http://www.imgt.org

IMGT® Databases and Tools for Immunoglobulin (IG) and T cell receptor (TR) analysis, and for Antibody humanization

http://www.imgt.org

Marie-Paule Lefranc
IMGT Founder and Director
Professor University Montpellier 2, CNRS, Montpellier, France

Federation of African Immunological Societies FAIS
7th International Conference,
Sharm El-Sheikh, 8-11 November 2009

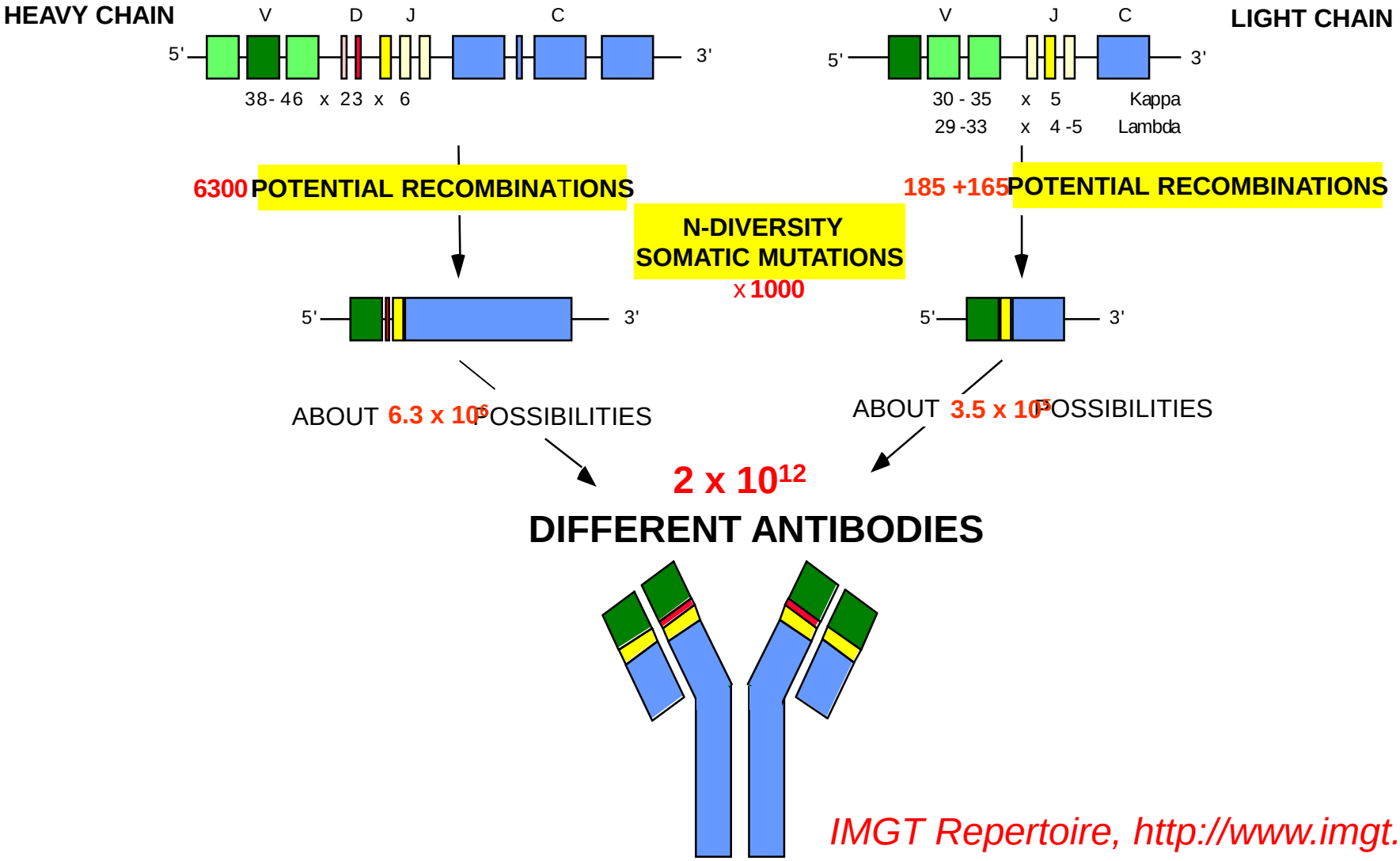
Outline

- IMGT® standards based on IMGT-ONTOLOGY
  - classification: gene nomenclature
  - description: labels et prototypes
  - numerotation: IMGT unique numbering
    IMGT Collier de Perles
- Tools and databases
  - sequences: IMGT/JunctionAnalysis
    IMGT/V-QUEST,
    IMGT/CLL-DB
    IMGT/DomainGapAlign
  - 3D structures: IMGT/3Dstructure-DB
    (IMGT/2Dstructure-DB cards)
- Go-between database: IMGT/mAb-DB

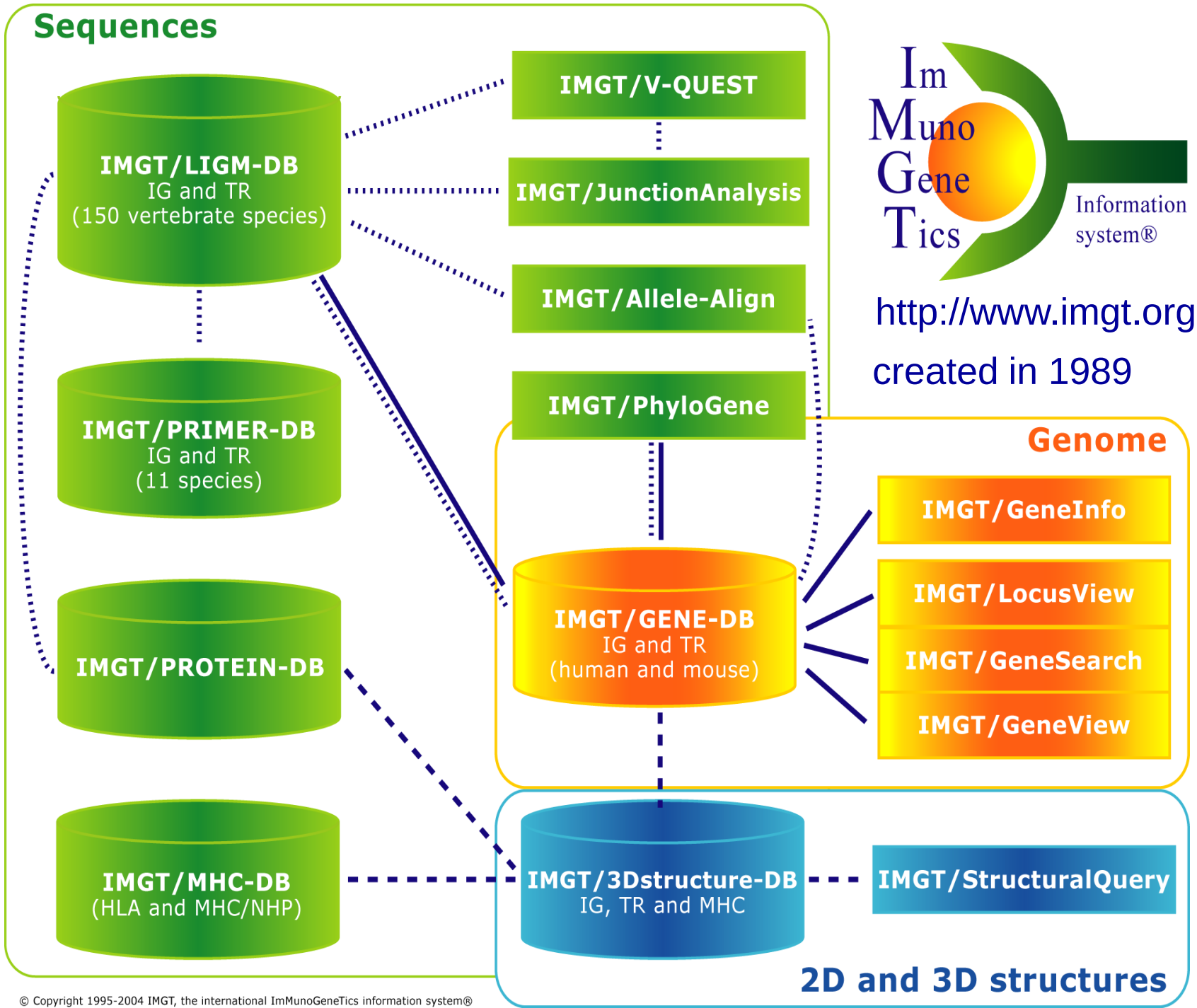
Immunoglobulin (IG) synthesis

http://www.imgt.org

150
FUNCTIONAL IG GENES



IMGT Repertoire, http://www.imgt.org



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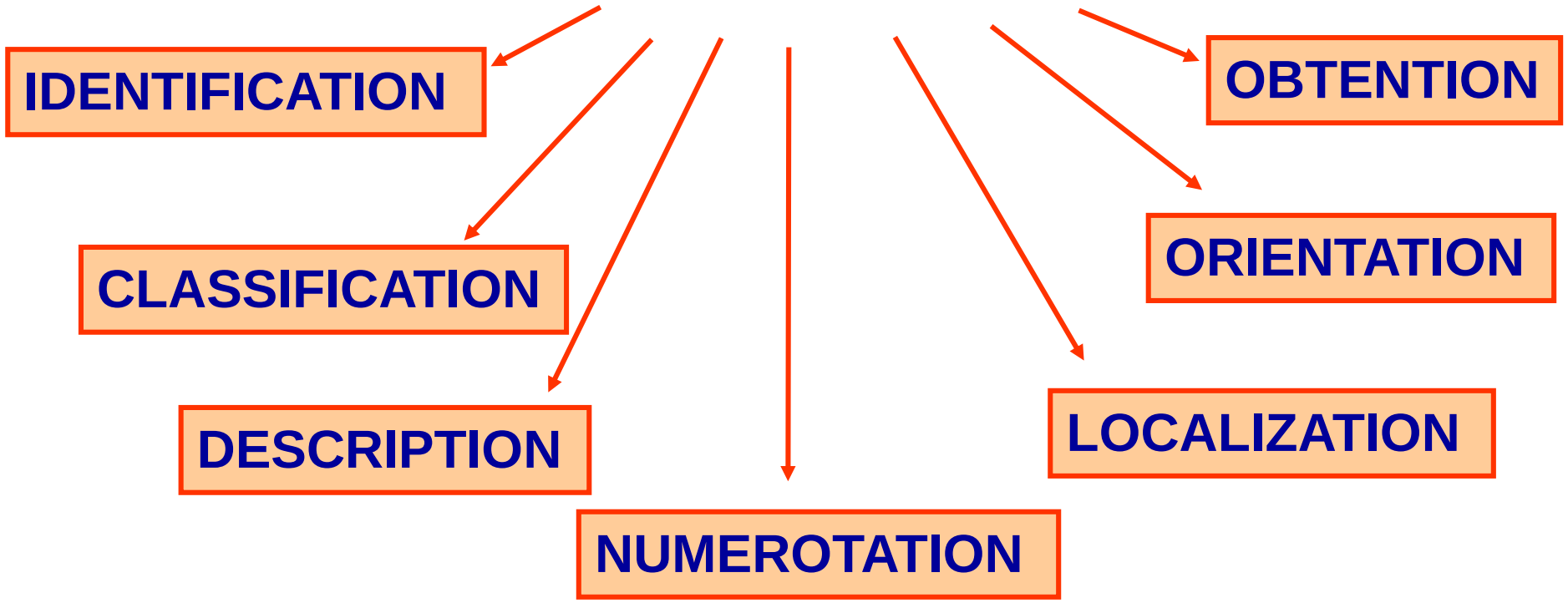
http://www.imgt.org

IMGT standards based on IMGT-ONTOLOGY

http://www.imgt.org

IMGT-ONTOLOGY seven axioms:

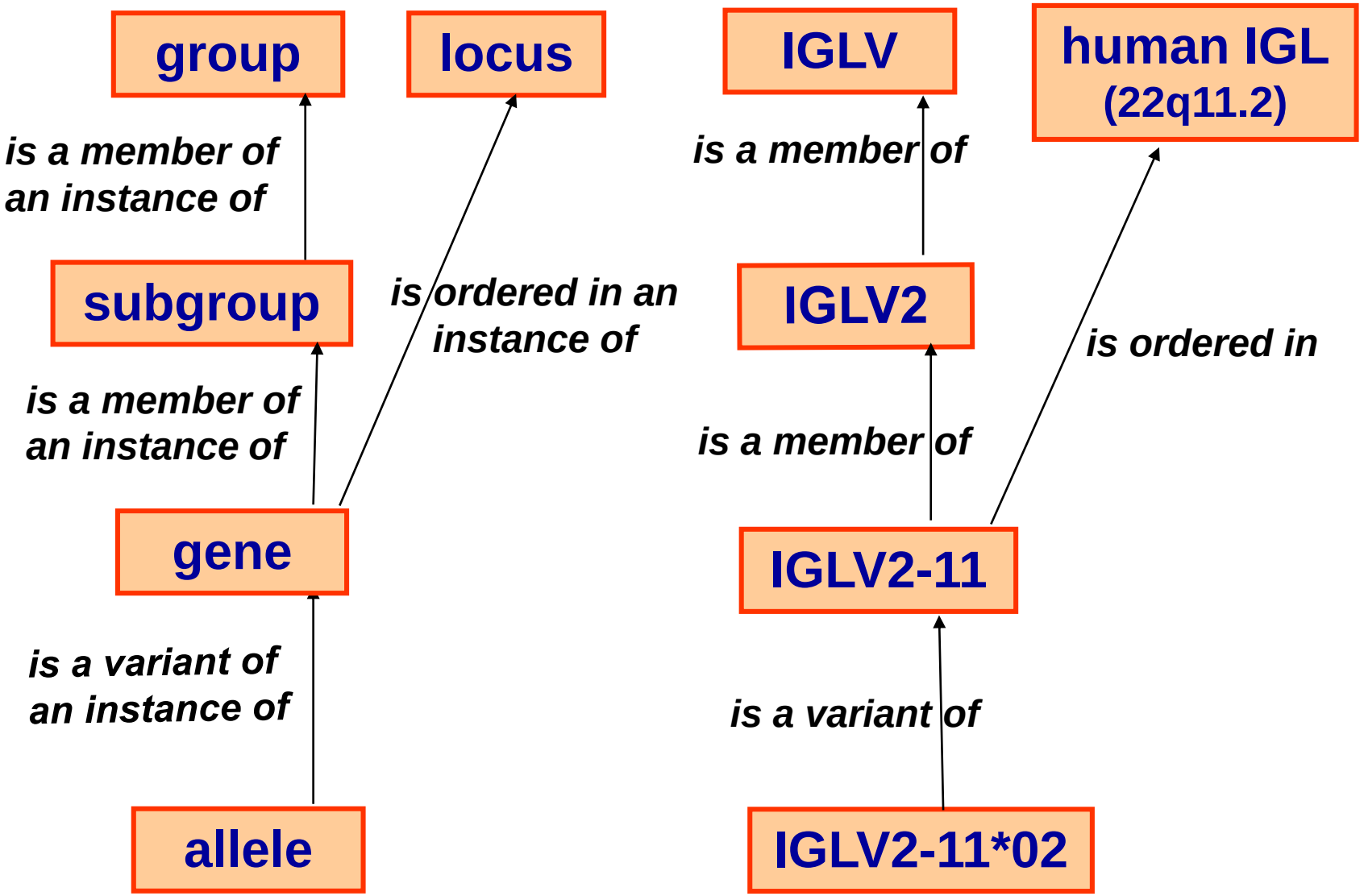
To share, reuse and represent knowledge in Immunogenetics and Life Sciences



Giudicelli and Lefranc, Bioinformatics (1999)

CLASSIFICATION axiom

http://www.imgt.org



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 genes (direct links from NCBI Entrez Gene) and alleles.

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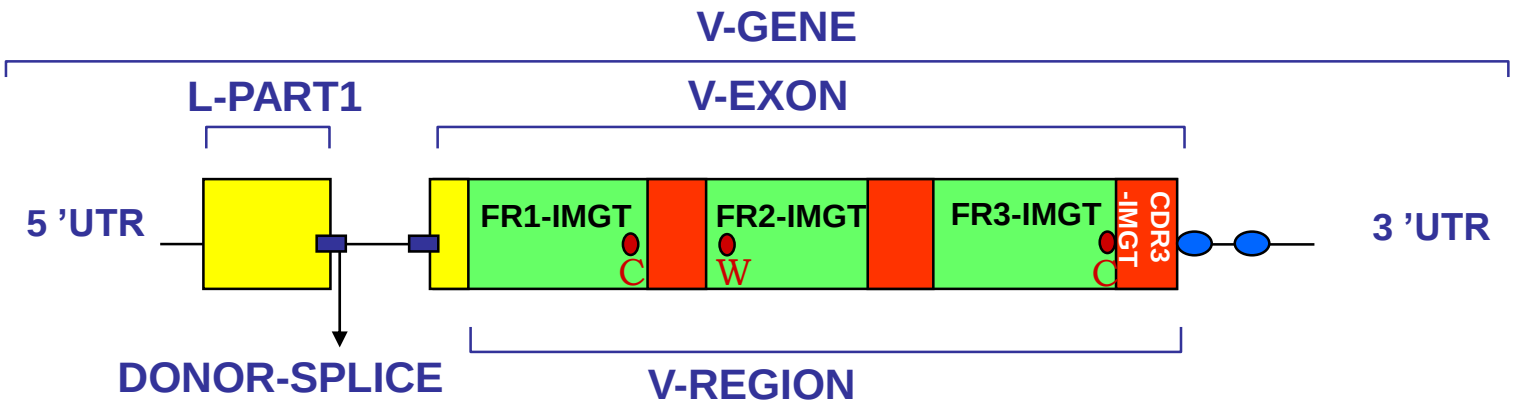
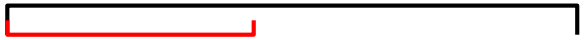
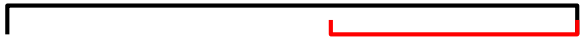
DESCRIPTION axiom

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	

http://www.imgt.org

Concepts of DESCRIPTION

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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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IMGT/LIGM-DB

http://www.imgt.org

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
FT                       /translation="QVHLVESGGAVFHPGRSLRLSRAASGFTFSSYGMHWVRQAP
FT                       AKGLEWVAVIWYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYC
FT                       AKHVTIAAAGRRGAGMDVWGQGTTVTVSS"
FT   V-REGION            1..296
FT                       /allele="IGHV3-33*01, putative"
FT                       /gene="IGHV3-33"
FT                       /CDR_length="[8.8.18]"
FT                       /putative_limit="3' side"
FT                       /translation="QVHLVESGGAVFHPGRSLRLSRAASGFTFSSYGMHWVRQAP
FT                       AKGLEWVAVIWYDGSNKYYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYC
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="IWYDGSNK"
FT   FR3-IMGT            175..288
FT                       /AA_IMGT="66 to 104, AA 73 is missing"
FT                       /translation="YYADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYC"
```

Done

DESCRIPTION

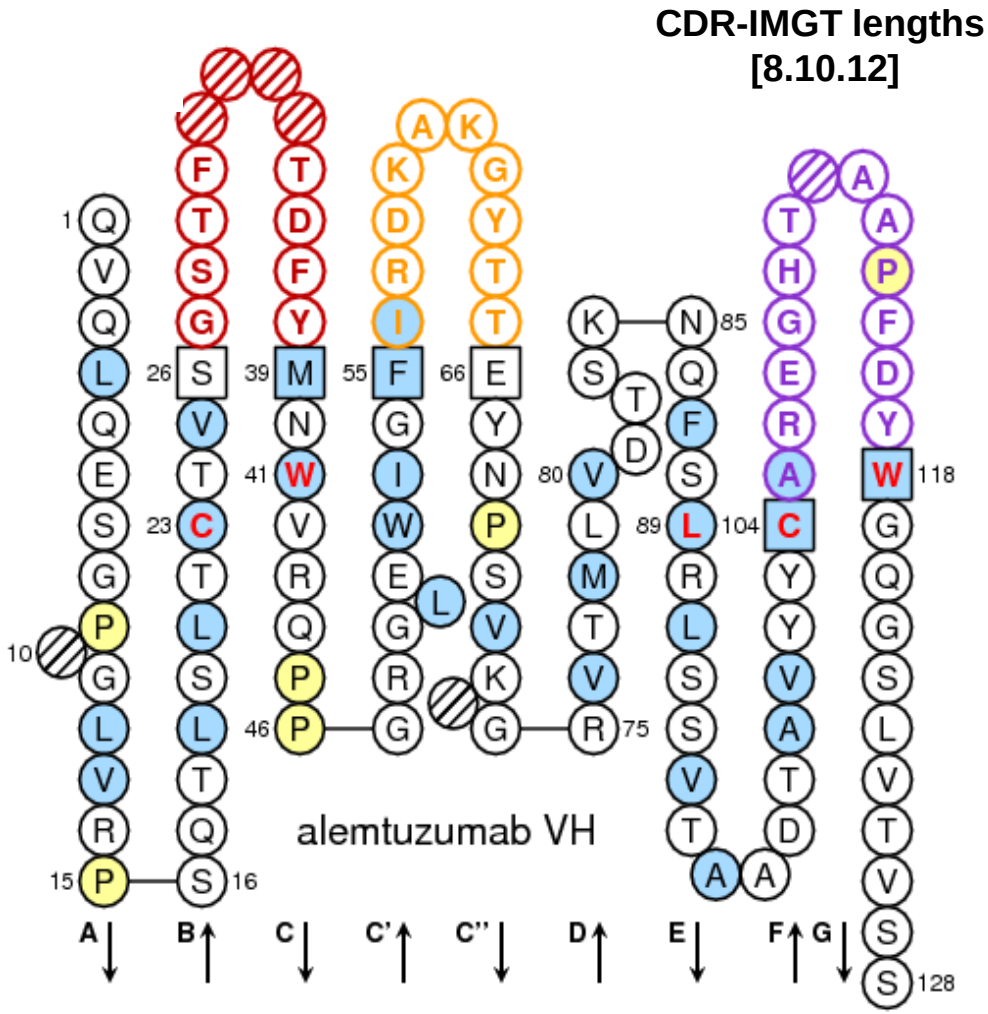
137 963 sequences from 235 species

IMGT-ONTOLOGY:
277 IMGT labels for sequences
285 IMGT labels for 3D structures

NUMEROTATION axiom

http://www.imgt.org

IMGT Collier de Perles



Lefranc et al. Dev. Comp. Immunol. 27, 55-77 (2003)

NUMEROTATION axiom

http://www.imgt.org

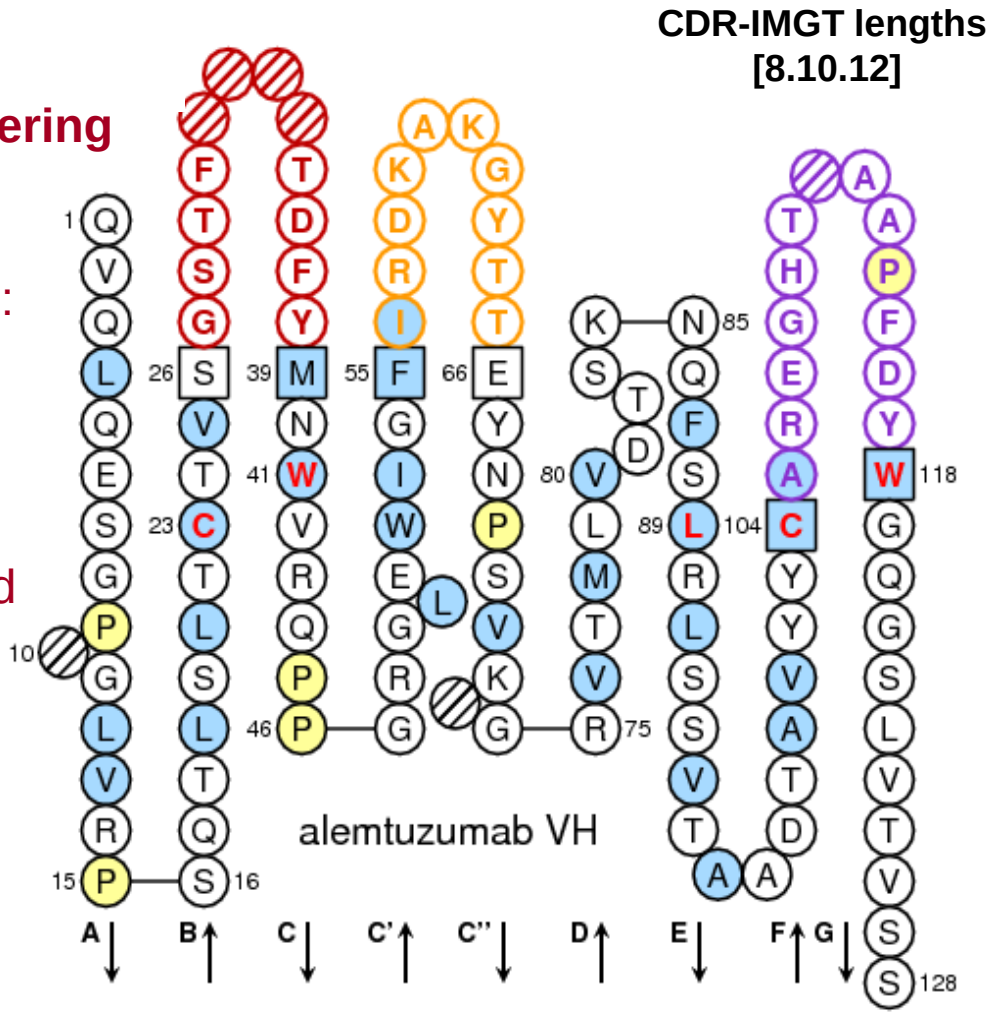
IMGT Collier de Perles

Based on the **IMGT unique numbering**

- conserved AA (and codons) are always at the same positions:
  - 1st-CYS **23**
  - 2nd-CYS **104**
  - J-PHE, J-TRP **118**

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

- CDR-IMGT lengths are crucial information

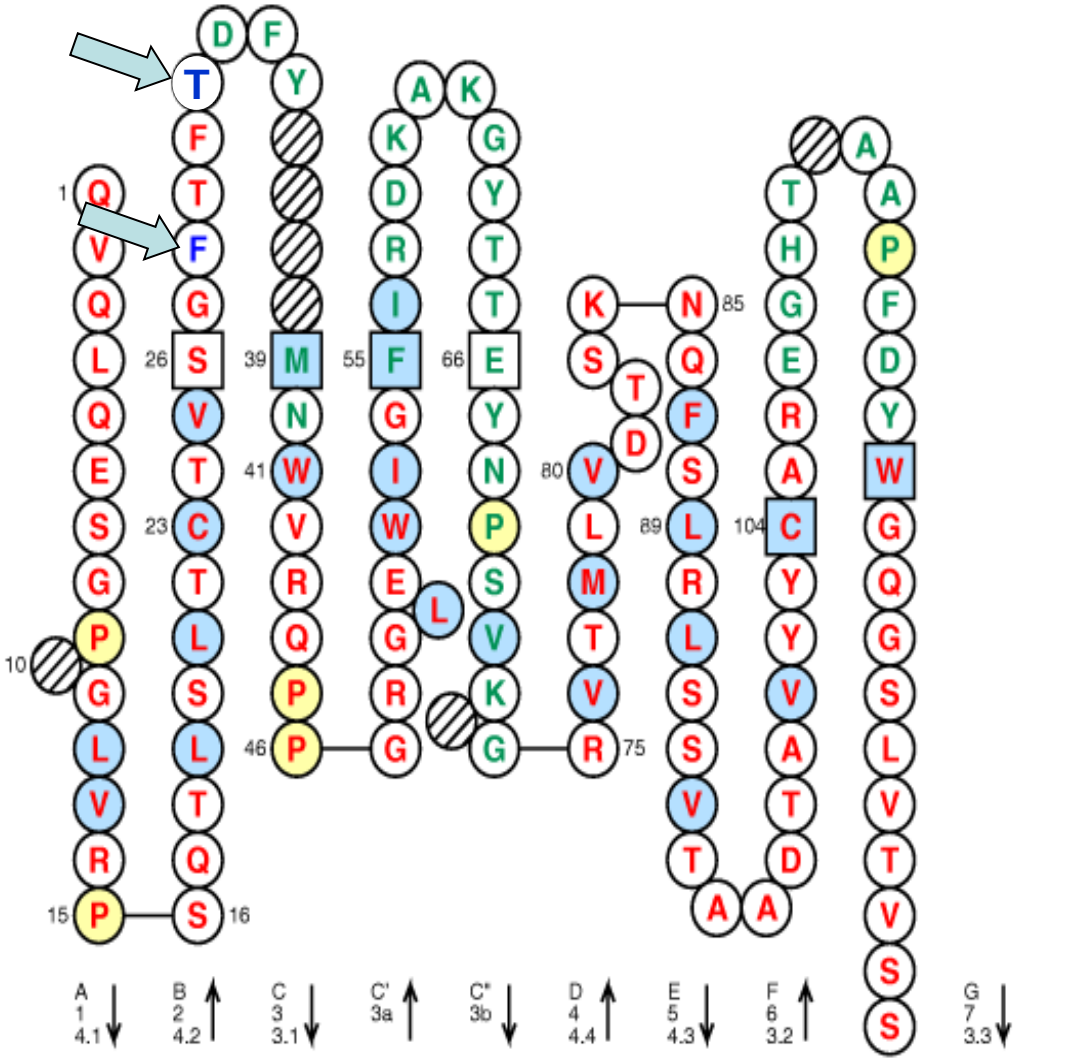


Lefranc et al. Dev. Comp. Immunol. 27, 55-77 (2003)

Alemtuzumab

http://www.imgt.org

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



human

rat

VH domain
[8.10.12]

IMGT Biotechnology page (http://www.imgt.org)

Concepts of NUMEROTATION

http://www.imgt.org

1. The IMGT-ONTOLOGY concepts of numerotation include:
- IMGT unique numbering
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2. The concepts bridge the gap between sequences and 3D structures, at the amino acid (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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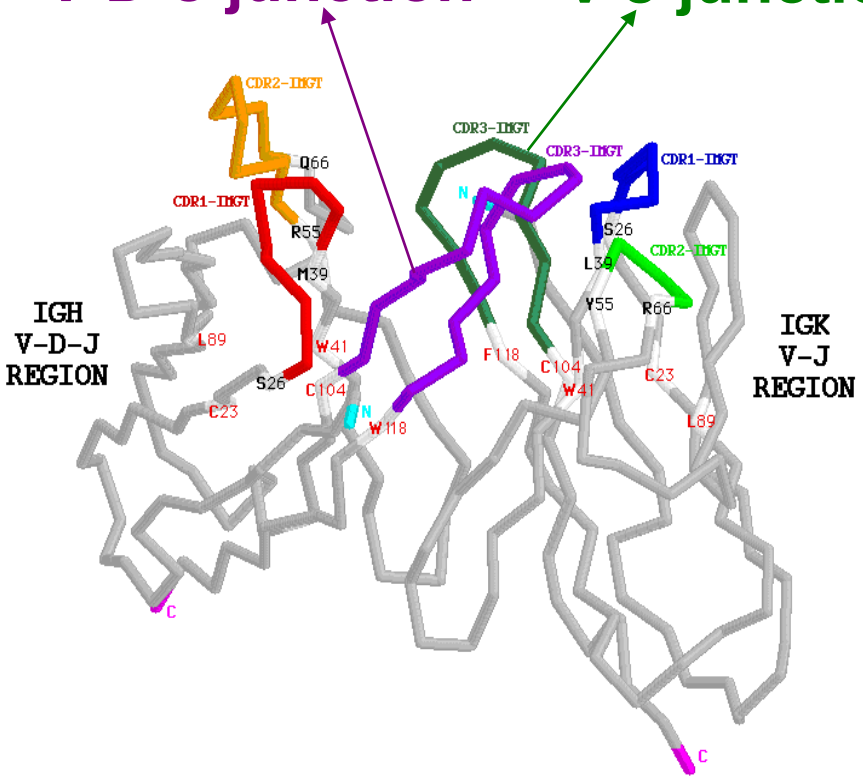
V-DOMAIN: VH and V-KAPPA

http://www.imgt.org

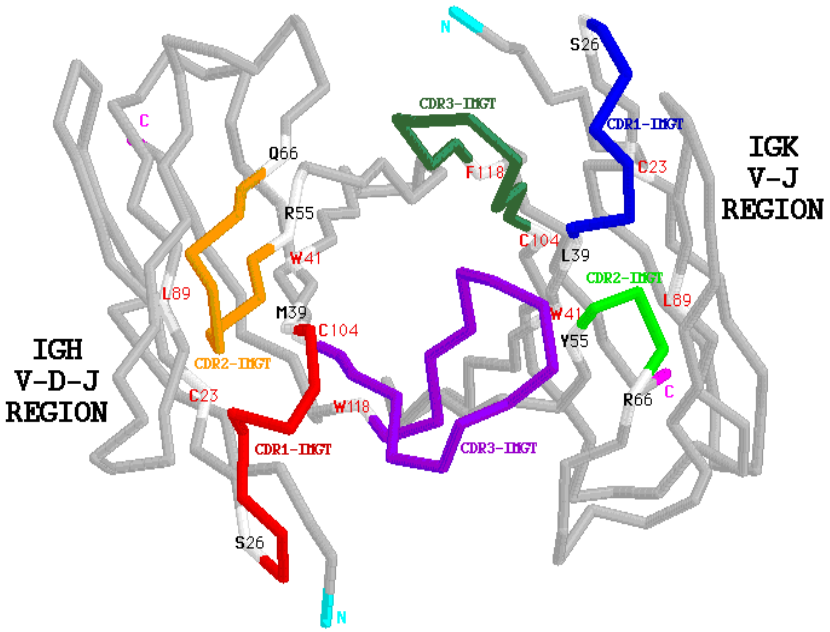
VH V-KAPPA

V-D-J junction V-J junction



Side view of the V-DOMAIN

VH V-KAPPA

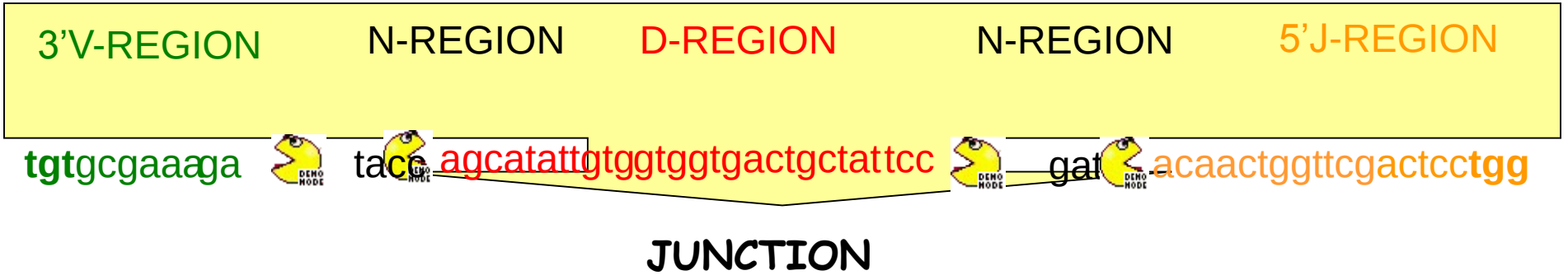


View from above the CDR-IMGT

CDR3-IMGT= Complementarity determining region (105-117)
V-D-J junction (104-118), V-J junction (104-118)

Immunoglobulin V-D-J generation of sequence diversity

http://www.imgt.org



C	A	P	Y	R	G	D	T	Y	D	Y	S	W
tgt	gcg	cca	tac	cgg	ggt	gac	act	tat	gat	tac	tcc	tgg

IMGT/JunctionAnalysis: analysis of the IG and TR junctions

THANK YOU
for using IMGT/JunctionAnalysis

THE
INTERNATIONAL
IMMUNOGENETICS
INFORMATION SYSTEM®

Analysis of the JUNCTIONs

	Input	V name	V-REGION	N1	D-REGION	N2
#1	M62724	IGHV7-4-1*02	tgtgcgagaga	aga	.tagcaatggctacaa....	aata
#2	Z47269	IGHV1-69*06	tgtgcgagag.	gggggggctaagg	....tcgaatttttggagtggtt.....	tcatgggt

	Input	J-REGION	J name	D name	Vmut	Dmut	Jmut	Ngc
#1	M62724	.....tttgactactgg	IGHJ4*02	IGHD5-24*01	0	2	0	1/7
#2	Z47269	...actggttcgacccctgg	IGHJ5*02	IGHD3-3*02	0	2	0	13/20

Translation of the JUNCTIONs

		104	105	106	107	108	109	110	111	111.1	111.2	111.3	112.4	112.3	112.2	112.1	112	113	114	115	116	117	118	frame	CDR3-IMGT length
			C	A	R	E	D	S	N	G									Y	K	I	F	D	Y	W	
#1	M62724		tgt	gcg	aga	gaa	gat	agc	aat	ggc									tac	aaa	ata	ttt	gac	tac	tgg	+	13
			C	A	R	G	G	A	K	V	E	F	L	E	W	F	H	G	Y	W	F	D	P	W		
#2	Z47269		tgt	gcg	aga	ggg	ggg	gct	aag	gtc	gaa	ttt	ttg	gag	tgg	ttt	cat	ggg	tac	tgg	ttc	gac	ccc	tgg	+	20

IMGT/JunctionAnalysis: analysis of the IG and TR junctions

IMGT/JunctionAnalysis Results

Locus IGH
Species Homo sapiens
IMGTrepertoire link Locus representation

Maximum number of mutations :
V-REGION : 2; D-REGION : 4; J-REGION : 2
Deletion criterium : Using patterns
Best D gene choice for a same score : Less mutations

http://www.imgt.org

Description of the JUNCTIONs

Click on mutated (underscored) nucleotid to see the original one: c

	Input	V name	V-REGION	P	N1	D-REGION	N2	P	J-REGION	J name	D name	Vmut	Dmut	Jmut	Ngc
#1	Z70256	IGHV2-26*01	tgtgtacg.....		tgttgt	.....gcagcgcctggtac	ccaaatatc		...actttgaccactgg	IGHJ4*02	IGHD6-13*01	1	2	1	5/15
#2	Z70257	IGHV3-7*02	tgtgcgag.		ggatgg	.....cagctcttatgcc	cgccc		ctactggtacttcgatctctgg	IGHJ2*01	IGHD2-2*01	0	2	0	9/11
#3	Z70606	IGHV4-31*03	tgtgcgagag.		c	.gactacg.....	cact		..atgcttttgatgtctgg	IGHJ3*01	IGHD4-17*01	0	0	0	3/5
#4	Z70608	IGHV4-39*05	tgtgc.		cagagta	.....acgatttttggagtggttatt.....	ccccgggggga		..atgcttttgatatctgg	IGHJ3*02	IGHD3-3*01	0	0	0	12/17
#5	Z70610	IGHV4-34*09	tgtgcgagag.		tcgggag	......cgatttttggagtggttatt.....	cccga	ca	tgatgcttttgatatctgg	IGHJ3*02	IGHD3-3*01	0	0	0	9/12
#6	Z70611	IGHV4-59*01	tgtgcgaga..		ca	.....tggtaactataa.	tgccggcgttg		...actggttcgacccctgg	IGHJ5*02	IGHD3-9*01	0	2	0	9/13
#7	Z70613	IGHV4-59*01	tgtgcgagag.			.....cagcagctggtac	ctccct		....ctttgactactgg	IGHJ4*02	IGHD6-13*01	0	0	0	4/6
#8	Z70614	IGHV4-59*01	tgtgcgaga..		cactataa	.....ttcggggacttat.....	cccctc		.....gactactgg	IGHJ4*02	IGHD3-16*01	0	2	0	7/14
#9	Z70615	IGHV4-59*01	tgtgcgagag.		ggctg	gtaaagaggg.....	tttcggaa		.tactggtacttcgatctctgg	IGHJ2*01	IGHD5-24*01	0	2	0	7/13
#10	Z70616	IGHV4-34*01	tgtgcgagag.		cgg	.....gtttggg.....	ttccc		...actggttcgacccctgg	IGHJ5*02	IGHD3-16*01	0	0	0	6/8
#11	Z70620	IGHV4-30-4*01	tgtgcgagaga		cc	.....ggggcgggatggtt.....	cgg		.gatgcttttgatatctgg	IGHJ3*02	IGHD3-16*01	1	4	0	5/5
#12	Z70621	IGHV4-39*01	tgtgcgagaca		ccacgatttatgg	.....ttcggggagtt.....	tgaccccc		.....ttgactactgg	IGHJ4*02	IGHD3-16*01	0	1	0	12/21
#13	Z70622	IGHV4-39*06	tgtgcgagaga	t	tgccccgctcctgccaaaat	gtattactatggttcgggga.....	tatgtacg		.....tttgactactgg	IGHJ4*03	IGHD3-10*01	0	0	0	15/28

Terminé

The 11 IMGT physicochemical AA classes

http://www.imgt.org

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

Pommié et al. J. Mol Recognit. 17, 17-32, 2004

IMGT/JunctionAnalysis: analysis of the IG and TR junctions

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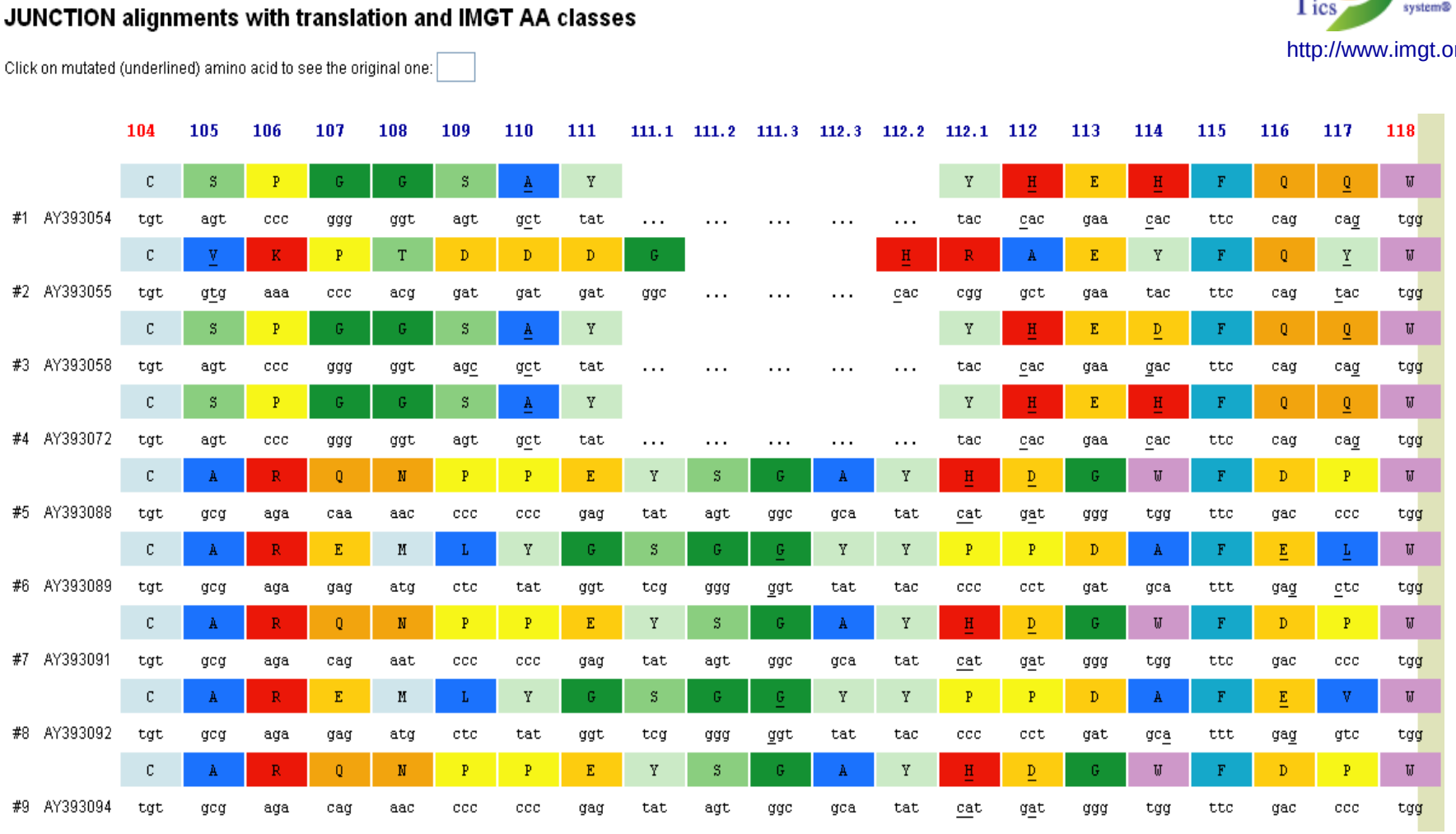
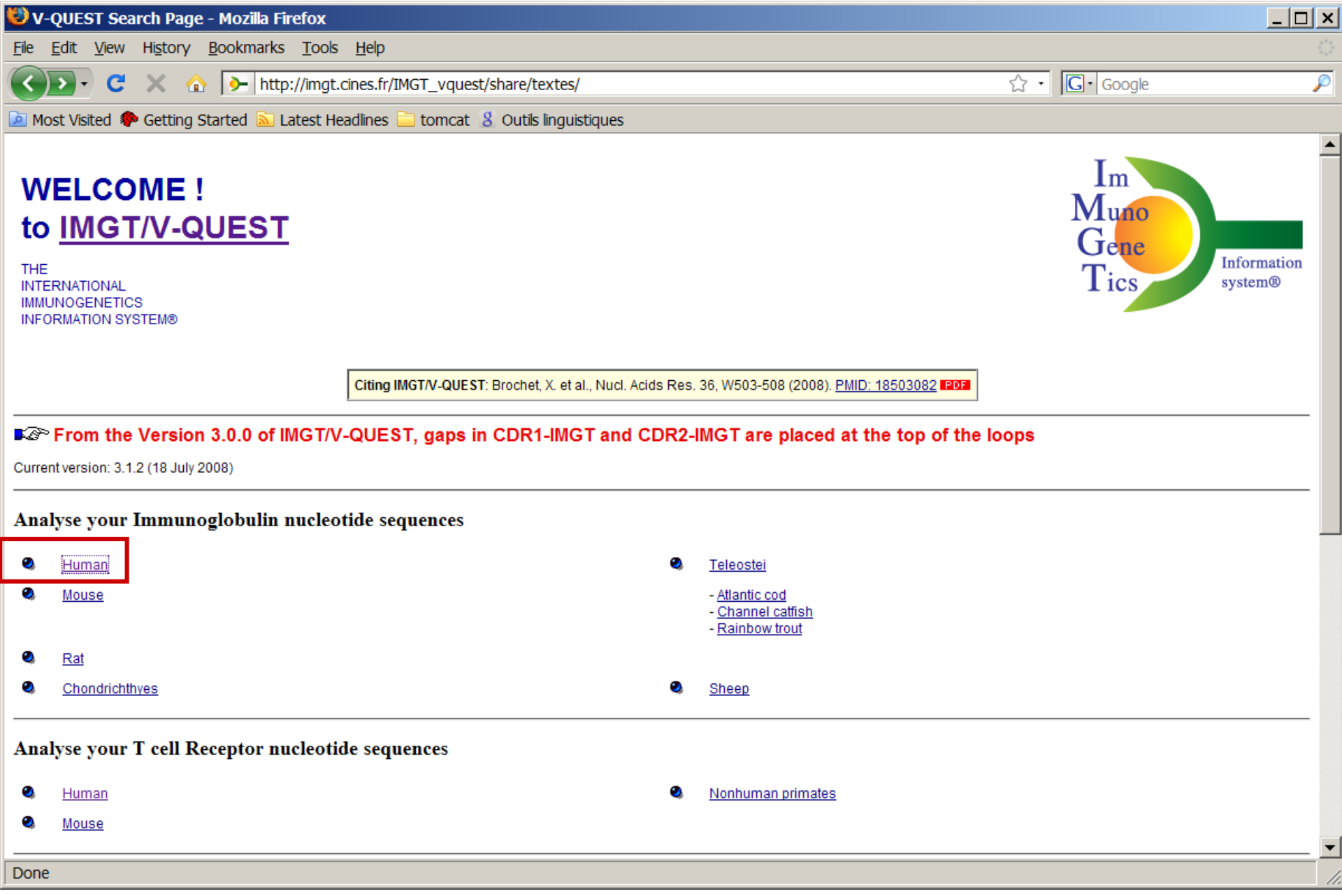


Yousfi Monod et al. Bioinformatics 20, i379-i385 (2004)
Pommié et al. J. Mol Recognit. 17, 17-32 (2004)

IMGT/V-QUEST http://www.imgt.org



IMGT/V-QUEST Search page

WELCOME !
to IMGT/V-QUEST Search page

THE
INTERNATIONAL
IMMUNOGENETICS
INFORMATION SYSTEM®

Im Muno Gene Tics Information system®

Citing IMGT/V-QUEST: Brochet, X. et al., Nucl. Acids Res. 36, W503-508 (2008). PMID: 18503082 PDF

From the Version 3.0.0 of IMGT/V-QUEST, gaps in CDR1-IMGT and CDR2-IMGT are placed at the top of the loops

Analyse your Immunoglobulin sequences

Your selection: Human

Your sequences are compared to the **Human *(Homo sapiens)* IG set** from the IMGT/V-QUEST reference directory s

Analysis by batches of up to 50 sequences in a single run

Nucleotide sequences

Sequence sets to test IMGT/V-QUEST are available here

Type (or copy/paste) your sequence(s) in FASTA format

```
>seq1
caggtgcagctggtgcagtctggagctgaggtgaagaagcctggggcctcagtgaaggtc
tcctgcaaggcttctggttacacctttaccagctatggtatcagctgggtgcgacaggcc
cctggacaagggcttgagtggatgggatggatcagcgcttacaatggtaacacaaactat
gcacagaagctccagggcagagtcaccatgaccacagacacatccacgagcacagcctac
atggagctgaggagcctgagatctgacgacacggccgtgtattactgtgcgagaggtata
cgtgcttttgatatctggggccaagggaccacggtcaccgtctcgagc
>seq1
caggtgcagctggtgcagtctggggctgaagtgaagaagcctgggtcctcggtgaaggtc
tcctgcaaggcttttggagtcaccttcagtagttacgctatcagctgggtgcgacaggcc
cctggacaagggcctgagtggatgggagggatcatccctttgttcggaaaggcaaactac
```

Or give the path access to a local file containing your sequence(s) in FASTA format

Browse...

Start | Clear the form

Done

IMGT/V-QUEST Selection for results display

http://www.imgt.org

```
>seq2
caggtgcagctggtgcagtctggggctgaagtgaagaagcctgggtcctcggtgaaggtc
tcctgcaaggcttttggagtcaccttcagtagttacgctatcagctgggtgcgacaggcc
cctggacaagggcctgagtggatgggagggatcatccctttgttcggaaaggcaaactac
```

Or give the path access to a local file containing your sequence(s) in FASTA format

Browse...

Start | Clear the form

Selection for results display

CLASSIFICATION

Export in text ☐ **Nb of nucleotides per line in alignments:** 60

A. Detailed view

1. ☑ Alignment for V-GENE
2. ☑ Alignment for D-GENE
3. ☑ Alignment for J-GENE
4. ☑ Results of IMGT/JunctionAnalysis
   - ○ with full list of eligible D-GENEs
   - ◉ without list of eligible D-GENEs
5. ☐ Sequence of the JUNCTION ('nt' and 'AA')
6. ☑ V-REGION alignment
7. ☑ V-REGION translation
8. ☑ V-REGION protein display
9. ☐ V-REGION mutation table
10. ☐ V-REGION mutation statistics
11. ☐ V-REGION mutation hot spots
12. IMGT Collier de Perles
    - ◉ link to IMGT/Collier-de-Perles tool
    - ○ IMGT Collier de Perles (for a nb of sequences < 5)
    - ○ no IMGT Collier de Perles
13. ☐ Sequences of V-, V-J- or V-D-J- REGION ('nt' and 'AA') with gaps in FASTA and access to IMGT/PhyloGene for V-REGION ('nt')
14. ☐ Annotation by IMGT/Automat

B. Synthesis view

1. ☑ Alignment for V-GENE
2. ☑ V-REGION alignment
3. ☑ V-REGION translation
4. ☑ V-REGION protein display
5. ☑ V-REGION protein display (with AA class colors)
6. ☑ V-REGION protein display (only AA changes displayed)
7. ☑ V-REGION most frequently occurring AA
8. ☑ Results of IMGT/JunctionAnalysis

Advanced parameters

Selection of IMGT reference directory set F+ORF+ in-frame P ◉ With all alleles ○ With allele *01 only

Search for insertions and deletions ◉ No ○ Yes (slower, the nb of submitted sequences in a single run is limited to 10)

Parameters for IMGT/JunctionAnalysis

Nb of D-GENEs in IGH JUNCTIONs (default is 1): default

Nb of accepted mutations: default in 3'V-REGION; default in D-REGION; default in 5'J-REGION

Done

IMGT/V-QUEST Selection for results display

http://www.imgt.org

```
>seq2
caggtgcagctggtgcagtctggggctgaagtgaagaagcctgggtcctcggtgaaggtc
tcctgcaaggcttttggagtcaccttcagtagttacgctatcagctgggtgcgacaggcc
cctggacaagggcctgagtggatgggagggatcatccctttgttcggaaaggcaaactac
```

Or give the path access to a local file containing your sequence(s) in FASTA format

Browse...

Start | Clear the form

Selection for results display

DESCRIPTION

Export in text ☐ **Nb of nucleotides per line in alignments:** 60

A. Detailed view

1. ☑ Alignment for V-GENE
2. ☑ Alignment for D-GENE
3. ☑ Alignment for J-GENE
4. ☑ Results of IMGT/JunctionAnalysis
   - ○ with full list of eligible D-GENEs
   - ◉ without list of eligible D-GENEs
5. ☐ Sequence of the JUNCTION ('nt' and 'AA')
6. ☑ V-REGION alignment
7. ☑ V-REGION translation
8. ☑ V-REGION protein display
9. ☐ V-REGION mutation table
10. ☐ V-REGION mutation statistics
11. ☐ V-REGION mutation hot spots
12. IMGT Collier de Perles
    - ◉ link to IMGT/Collier-de-Perles tool
    - ○ IMGT Collier de Perles (for a nb of sequences < 5)
    - ○ no IMGT Collier de Perles
13. ☐ Sequences of V-, V-J- or V-D-J- REGION ('nt' and 'AA') with gaps in FASTA and access to IMGT/PhyloGene for V-REGION ('nt')
14. ☐ Annotation by IMGT/Automat

B. Synthesis view

1. ☑ Alignment for V-GENE
2. ☑ V-REGION alignment
3. ☑ V-REGION translation
4. ☑ V-REGION protein display
5. ☑ V-REGION protein display (with AA class colors)
6. ☑ V-REGION protein display (only AA changes displayed)
7. ☑ V-REGION most frequently occurring AA
8. ☑ Results of IMGT/JunctionAnalysis

Advanced parameters

Selection of IMGT reference directory set F+ORF+ in-frame P ◉ With all alleles ○ With allele *01 only

Search for insertions and deletions ◉ No ○ Yes (slower, the nb of submitted sequences in a single run is limited to 10)

Parameters for IMGT/JunctionAnalysis

Nb of D-GENEs in IGH JUNCTIONs (default is 1): default

Nb of accepted mutations: default in 3'V-REGION; default in D-REGION; default in 5'J-REGION

Done

IMGT/V-QUEST Selection for results display

http://www.imgt.org

```
>seq2
caggtgcagctggtgcagtctggggctgaagtgaagaagcctgggtcctcggtgaaggtc
tcctgcaaggcttttggagtcaccttcagtagttacgctatcagctgggtgcgacaggcc
cctggacaagggcctgagtggatgggagggatcatccctttgttcggaaaggcaaactac
```

Or give the path access to a local file containing your sequence(s) in FASTA format

Browse...

Start | Clear the form

Selection for results display

NUMEROTATION

Export in text ☐ **Nb of nucleotides per line in alignments:** 60

A. Detailed view

1. ☑ Alignment for V-GENE
2. ☑ Alignment for D-GENE
3. ☑ Alignment for J-GENE
4. ☑ Results of IMGT/JunctionAnalysis
   - ○ with full list of eligible D-GENEs
   - ◉ without list of eligible D-GENEs
5. ☐ Sequence of the JUNCTION ('nt' and 'AA')
6. ☑ V-REGION alignment
7. ☑ V-REGION translation
8. ☑ V-REGION protein display
9. ☐ V-REGION mutation table
10. ☐ V-REGION mutation statistics
11. ☐ V-REGION mutation hot spots
12. IMGT Collier de Perles
    - ◉ link to IMGT/Collier-de-Perles tool
    - ○ IMGT Collier de Perles (for a nb of sequences < 5)
    - ○ no IMGT Collier de Perles
13. ☐ Sequences of V-, V-J- or V-D-J- REGION ('nt' and 'AA') with gaps in FASTA and access to IMGT/PhyloGene for V-REGION ('nt')
14. ☐ Annotation by IMGT/Automat

B. Synthesis view

1. ☑ Alignment for V-GENE
2. ☑ V-REGION alignment
3. ☑ V-REGION translation
4. ☑ V-REGION protein display
5. ☑ V-REGION protein display (with AA class colors)
6. ☑ V-REGION protein display (only AA changes displayed)
7. ☑ V-REGION most frequently occurring AA
8. ☑ Results of IMGT/JunctionAnalysis

Advanced parameters

Selection of IMGT reference directory set F+ORF+ in-frame P ◉ With all alleles ○ With allele *01 only

Search for insertions and deletions ◉ No ○ Yes (slower, the nb of submitted sequences in a single run is limited to 10)

Parameters for IMGT/JunctionAnalysis

Nb of D-GENEs in IGH JUNCTIONs (default is 1): default

Nb of accepted mutations: default in 3'V-REGION; default in D-REGION; default in 5'J-REGION

Done

IMGT/V-QUEST 'Detailed view': Result summary

http://www.imgt.org

Sequence number 1: AF184762

Sequence compared with the human IG set from the IMGT reference directory

>AF184762
atggagtttgggctgagctgggttttccttgttgctattttaaaaggtgtccactgtgag
gtgcagctggtggagtctgggggaggcttagtccagcctgggggatccctgaaactctcc
tgtgcagcctctgggttcaccctcagtggctcaaatgtgcactgggtccgccaggcctcc
gggaaagggctggagtgggttggccgtatcaaaaggaatgctgagtctgacgcgacagca
tatgctgcgtcgatgagaggcaggctcaccatctccagagatgattcaaagaacacggcg
tttctgcaaatgaacagcctgaaaagcgatgacacggccatgtattattgtgtgatccgg
ggagatgtttacaaccgacagtggggccagggaaccctggtcaccgtctcctcagcatcc
ccgaccagccccaaggtcttcccgctgagcctctgcagcacccagccagat

Automatic evaluation

Result summary:	**Productive IGH rearranged sequence** (no stop codon and in frame junction)		
V-GENE and allele	IGHV3-73*01	score = 1240	identity = **91,50%** (269/294 nt)
J-GENE and allele	IGHJ1*01 (b)	score = 179	identity = 82,69% (43/52 nt)
D-GENE and allele by IMGT/JunctionAnalysis	IGHD3-10*01	D-REGION is in reading frame 3	
[CDR1-IMGT.CDR2-IMGT.CDR3-IMGT] lengths and AA JUNCTION	[8.10.10]	CVIRGDVYNRQW	

(b) Other possibilities: IGHJ4*02 and IGHJ5*02 (highest number of consecutive identical nucleotides)

IMGT/V-QUEST provides **22 different output results** (analysis of IG nucleotide sequences and of their translation)

IMGT/V-QUEST 'Detailed view':
Result summary table

http://www.imgt.org

Number of analysed sequences: 4

seq1 seq2 seq3 seq4

☞ **This release of IMGT/V-QUEST uses IMGT/JunctionAnalysis for the analysis of the JUNCTION**

☞ **Hyphens (-) show nucleotide identity, dots (.) represent gaps**

Sequence number 1: seq1

Sequence compared with the human IG set from the IMGT reference directory

```
>seq1
caggtgcagctggtgcagtctggagctgaggtgaagaagcctggggcctcagtgaaggtc
tcctgcaaggcttctggttacacctttaccagctatggtatcagctgggtgcgacaggcc
cctggacaagggcttgagtggatgggatggatcagcgcttacaatggtaacacaaactat
gcacagaagctccagggcagagtcaccatgaccacagacacatccacgagcacagcctac
atggagctgaggagcctgagatctgacgacacggccgtgtattactgtgcgagaggtata
cgtgcttttgatatctggggccaagggaccacggtcaccgtctcgagc
```

CLASSIFICATION

Result summary:	Productive IGH rearranged sequence (no stop codon and in-frame junction)		
V-GENE and allele	IGHV1-18*01	score = 1426	identity = 99,65% (287/288 nt)
J-GENE and allele	IGHJ3*02 (a)	score = 164	identity = 81,63% (40/49 nt)
D-GENE and allele by IMGT/JunctionAnalysis	IGHD2-2*02	D-REGION is in reading frame 3	
[CDR1-IMGT.CDR2-IMGT.CDR3-IMGT] lengths and AA JUNCTION	[8.8.9]	CARGIRAFDIW	

(a) Other possibilities: IGHJ6*02 (highest number of consecutive identical nucleotides)

Done

IMGT/V-QUEST 'Detailed view':
Result summary table

http://www.imgt.org

Number of analysed sequences: 4

seq1 seq2 seq3 seq4

☞ **This release of IMGT/V-QUEST uses IMGT/JunctionAnalysis for the analysis of the JUNCTION**

☞ **Hyphens (-) show nucleotide identity, dots (.) represent gaps**

Sequence number 1: seq1

Sequence compared with the human IG set from the IMGT reference directory

```
>seq1
caggtgcagctggtgcagtctggagctgaggtgaagaagcctggggcctcagtgaaggtc
tcctgcaaggcttctggttacacctttaccagctatggtatcagctgggtgcgacaggcc
cctggacaagggcttgagtggatgggatggatcagcgcttacaatggtaacacaaactat
gcacagaagctccagggcagagtcaccatgaccacagacacatccacgagcacagcctac
atggagctgaggagcctgagatctgacgacacggccgtgtattactgtgcgagaggtata
cgtgcttttgatatctggggccaagggaccacggtcaccgtctcgagc
```

For D-GENE,
- other potential D
- mutation parameter
- amino acid sequence

Result summary:	Productive IGH rearranged sequence (no stop codon and in-frame junction)		
V-GENE and allele	IGHV1-18*01	score = 1426	identity = 99,65% (287/288 nt)
J-GENE and allele	IGHJ3*02 (a)	score = 164	identity = 81,63% (40/49 nt)
D-GENE and allele by IMGT/JunctionAnalysis	IGHD2-2*02	D-REGION is in reading frame 3	
[CDR1-IMGT.CDR2-IMGT.CDR3-IMGT] lengths and AA JUNCTION	[8.8.9]	CARGIRAFDIW	

(a) Other possibilities: IGHJ6*02 (highest number of consecutive identical nucleotides)

Done

IMGT/V-QUEST 'Detailed view':
Result summary table

http://www.imgt.org

Number of analysed sequences: 4

seq1 seq2 seq3 seq4

☞ **This release of IMGT/V-QUEST uses IMGT/JunctionAnalysis for the analysis of the JUNCTION**

☞ **Hyphens (-) show nucleotide identity, dots (.) represent gaps**

Sequence number 1: seq1

Sequence compared with the human IG set from the IMGT reference directory

```
>seq1
caggtgcagctggtgcagtctggagctgaggtgaagaagcctggggcctcagtgaaggtc
tcctgcaaggcttctggttacacctttaccagctatggtatcagctgggtgcgacaggcc
cctggacaagggcttgagtggatgggatggatcagcgcttacaatggtaacacaaactat
gcacagaagctccagggcagagtcaccatgaccacagacacatccacgagcacagcctac
atggagctgaggagcctgagatctgacgacacggccgtgtattactgtgcgagaggtata
cgtgcttttgatatctggggccaagggaccacggtcaccgtctcgagc
```

DESCRIPTION

NUMEROTATION

Result summary:	Productive IGH rearranged sequence (no stop codon and in-frame junction)		
V-GENE and allele	IGHV1-18*01	score = 1426	identity = 99,65% (287/288 nt)
J-GENE and allele	IGHJ3*02 (a)	score = 164	identity = 81,63% (40/49 nt)
D-GENE and allele by IMGT/JunctionAnalysis	IGHD2-2*02	D-REGION is in reading frame 3	
[CDR1-IMGT.CDR2-IMGT.CDR3-IMGT] lengths and AA JUNCTION	[8.8.9]	CARGIRAFDIW	

(a) Other possibilities: IGHJ6*02 (highest number of consecutive identical nucleotides)

Done

IMGT/V-QUEST 'Synthesis view':
Summary table

http://www.imgt.org

Number of analysed sequences: 7

CLASSIFICATION

Sequences compared with the human IG set from the IMGT reference directory

DESCRIPTION **NUMEROTATION**

Summary table:

Sequence ID	V-GENE and allele	Functionality	V-REGION score	V-REGION identity % (nt)	J-GENE and allele	D-GENE and allele	D-REGION reading frame	CDR-IMGT lengths	AA JUNCTION	JUNCTION frame
seq1	IGHV1-69*06	Productive	1050	95,63% (219/229 nt)	IGHJ3*02	IGHD3-16*02	2	[8.8.21]	CARGGDYDYIWGSYRASDAFDIW	in-frame
seq2	IGHV1-69*06	Productive	1300	94,79% (273/288 nt)	IGHJ4*01	IGHD6-13*01	1	[8.8.21]	CARERVGAYTSSWYGDYVSFDYW	in-frame
seq3	IGHV4-34*01	Productive	1411	99,30% (283/285 nt)	IGHJ6*02	IGHD2-2*02	3	[8.7.20]	CWIVVVPAAIVPNYYYYGMDVW	in-frame
seq4	IGHV4-34*01	Productive	1294	95,09% (271/285 nt)	IGHJ6*02	IGHD3-10*01	2	[8.7.20]	CARDFSPSPPGHYDARNDMDVW	in-frame
seq5	IGHV4-34*01	Productive	1285	94,74% (270/285 nt)	IGHJ6*03	IGHD3-22*01	2	[8.7.21]	CARWYYFDTSGYYPRNFYYMDVW	in-frame
seq6	IGHV4-34*01	Productive	1258	93,68% (267/285 nt)	IGHJ6*02	IGHD2-2*02	3	[8.7.25]	CARGHKTAIREPPTIGPIYYSYDMDVW	in-frame
seq7	IGHV4-34*01	Productive	1420	100,00% (285/285 nt)	IGHJ5*02	IGHD2-2*01	3	[8.7.25]	CARGDWRIVVVPAAVDTAMAANWFDPW	in-frame

Results of IMGT/JunctionAnalysis for : IGH junctions

Alignment with the closest alleles:

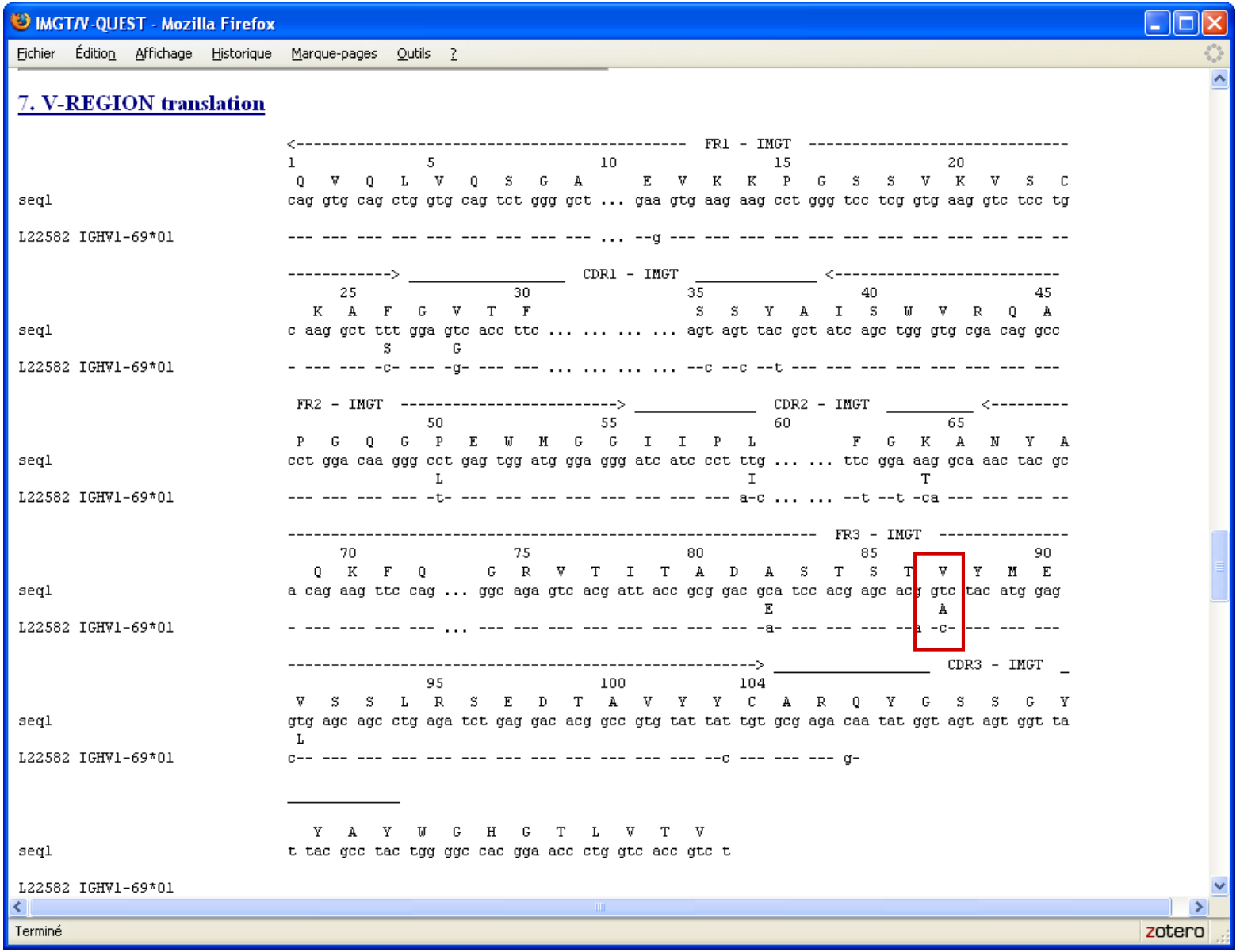
The analysed sequences are aligned with the closest allele (with number of aligned sequences in parentheses):

IGHV1-69*06(2) IGHV4-34*01(5)

Terminé zotero

IMGT/V-QUEST 'Detailed view':
7. V-REGION translation

http://www.imgt.org



IMGT/V-QUEST 'Synthesis view':
8. Results of IMGT/JunctionAnalysis

http://www.imgt.org

8. Results of IMGT/JunctionAnalysis

Results for the IGH junctions

Analysis of the JUNCTIONs

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

Input	V name	3'V-REGION	P	N1	P	D-REGION	N2	5'J-REGION	J name	D name	Vmut	Dmut	Jmut	Ngc
seq1	IGHV1-18*01	tgtgcgagaga		gcactcctcggc		...ctacagta.....	tgcggcggaaaggggt	....ctttcattactgg	IGHJ4*02	IGHD4-4*01	0	0	2	20/28
seq2	IGHV3-30*04	tgtgcgagaga		tcgga		..gtatagcagtggc.....	ccagt	actactttgactactgg	IGHJ4*02	IGHD6-19*01	0	0	0	6/10
seq3	IGHV3-30*04	tgtgcgagag.		gaaggacgaag		.....ggttcggggag.....	acccggc	......tacttccagcactgg	IGHJ1*01	IGHD3-10*01	0	0	0	12/18
seq4	IGHV3-30*04	tgtgcgagaga	t	tcctcctaccc	ccc	gggtatagcagcagctgg...	ag	......ttgantactgg	IGHJ4*02	IGHD6-13*01	0	0	1	8/13

Translation of the JUNCTIONs

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

		104	105	106	107	108	109	110	111	111.1	111.2	112.3	112.2	112.1	112	113	114	115	116	117	118	Frame	CDR3-IMGT length	Molecular mass	pI
		C	A	R	E	H	S	S	A	Y	S	M	R	R	K	G	V	F	H	Y	W				
#1	seq1	tgt	gcg	aga	gag	cac	tcc	tcg	gcc	tac	agt	atg	cgg	cgg	aaa	ggg	gtc	ttt	cat	tac	tgg	+	18	2,471.81	10.28
		C	A	R	D	R	S	I	A	V				A	Q	Y	Y	F	D	Y	W				
#2	seq2	tgt	gcg	aga	gat	cgg	agt	ata	gca	gtg	...	...	...	gcc	cag	tac	tac	ttt	gac	tac	tgg	+	15	2,127.37	6.58
		C	A	R	G	R	T	K	G	S			G	R	P	G	Y	F	Q	H	W				
#3	seq3	tgt	gcg	aga	gga	agg	acg	aag	ggt	tcg	...	...	ggg	aga	ccc	ggc	tac	ttc	cag	cac	tgg	+	16	2,064.32	11.72
		C	A	R	D	S	S	Y	P	P	G		I	A	A	A	G	V	X	Y	W				
#4	seq4	tgt	gcg	aga	gat	tcc	tcc	tac	ccc	ccg	ggt	...	ata	gca	gca	gct	gga	gtt	gan	tac	tgg	+	17	1,884.1	6.44

Done

IMGT/V-QUEST 'Detailed view':
9. V-REGION mutation table

http://www.imgt.org

Nucleotide substitution

Amino acid change

9. V-REGION mutation table

FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT
g33>a	g83>t, G28>V (- - -)	t149>c, L50>P (- - -)	a175>t, I59>L (+ + +)	a245>c, E82>A (- - -)	g319>c
c77>t, S26>F (- - -)	c105>t		c177>g, I59>L (+ + +)	a258>g	
	c108>t		t186>c	c260>t, A87>V (+ - +)	
	t111>c		t189>a	c271>g, L91>V (+ - +)	
			c191>a, T64>K (- - -)	c309>t	
			a192>g, T64>K (- - -)		

Terminé

zotero

IMGT/V-QUEST 'Detailed view':
9. V-REGION mutation table

http://www.imgt.org

Nucleotide substitution

Amino acid change

9. V-REGION mutation table

FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT
g33>a c77>t, S26>F (- - -)	g83>t, G28>V (- - -) c105>t c108>t t111>c	t149>c, L50>P (- - -)	a175>t, I59>L (+ + +) c177>g, I59>L (+ + +) t186>c t189>a c191>a, T64>K (- - -) a192>g, T64>K (- - -)	a245>c, E82>A (- - -) a258>g c260>t, A87>V (+ - +) c271>g, L91>V (+ + +) c309>t	g319>c

Terminé

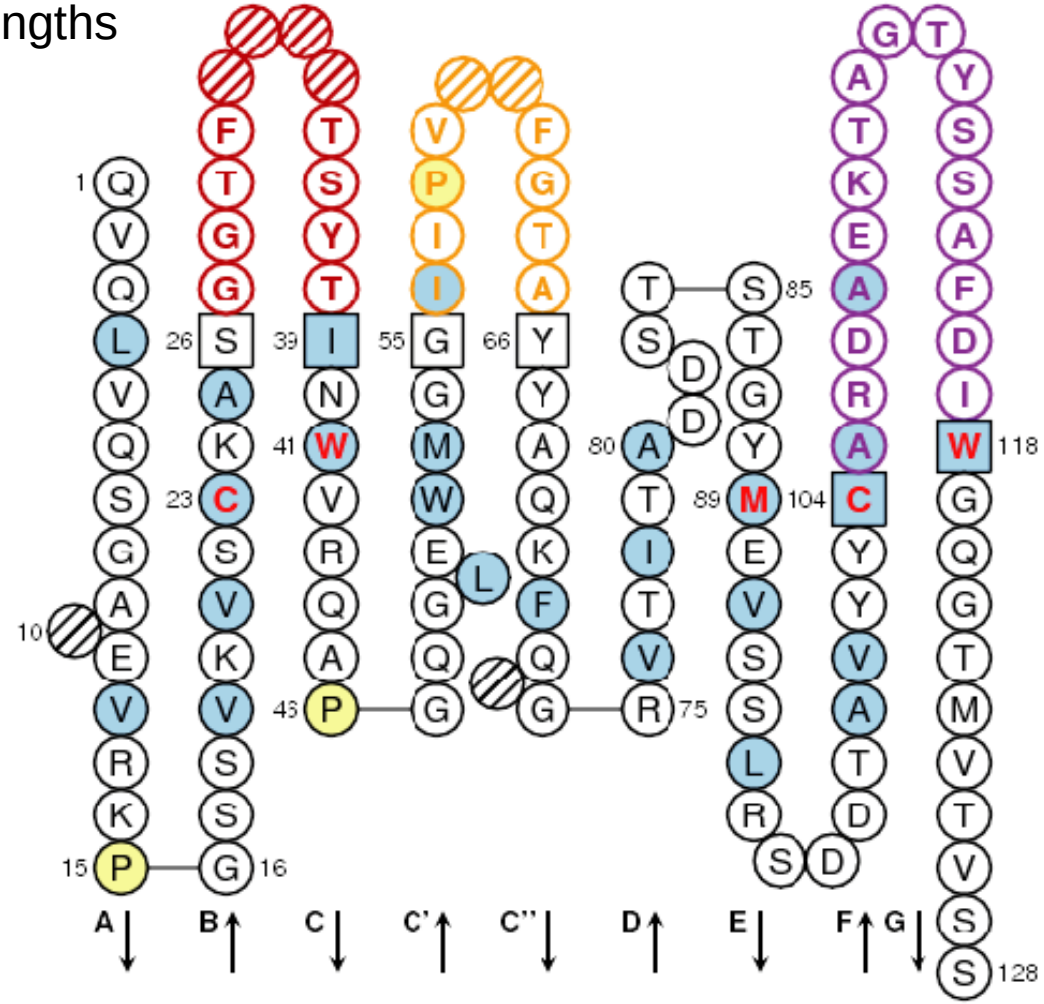
zotero

Hydropathy (+ : conserved classes)
Volume (- : different classes)
Physicochemical properties (+ : conserved classes)

IMGT/V-QUEST 'Detailed view':
12. Link to the IMGT/Collier-de-Perles tool

http://www.imgt.org

CDR-IMGT lengths
[8.8.17]



IMGT Collier de Perles for V-DOMAIN

Chronic lymphocytic leukemia (CLL) and IG

http://www.imgt.org

1. Two types de CLL with different clinical outcomes:

   ≥ 98% identity, IGHV 'nonmutated': agressive disease, unfavorable pronostic

   < 98% identity, IGHV 'mutated': less agressive disease, favorable pronostic

   Hamblin et al. Blood 1999, Damle et al. Blood 1999

2. Biased repertoire of the IG in the CLL

   Chiorazzi et al. N Engl J Med 2005; Ghia et al. Blood 2005; Stamatopoulos et al. Blood 2005

3. Stereotypes: limited nb of antibodies and therefore of Ag in leukemogenesis

   Tobin et al. Blood 2004; Ghia et al. Blood 2005; Stamatopoulos et al. Blood 2007

Results of the collaboration:

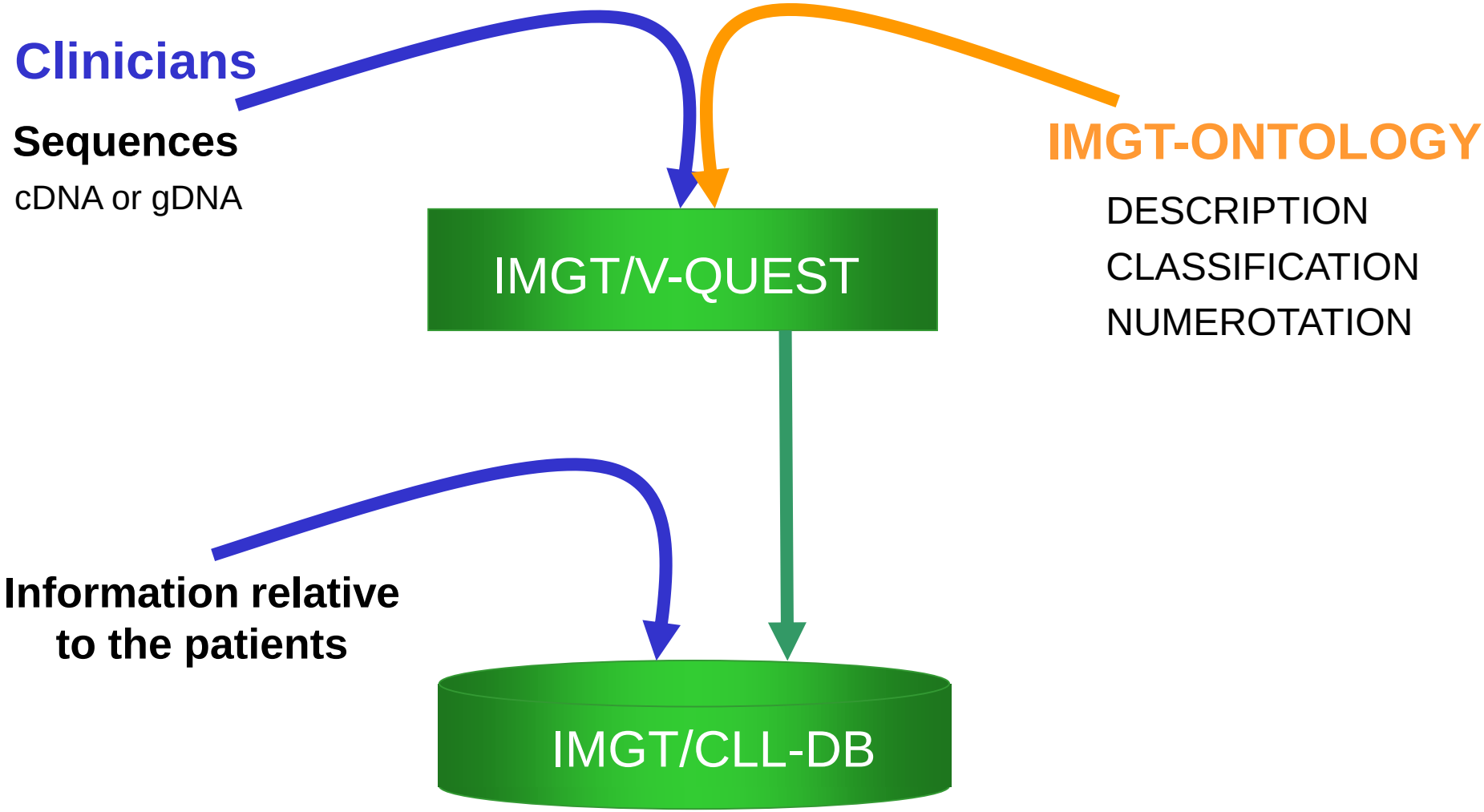
1. Recommandations of the European Research Initiative on CLL (ERIC) network

   Ghia et al. Leukemia 2007; Davi et al. Leukemia 2008

2. A book: *Immunoglobulin gene analysis in CLL, Ghia, Rosenquist and Davi. 8 chapters. 2009*
3. A database: IMGT/CLL-DB, Europe-USA Group, 2009

IMGT/CLL-DB

http://www.imgt.org



IMGT/CLL-DB

http://www.imgt.org

Sequence number 1: CLL000000011

Sequence compared with the human IG set from the IMGT reference directory

```
>CLL000000011
caggtgcagctgcaggagtcgggcccaggactggtgaagccttcacagaccctgtccctc
acctgcactgtctctggtggctccatcagcagtggtggttactactggagctggatccgc
cagcacccagggaagggcctggagtggattgggtacatctattacagtgggagcacctac
tacaacccgtccctcaagagtcgagttaccatatcagtagacacgtctaagaaccagttc
tccctgaagctgagctctgtgactgccgcggacacggccgtgtattactgtgcaaaggga
gctacggtgacccactttgactactggggccagggaaccctggtcaccgtctcctcag
```

IMGT/V-QUEST results

Result summary:	Productive IGH rearranged sequence (no stop codon and in frame junction)		
V-GENE and allele	IGHV4-31*03	score = 1450	identity = 100,00% (291/291 nt)
J-GENE and allele	IGHJ4*02	score = 222	identity = 95,83% (46/48 nt)
D-GENE and allele by IMGT/JunctionAnalysis	IGHD4-17*01	D-REGION is in reading frame 3	
[CDR1-IMGT.CDR2-IMGT.CDR3-IMGT] lengths and AA JUNCTION	[10.7.11]	CAKGATVTHFDYW	

1. Alignment for V-GENE and allele identification

Closest V-REGIONs (evaluated from the V-REGION first nucleotide to the 2nd-CYS codon)

		Score	Identity
Z14237	IGHV4-31*03	1450	100,00% (291/291 nt)
M99683	IGHV4-31*02	1441	99,66% (290/291 nt)
M95120	IGHV4-31*04	1441	99,66% (290/291 nt)
X92270	IGHV4-31*06	1441	99,66% (289/290 nt)
X92271	IGHV4-31*07	1441	99,66% (289/290 nt)

Alignment with FR-IMGT and CDR-IMGT delimitations

```
                          <---------------------------------- FR1-IMGT ---------------------------------->_____________ CDR1-IMGT ___________<-----
CLL000000011              caggtgcagctgcaggagtcgggccca...ggactggtgaagccttcacagaccctgtccctcacctgcactgtctctggtggctccatcagc......agtggtggttactactggagc
Z14237 IGHV4-31*03        ----------------------------...-------------------------------------------------------------......----------------------
M99683 IGHV4-31*02        ----------------------------...-----------------------------------------t-------------------......----------------------
M95120 IGHV4-31*04        -------g--------------------...-------------------------------------------------------------......----------------------
X92270 IGHV4-31*06        ----------------------------...-------------------------------------------------------------......------a---------------
X92271 IGHV4-31*07        ----------------------------...-----------------------------------------------a---------......----------------------
```

IMGT/CLL-DB

Mozilla Firefox

Fichier Édition Affichage Historique Marque-pages Outils ?

Your query:

IG chain type= 'Ig-Heavy'
V-REGION identity %>= '98.0%'
V-GENE and allele= 'IGHV1-69'
V-REGION identity %<= '100.0%'

Number of resulting sequences: 380

Number of resulting patients: 379 Click on Patient ID for IMGT/CLL-DB Patient card

IMGT Information system®

http://www.imgt.org

Select page | Clear page | Invert selection

IMGT/V-QUEST Synthesis view or Download selected Sequences in FASTA or Excel

Download all FASTA sequences or Excel file

Résultats de IMGT/V-QUEST

380 items found, displaying 1 to 50.

[First/Prev] **1**, 2, 3, 4, 5, 6, 7, 8 [Next/Last]

N°		IMGT/CLL-DB accession number	Sequence ID	Laboratory ID	Patient ID	Functionality	V-GENE and allele	V identity %	D-GENE and allele by IMGT/JunctionAnalysis	D reading frame	J-GENE and allele	JUNCTION AA	JUNCTION frame	CDR1-IMGT length
1	☑	CLL000000006	NY-01-0006-H1	CLL008VH1M	NY-01-0006	productive	IGHV1-69*01	100	IGHD3-10*01	2	IGHJ5*02	CARVWGGSGSYYIWFDPW	in-frame	8
2	☑	CLL000000008	NY-01-0008-H1	CLL014VH1M	NY-01-0008	productive	IGHV1-69*01	100	IGHD3-3*01	2	IGHJ6*03	CATKNDFWSGYYEGYYYYYYMDVW	in-frame	8
3	☑	CLL000000009	NY-01-0009-H1	CLL017VH1M	NY-01-0009	productive	IGHV1-69*02	100	IGHD3-3*01	2	IGHJ4*02	CATNYDFWSGYPYW	in-frame	8
4	☑	CLL000000030	NY-01-0030-H1	CLL051VH1M	NY-01-0030	productive	IGHV1-69*01	100	IGHD3-3*01	3	IGHJ6*03	CARVEIFGVVNLNYYYYYMDVW	in-frame	8
5	☑	CLL000000043	NY-01-0043-H1	CLL068VH1M	NY-01-0043	productive	IGHV1-69*06	100	IGHD3-16*02	2	IGHJ3*02	CARGGDYDYVWGSYRSNDAFDIW	in-frame	8
6	☑	CLL000000044	NY-01-0043-H2	CLL068VH3M	NY-01-0043	productive	IGHV1-69*06	100	IGHD3-16*02	2	IGHJ3*02	CARGGDYDYVWGSYRSNDAFDIW	in-frame	8
7	☑	CLL000000062	NY-01-0061-H1	CLL1001VH1M	NY-01-0061	productive	IGHV1-69*01	100	IGHD3-3*01	2	IGHJ6*02	CAREGNDDFWSGYYPNYYYYGMDVW	in-frame	8
8	☑	CLL000000071	NY-01-0070-H1	CLL1012VH1M	NY-01-0070	productive	IGHV1-69*01	100	IGHD3-3*01	3	IGHJ6*03	CARVEIFGVVGLSYYYYYMDVW	in-frame	8
9	☑	CLL000000074	NY-01-0073-H1	CLL1015VH1M	NY-01-0073	productive	IGHV1-69*01	100	IGHD3-3*01	2	IGHJ2*01	CARAEKYYDFWSGYSPRSYWYFDLW	in-frame	8
10	☑	CLL000000081	NY-01-0080-H1	CLL1025VH1M	NY-01-0080	productive	IGHV1-69*12	100	IGHD3-16*02	2	IGHJ2*01	CARVGPYDYVWGSYRYNLTDWYFDLW	in-frame	8
11	☑	CLL000000096	NY-01-0093-H1	CLL1041VH1	NY-01-0093	productive	IGHV1-69*01	100	IGHD3-3*01	3	IGHJ6*02	CAGGRLPITIFGVVITSGDGYYYGMDVW	in-frame	8
12	☑	CLL000000113	NY-01-0108-H1	CLL1073VH1	NY-01-0108	productive	IGHV1-69*01	100	IGHD1-26*01	3	IGHJ6*02	CAREGVSGSYQVYYYYYGMDVW	in-frame	8
13	☑	CLL000000131	NY-01-0126-H1	CLL1102VH1	NY-01-0126	productive	IGHV1-69*01	100	IGHD3-3*01	2	IGHJ6*03	CASGEQYYDFWSGYWDYYYMDVW	in-frame	8
14	☑	CLL000000132	NY-01-0127-H1	CLL1104VH1	NY-01-0127	productive	IGHV1-69*04	100	IGHD3-9*01	2	IGHJ5*02	CASVTGGYDILTGYSWFDPW	in-frame	8
15	☑	CLL000000135	NY-01-0130-H1	CLL1111VH1	NY-01-0130	productive	IGHV1-69*01	100	IGHD3-16*02	3	IGHJ6*02	CASAPLEITFGGVIVRWADYYYYYGMDVW	in-frame	8
16	☑	CLL000000137	NY-01-0132-H1	CLL1114VH1	NY-01-0132	productive	IGHV1-69*05	98,96	IGHD3-3*01	3	IGHJ6*03	CARDLDGHTIFGVVPLYYYYMDVW	in-frame	8
17	☑	CLL000000149	NY-01-0143-H1	CLL112VH1M	NY-01-0143	productive	IGHV1-69*01	100	IGHD2-21*02	2	IGHJ6*03	CARYGGGYNLFSYQLYYYYYMDVW	in-frame	8
18	☑	CLL000000153	NY-01-0147-H1	CLL1136VH1	NY-01-0147	productive	IGHV1-69*01	100	IGHD2-2*01	3	IGHJ6*03	CAREAVPAAMQGLVVSQRYYYYYMDVW	in-frame	8
19	☑	CLL000000166	NY-01-0160-H1	CLL1150VH1	NY-01-0160	productive	IGHV1-69*01	100	IGHD3-9*01	1	IGHJ5*02	CAREREQRFDWLFYNWFDPW	in-frame	8

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IMGT/DomainGapAlign

Sequence name: alemtuzumab_H

http://www.imgt.org

Move your mouse over the amino acids in bold for the characterization of AA class changes

Closest reference gene and allele(s) from the IMGT domain directory

V gene and allele	Species	Domain	Smith-Waterman Score	Identity percentage	Overlap
IGHV4-59*01	Homo sapiens	1	494	73.0	100

J gene and allele	Species	Domain	Smith-Waterman Score	Identity percentage	Overlap
IGHJ4*01	Homo sapiens	1	94	92.9	14
IGHJ4*02	Homo sapiens	1	94	92.9	14
IGHJ4*03	Homo sapiens	1	94	92.9	14

Alignment with the closest genes and alleles from the IMGT domain directory

```
                FR1-IMGT          CDR1-IMGT     FR2-IMGT      CDR2-IMGT                 FR3-IMGT                CDR3-IMGT   FR4-IMGT
                (1-26)            (27-38)       (39-55)       (56-65)                   (66-104)                (105-117)   (118-128)
                   A        B        BC       C       C'       C'C"      C"      D        E        F        FG          G
                (1-15)   (16-26)   (27-38)   (39-46) (47-55)   (56-65)   (66-74) (75-84)  (85-96)  (97-104) (105-117)   (118-128)
                ------>  ------>   ------>   ------> ------>   ------>   ------> ------>  ------>  ------>            ------>
1          10  15 16    23 26 27        38 3941  46 47     55 56      65 66     74 75   80 84 85  89    96 97   104 105 11112 117 118      128
|........|....| |......|..| |..........| |.|....| |.......| |........| |.......| |....|..| |...|......| |......| |.....||....| |..........|
alemtuzumab_H   QVQLQESGP.GLVRP SQTLSLTCTVS GFTF....TDFY MNWVRQPP GRGLEWIGF IRDKAKGYTT EYNPSVK.G RVTMLVDTSK NQFSLRLSSVTA ADTAVYYC AREGHTAAPFDYW GQGSLVTVSS.
IGHV4-59*01     QVQLQESGP.GLVKP SETLSLTCTVS GGSI....SSYY WSWIRQPP GKGLEWIGY IYYS...GST NYNPSLK.S RVTISVDTSK NQFSLKLSSVTA ADTAVYYC AR        FDYW GQGTLVTVSS.
(Homo sapiens)          R   Q        FTF   TDF  MN V      R      F  RDK   YT  E   V  G   ML          R                                S
|-------------------------------------------------------------------------------------------------------------------------------------|--N--||-----J-REGION-----|
                                                                V-REGION
```

Region(s) and domain(s) identified in your sequence (corresponding to the closest genes and alleles)

Without gaps — Sequence in FASTA format — Download

With gaps — Sequence in FASTA format — Download

```
QVQLQESGPGLVRPSQTLSLTCTVSGFTFTDFYMNWVRQPPGRGLEWIGF
IRDKAKGYTTEYNPSVKGRVTMLVDTSKNQFSLRLSSVTAADTAVYYCAR
EGHTAAPFDYWGQGSLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLV
KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQ
TYICNVNHKPSNTKVDKKVEAPELLGGPSVFLFPPKPKDTLMISRTPEVT
CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH
QDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTK
NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKL
TVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
```

IMGT Collier de Perles

Towards «Potential immunogenicity evaluation»

http://www.imgt.org

- Comparison with the closest human germline genes
- 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**

Magdelaine-Beuzelin C. et al. Crit. Rev. Oncol. Hemat. 64, 210-225 (2007)

Towards «Potential immunogenicity evaluation»

http://www.imgt.org

- Characteristics of the AA class changes

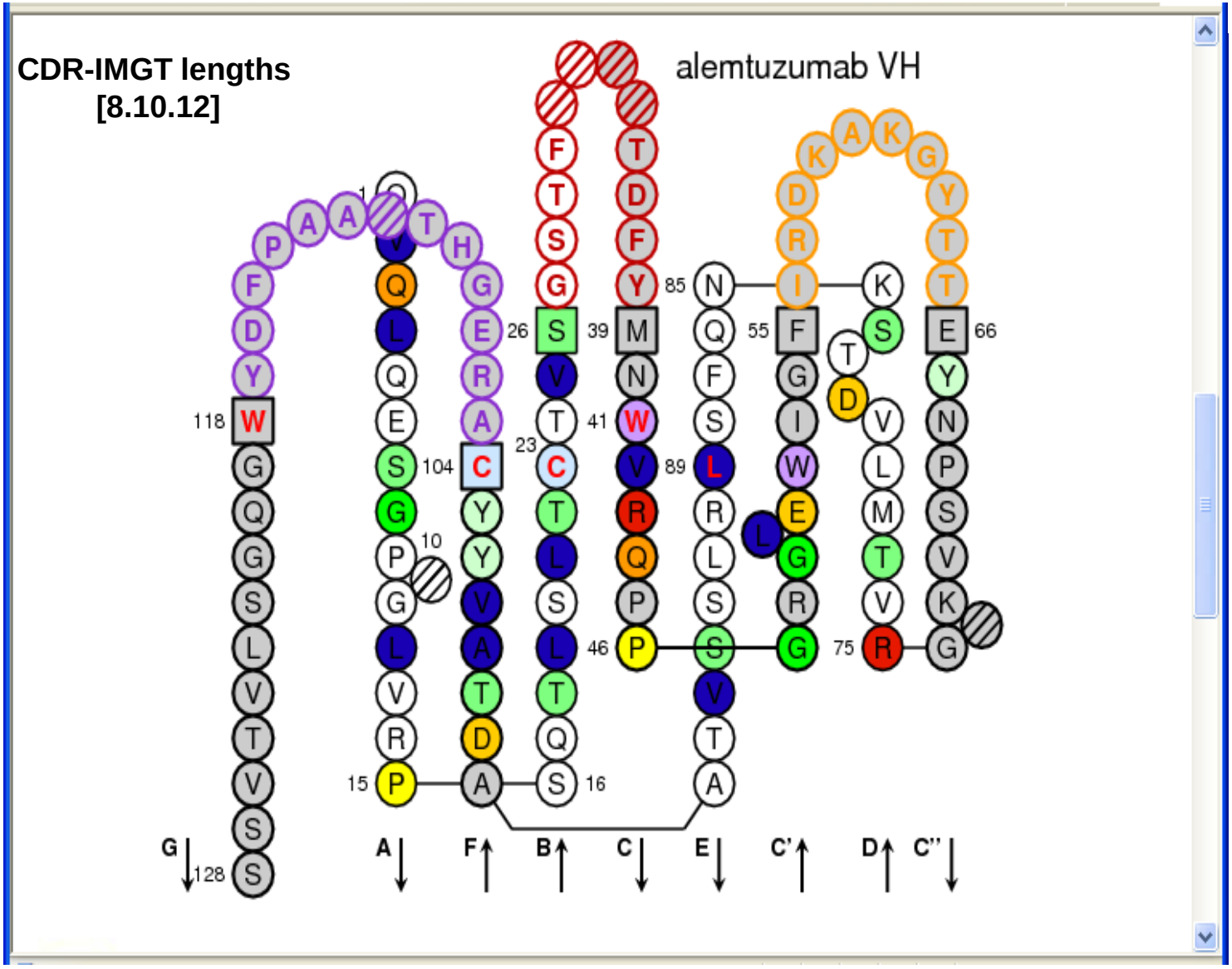
Sequence name	V-REGION identity percentage	CDR-IMGT lengths	Number of different AA in FR-IMGT	Number of AA class changes	List of AA class changes
alemtuzumab_H	73.0%	[8,10,13]	14	25	K14>R (+ + +) very similar E17>Q (+ + -) similar G28>F (- - -) very dissimilar S29>T (+ - +) similar I30>F (+ - -) dissimilar S35>T (+ - +) similar S36>D (- - -) very dissimilar Y37>F (- + -) dissimilar W39>M (+ - -) dissimilar S40>N (- - -) very dissimilar I42>V (+ - +) similar K48>R (+ + +) very similar Y55>F (- + -) dissimilar Y57>R (- - -) very dissimilar Y58>D (- - -) very dissimilar S59>K (- - -) very dissimilar G63>Y (+ - -) dissimilar S64>T (+ - +) similar N66>E (+ - -) dissimilar L71>V (+ - +) similar S74>G (+ + -) similar I78>M (+ + -) similar S79>L (- - -) very dissimilar K90>R (+ + +) very similar T121>S (+ - +) similar

V-REGION identity percent

14/91 different AA in FR-IMGT

IMGT Collier de Perles amino acid profile

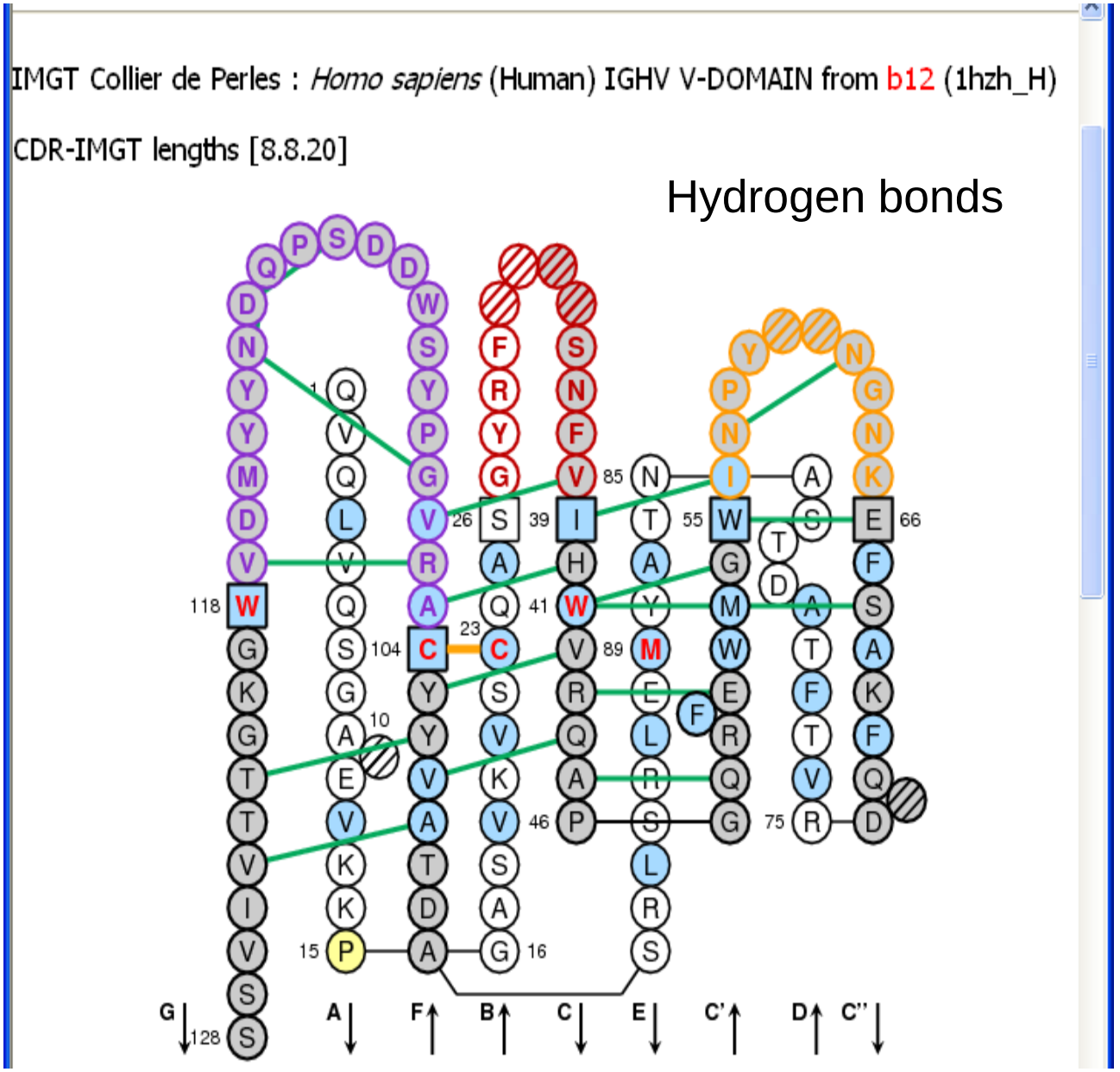
http://www.imgt.org



Pommié et al. J. Mol Recognit. 17, 17-32 (2004)

IMGT/3Dstructure-DB

http://www.imgt.org



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

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

http://www.imgt.org

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)

http://www.imgt.org

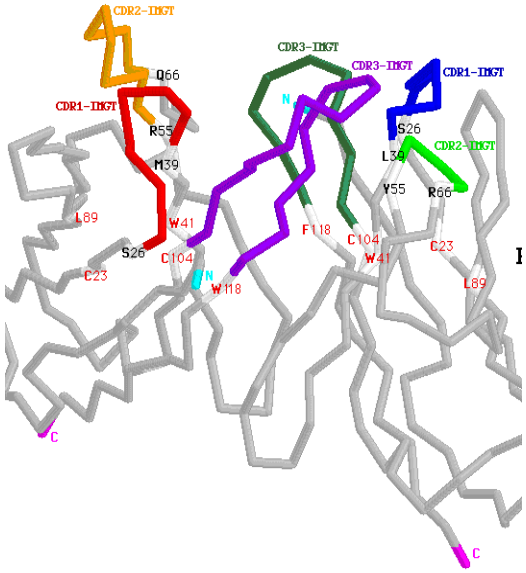
Summary:

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		Chain	Total	Polar	Hydrogen
R@P	38	TYR	Y	V-KAPPA	1ce1_L	3	SER	S	1ce1_P	1	0	0
R@P	38	TYR	Y	V-KAPPA	1ce1_L	5	PRO	P	1ce1_P	21	0	0
R@P	56	ASN	N	V-KAPPA	1ce1_L	3	SER	S	1ce1_P	3	2	0
R@P	107	HIS	H	V-KAPPA	1ce1_L	4	SER	S	1ce1_P	20	4	1
R@P	107	HIS	H	V-KAPPA	1ce1_L	5	PRO	P	1ce1_P	12	2	0
R@P	107	HIS	H	V-KAPPA	1ce1_L	6	SER	S	1ce1_P	14	3	1
R@P	108	ILE	I	V-KAPPA	1ce1_L	5	PRO	P	1ce1_P	12	1	0
R@P	108	ILE	I	V-KAPPA	1ce1_L	6	SER	S	1ce1_P	12	3	0
R@P	109	SER	S	V-KAPPA	1ce1_L	6	SER	S	1ce1_P	11	2	0
R@P	114	ARG	R	V-KAPPA	1ce1_L	6	SER	S	1ce1_P	18	3	1
R@P	114	ARG	R	V-KAPPA	1ce1_L	7	ALA	A	1ce1_P	4	2	0
R@P	114	ARG	R	V-KAPPA	1ce1_L	8	ASP	D	1ce1_P	6	2	0
R@P	116	ARG	R	V-KAPPA	1ce1_L	2	THR	T	1ce1_P	1	1	0
R@P	116	ARG	R	V-KAPPA	1ce1_L	4	SER	S	1ce1_P	9	4	1
R@P	116	ARG	R	V-KAPPA	1ce1_L	6	SER	S	1ce1_P	20	6	1
R@P	116	ARG	R	V-KAPPA	1ce1_L	7	ALA	A	1ce1_P	7	2	0

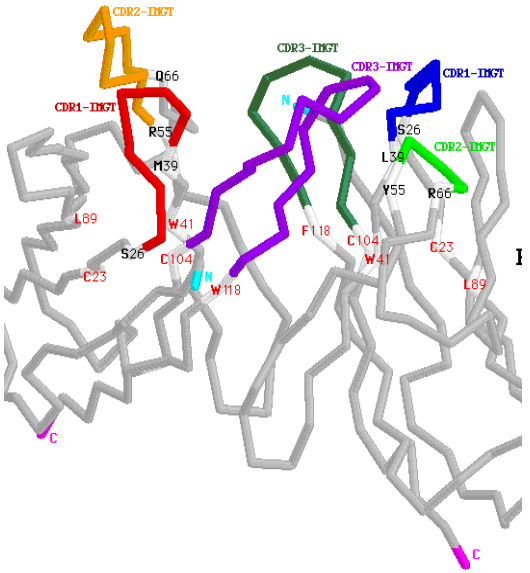


Kaas Q. et al.
Nucl. Acids Res. (2004)

Contacts VH-(Ligand)

Im Muno Gene Tics Information system®
http://www.imgt.org

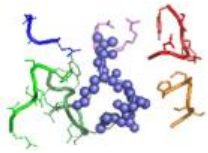
	IMGT Num	Residue		Domain	Chain		IMGT Num	Residue		Domain	Chain	Total	Polar	Hydrogen
R@P	38	TYR	Y	VH	1ce1_H	R@P	2	THR	T		1ce1_P	4	0	0
R@P	38	TYR	Y	VH	1ce1_H	R@P	7	ALA	A		1ce1_P	13	1	0
R@P	38	TYR	Y	VH	1ce1_H	R@P	8	ASP	D		1ce1_P	14	2	2
R@P	55	PHE	F	VH	1ce1_H	R@P	6	SER	S		1ce1_P	5	0	0
R@P	55	PHE	F	VH	1ce1_H	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	naptumomab 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	aflibercept	INN	FUSION-FLT1-KDR-FC-GAMMA-1	*Homo sapiens*	L95 (2006)	R57 (2007)	862111-32-8
15	8750	rilonacept, 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	8942	anrukinzumab	INN	IG-GAMMA-1_KAPPA	*Humanized*	L98 (2007)	R60 (2008)	910649-32-0

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IMGT/2Dstructure-DB

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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)
	[V-REGION EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAED]N-AND[J-REGION][CH1 TAVYYCSRWGGDGFYAMDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS][HINGE-REGION][

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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)

Chain sequence

```
[                                          V-REGION
EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAED
       ]N-AND[    J-REGION     ][                                                  CH1
TAVYYCSRWGGDGFYAMDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS
                                        ][HINGE-REGION ][
GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDTPPPCPRCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS
                 CH2                                                              ][
HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE
                                       CH3                                                 ]
LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
```

Sequence in FASTA format *Sequence in IMGT format*

V-DOMAIN

IMGT domain description	VH
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*

```
                          [   CDR1    ]                  [  CDR2  ]
EVQLVESGG.GLVQPGGSLRLSCAASGFNI....KDTYIHWVRQAPGKGLEWVARIYPT..NGYTRYADSVK.GRFTISADTSKNTAYLQ
               [   CDR3    ]
MNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVSS
```

IMGT/DomainGapAlign results

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mAb-DB

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

Search by:

Search Reset

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

Search Reset

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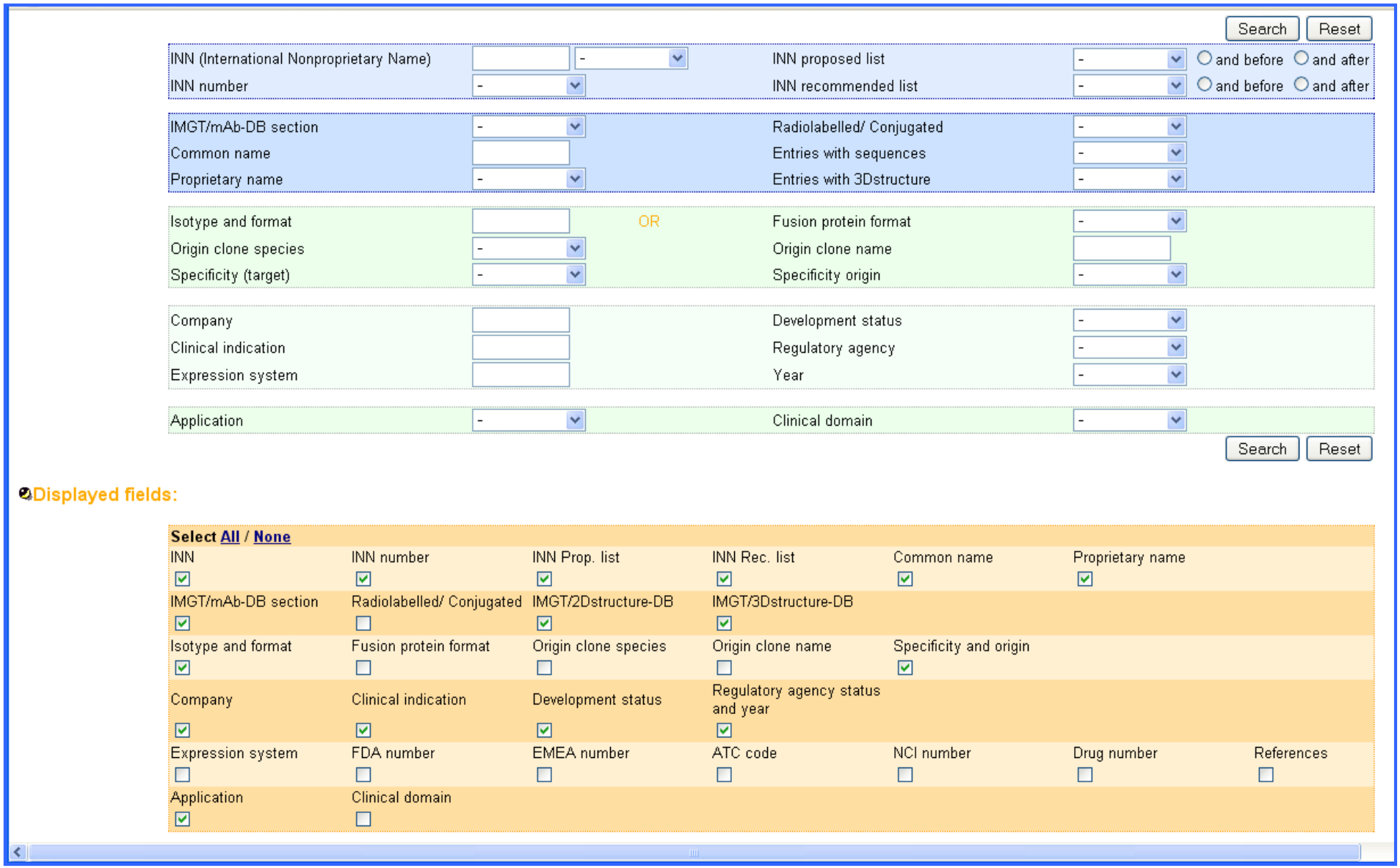
IMGT/mAb-DB



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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	IgG1κ	ERBB2 (Epidermal Growth Factor Receptor 2; HER-2; p185c-erbB2; NEU; EGFR2) [*Homo sapiens*]	F. 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

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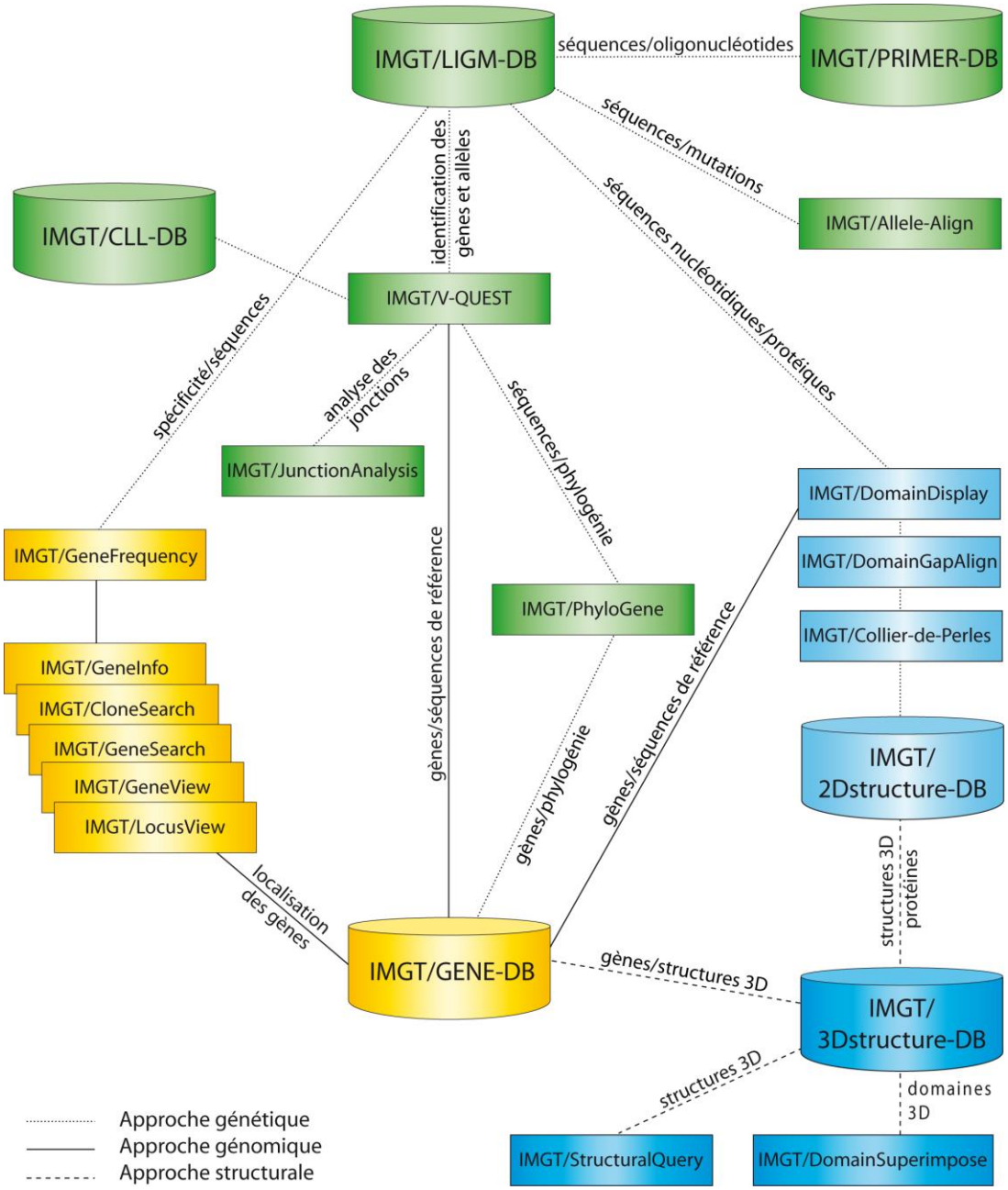

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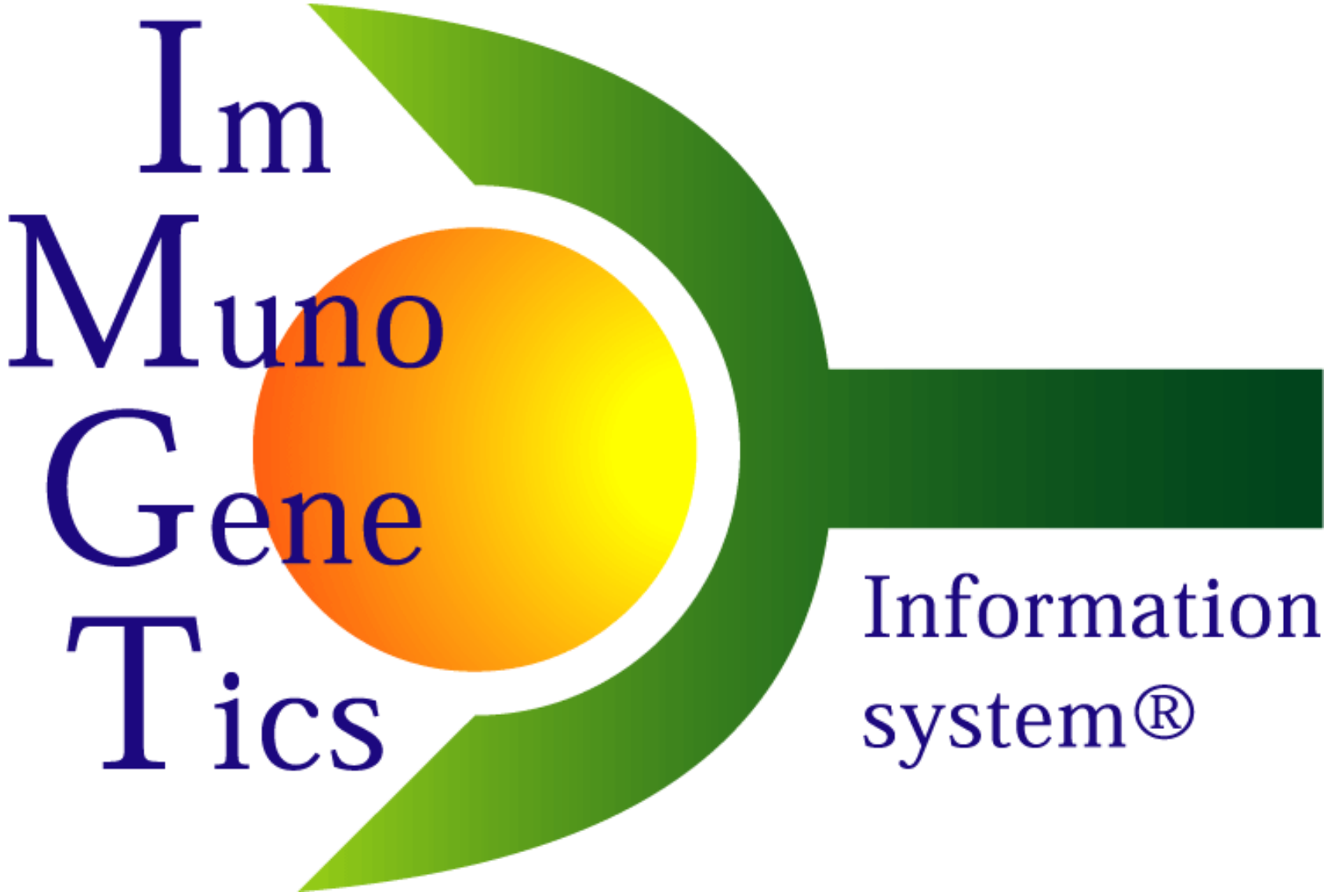
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