expression system	<input type="text"/>	Year	- <input type="text"/>	
Application	- <input type="text"/>	Clinical domain	- <input type="text"/>	

IMGT/mAb-DB

INN (International Nonproprietary Name)	<input type="text"/>	- <input type="text"/>	INN proposed list	- <input type="text"/>	<input type="radio"/> and before <input type="radio"/> and after
INN number	- <input type="text"/>		INN recommended list	- <input type="text"/>	<input type="radio"/> and before <input type="radio"/> and after
IMGT/mAb-DB section	- <input type="text"/>		Radiolabelled/ Conjugated	- <input type="text"/>	
Common name	<input type="text"/>		Entries with sequences	- <input type="text"/>	
Proprietary name	- <input type="text"/>		Entries with 3Dstructure	- <input type="text"/>	
Isotype and format	<input type="text"/>	OR	Fusion protein format	- <input type="text"/>	
Origin clone species	- <input type="text"/>		Origin clone name	<input type="text"/>	
Specificity (target)	- <input type="text"/>		Specificity origin	- <input type="text"/>	
Company	<input type="text"/>		Development status	- <input type="text"/>	
Clinical indication	<input type="text"/>		Regulatory agency	- <input type="text"/>	
Expression system	<input type="text"/>		Year	- <input type="text"/>	
Application	- <input type="text"/>		Clinical domain	- <input type="text"/>	

Displayed fields:

Select All / None						
INN	INN number	INN Prop. list	INN Rec. list	Common name	Proprietary name	
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	
IMGT/mAb-DB section	Radiolabelled/ Conjugated	IMGT/2Dstructure-DB	IMGT/3Dstructure-DB			
<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>			
Isotype and format	Fusion protein format	Origin clone species	Origin clone name	Specificity and origin		
<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>		
Company	Clinical indication	Development status	Regulatory agency status and year			
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>			
Expression system	FDA number	EMEA number	ATC code	NCI number	Drug number	References
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Application	Clinical domain					
<input checked="" type="checkbox"/>	<input type="checkbox"/>					

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<http://www.imgt.org>

Your query: **IMGT/mAb-DB INN = trastuzumab**

Number of results: **1**

IMGT/mAb-DB id	INN (International Nonproprietary Name)	INN Num.	INN Prop. list	INN Rec. list	Common name	Proprietary name	IMGT/mAb-DB section	IMGT/ 2D	IMGT/ 3D	Isotype and format	Specificity (target) [origin]	Company	Clinical indication	Development status	Regulatory agency status and year	Application
97	trastuzumab	7637	78 (1997)	40 (1998)	4D5V8, Herceptin	HERCEPTIN®	Humanized	7637	1n8z	IgG1k	ERBB2 (Epidermal Growth Factor Receptor 2; HER-2; p185c-erbB2; NEU; EGFR2) [<i>Homo sapiens</i>]	E. Hoffmann-La Roche Ltd. (Basel Switzerland) (EU) / Genentech Inc. (S. San Francisco CA USA) (US)	Breast cancers (as adjuvant)	Phase III		
													Metastatic breast cancers overexpressing ERBB2	Phase M	AMM Market authorization (Roche) August 2000, FDA approval October 1998	Therapeutic
													Non-small-cell lung cancers	Phase II		

Created: 03/04/2009
Last updated:

IMGT/mAb-DB has been developed by Yan Wu and Patrice Duroux (LIGM, Montpellier, France)
IMGT/mAb-DB scientific officer: Marie-Paule Lefranc (Marie-Paule.Lefranc@igh.cnrs.fr)

[IMGT/mAb-DB Documentation](#)
[Monoclonal antibodies with clinical indications](#)

Conclusions

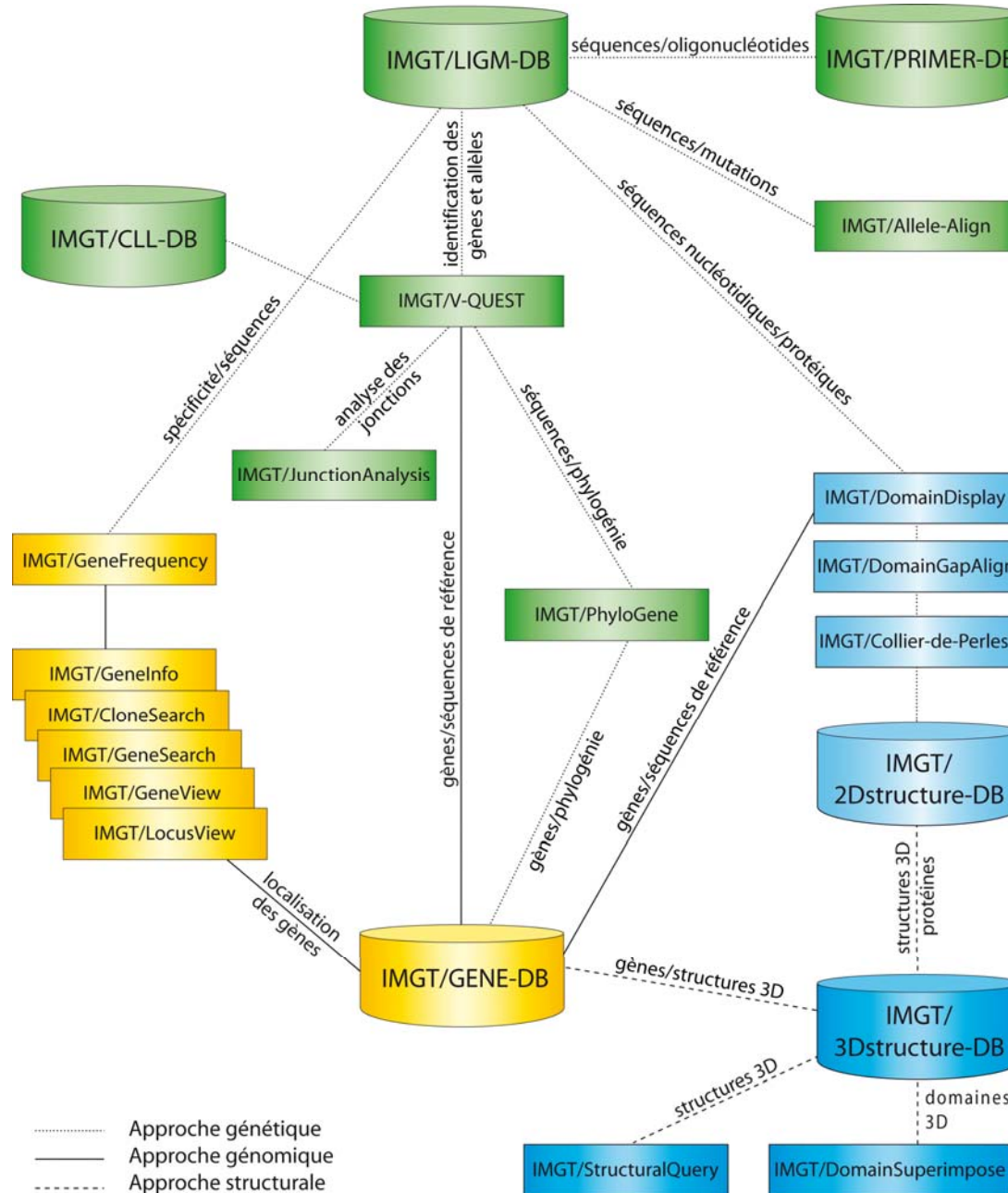


<http://www.imgt.org>

IMGT/Colliers de Perles provide a standardized way:

- to compare immunoglobulin variable domains
- to delimit the FR-IMGT and CDR-IMGT in the process of antibody humanization and engineering.

They provide an invaluable help for sequence-related characterization of specificity or potential immunogenicity.



- 6 databases
- 15 online tools

- Sequences
- Genes
- Structures

- Immunoglobulins (IG) (or antibodies)
- T cell receptors (TR)
- MHC
- IgSF and MhcSF

Acknowledgements



<http://www.imgt.org>

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«ImmunoGrid», 6th PCRDT, STREPS IST



and the companies that support the IMGT efforts of standardization.



Many thanks to the IMGT® team at Montpellier, France

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