Plateforme IMGT®
Bases de données anticorps

http://www.imgt.org

Marie-Paule Lefranc

IMGT Founder and Director

Professor, Montpellier 2 University, CNRS, Montpellier, France

Module Anticorps monoclonaux

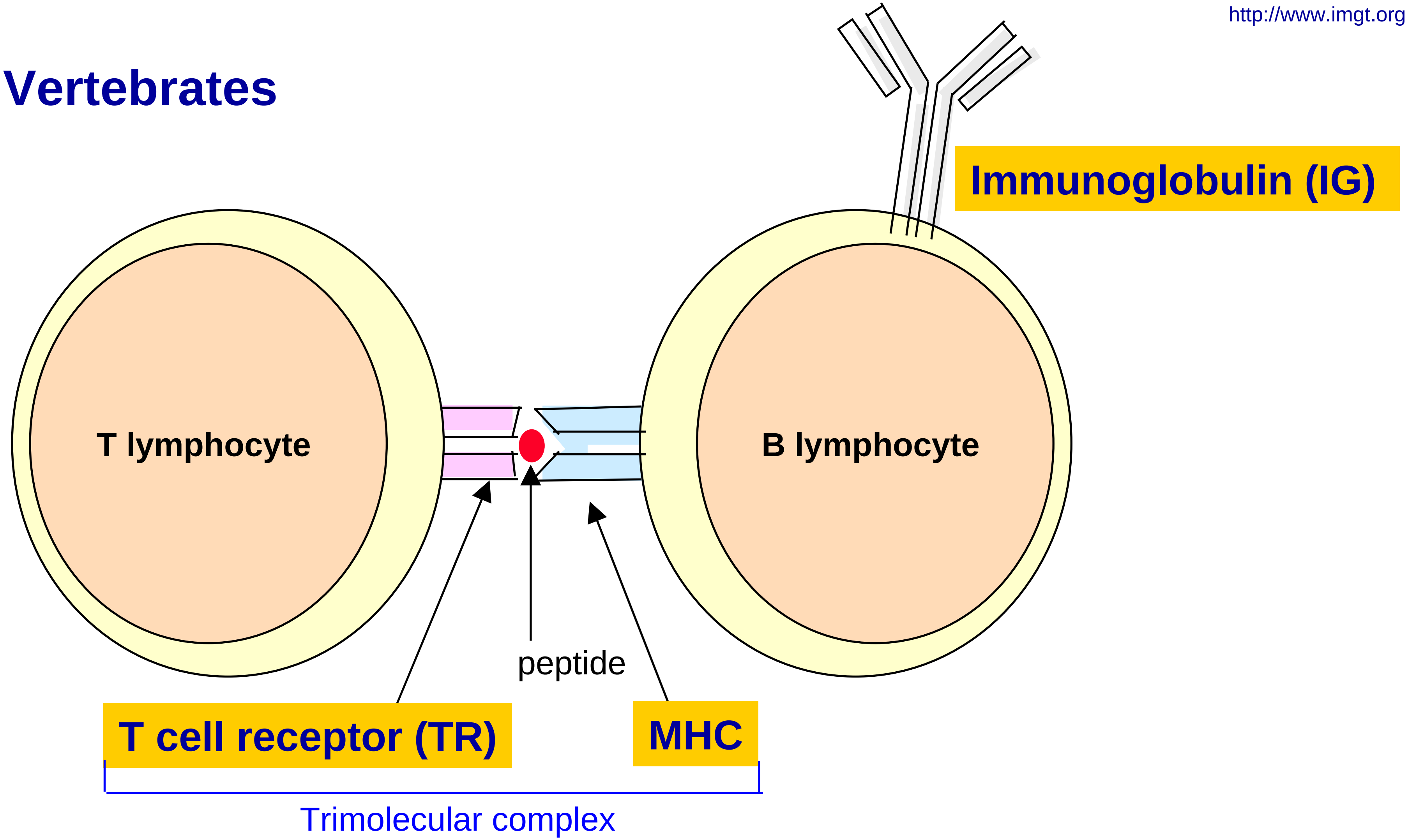
Parcours Immunotechnologies et Biothérapies

UPMC, Paris, 11 0ctobre 2010

IMGT®: the adaptive immune response

http://www.imgt.org

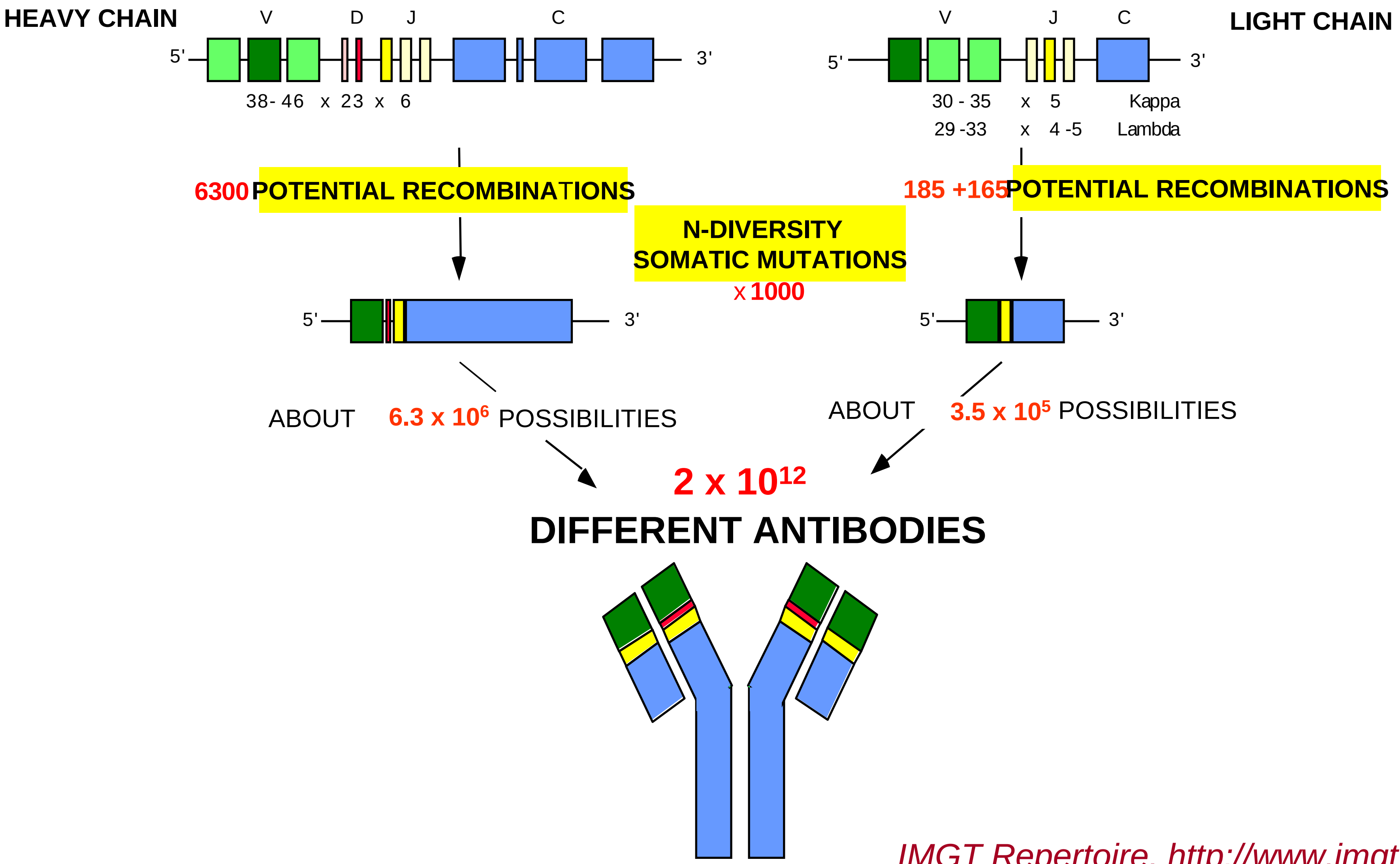
Vertebrates



Immunoglobulin (IG) synthesis

http://www.imgt.org

150
FUNCTIONAL IG GENES



HEAVY CHAIN

38- 46 x 23 x 6

LIGHT CHAIN

30 - 35 x 5 Kappa
29 -33 x 4 -5 Lambda

6300 POTENTIAL RECOMBINATIONS

185 +165 POTENTIAL RECOMBINATIONS

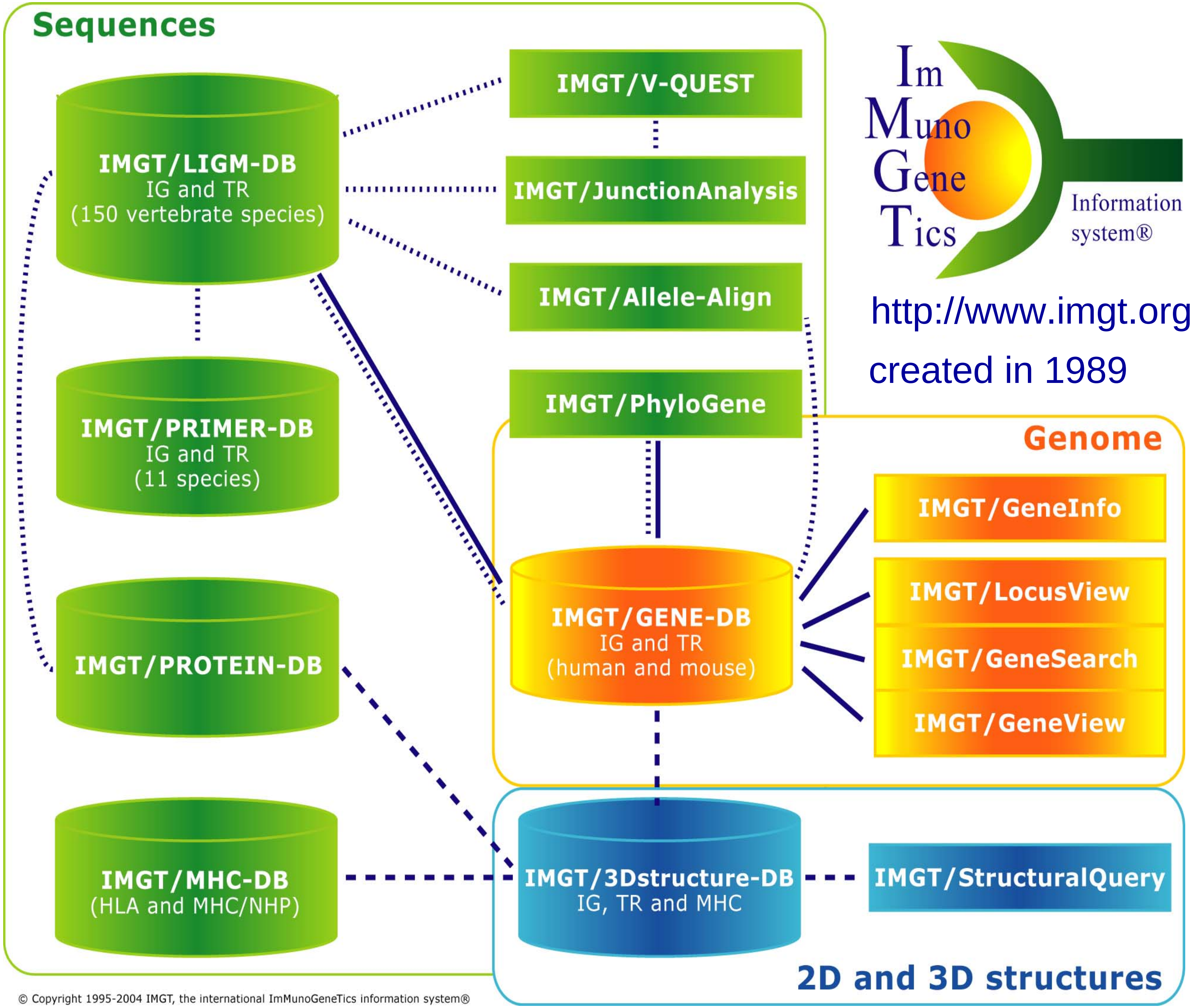
N-DIVERSITY
SOMATIC MUTATIONS
x 1000

ABOUT **6.3 x 10^6** POSSIBILITIES

ABOUT **3.5 x 10^5** POSSIBILITIES

2 x 10^{12}
DIFFERENT ANTIBODIES

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



ImMunoGeneTics Information system®

http://www.imgt.org

created in 1989

Sequences

IMGT/LIGM-DB
IG and TR
(150 vertebrate species)

IMGT/PRIMER-DB
IG and TR
(11 species)

IMGT/PROTEIN-DB

IMGT/MHC-DB
(HLA and MHC/NHP)

IMGT/V-QUEST

IMGT/JunctionAnalysis

IMGT/Allele-Align

IMGT/PhyloGene

Genome

IMGT/GENE-DB
IG and TR
(human and mouse)

IMGT/GeneInfo

IMGT/LocusView

IMGT/GeneSearch

IMGT/GeneView

2D and 3D structures

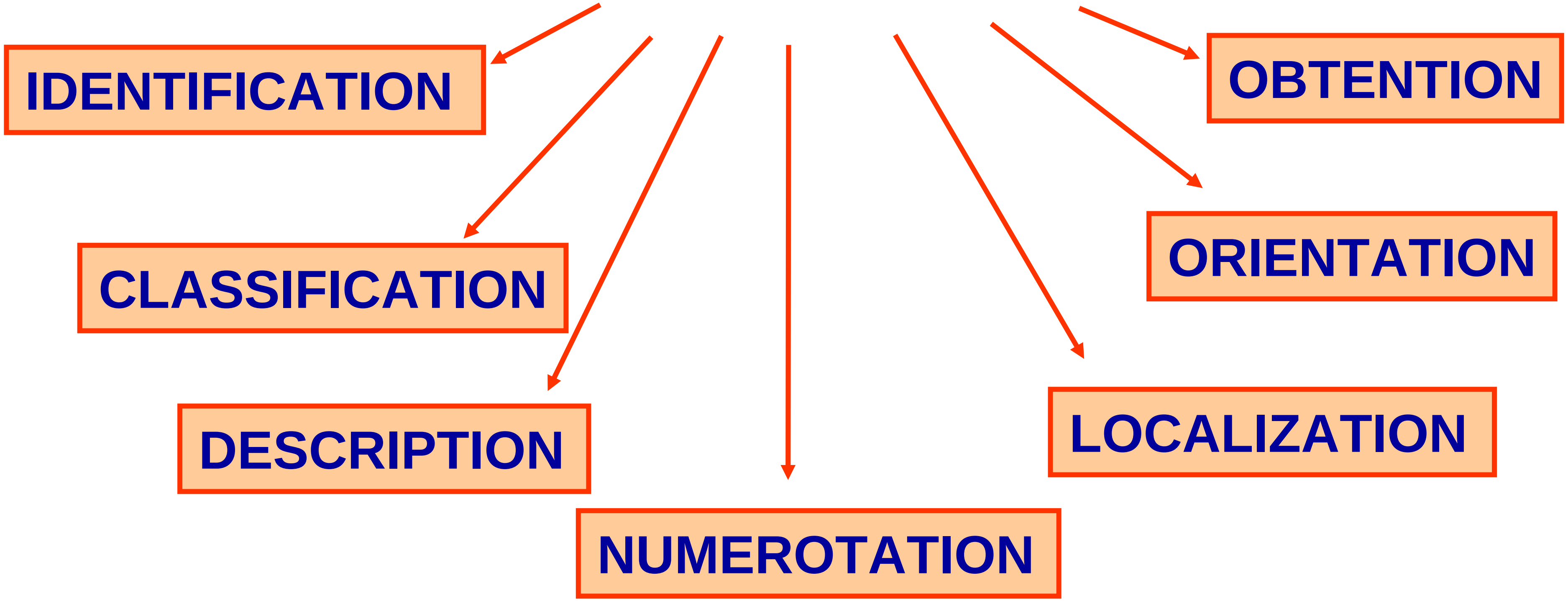
IMGT/3Dstructure-DB
IG, TR and MHC

IMGT/StructuralQuery

IMGT standards based on IMGT-ONTOLOGY

IMGT-ONTOLOGY seven axioms:

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



IDENTIFICATION

CLASSIFICATION

DESCRIPTION

NUMEROTATION

LOCALIZATION

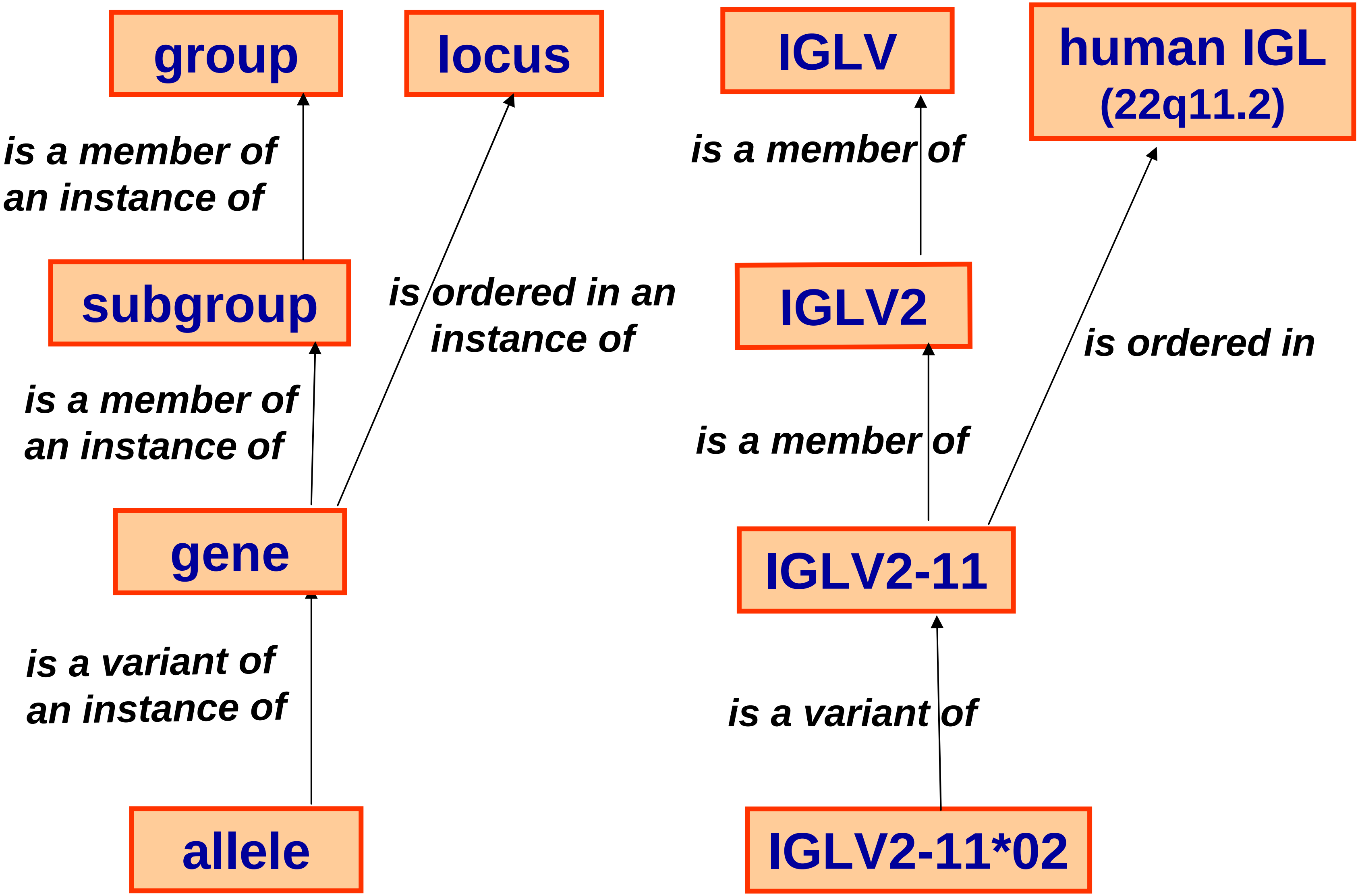
ORIENTATION

OBTENTION

Giudicelli and Lefranc, Bioinformatics (1999)

CLASSIFICATION axiom

http://www.imgt.org



group

is a member of
an instance of

subgroup

is a member of
an instance of

gene

is a variant of
an instance of

allele

locus

is ordered in an
instance of

IGLV

is a member of

IGLV2

is a member of

IGLV2-11

is a variant of

IGLV2-11*02

human IGL
(22q11.2)

is ordered in

« 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.

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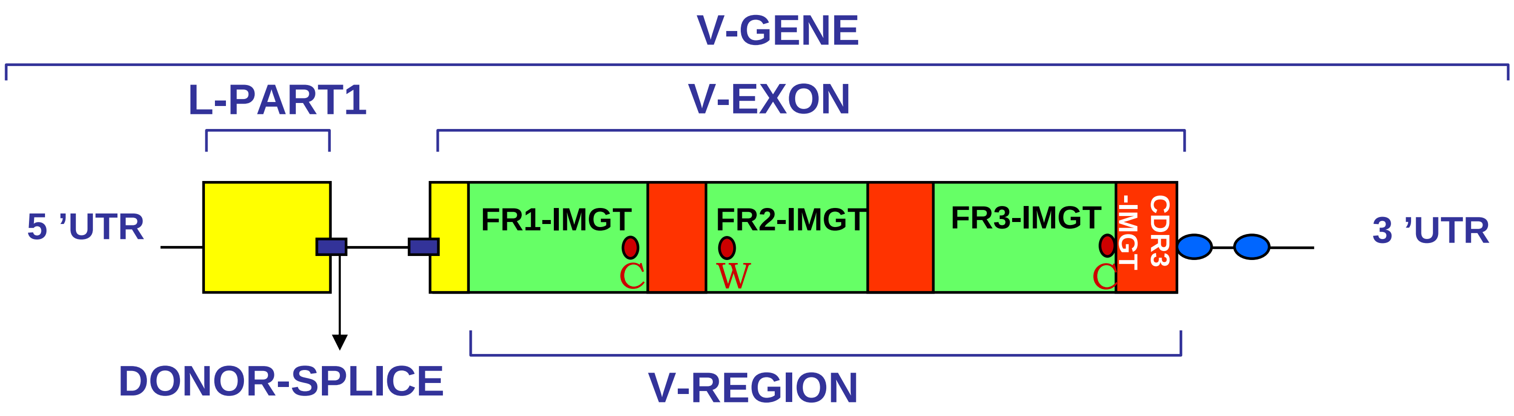
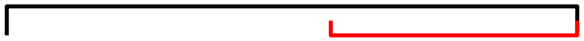
DESCRIPTION axiom

http://www.imgt.org

PROTOTYPE for a V-GENE

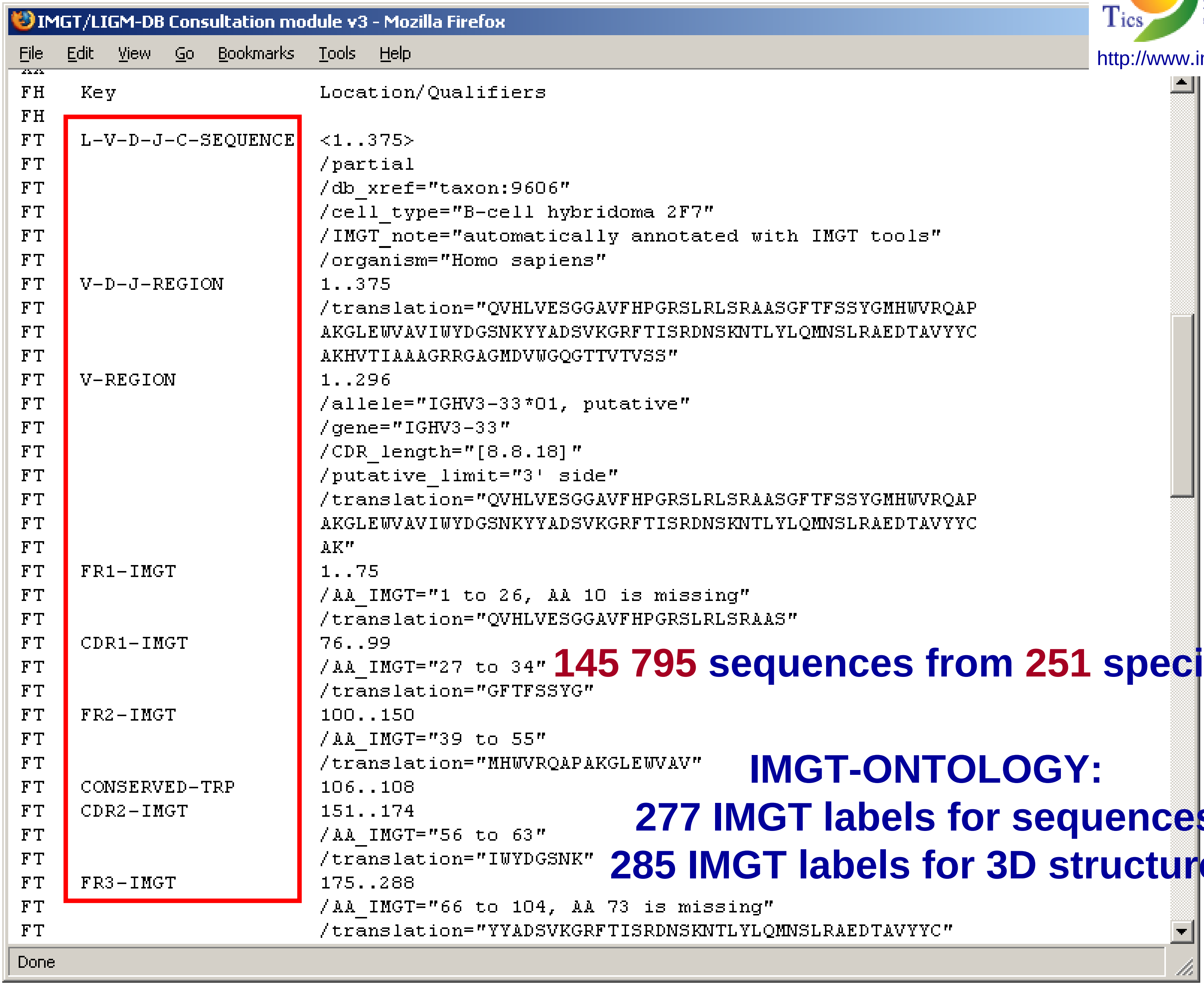


Label 1	Label 2	Relations entre Labels
V-GENE	V-EXON	
FR3-IMGT	CDR3-IMGT	
L-PART1	DONOR-SPLICE	
V-REGION	FR1-IMGT	
V-REGION	CDR3-IMGT	

IMGT/LIGM-DB

http://www.imgt.org

DESCRIPTION



```
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"
```

145 795 sequences from 251 species

IMGT-ONTOLOGY:

277 IMGT labels for sequences

285 IMGT labels for 3D structures

Concepts of DESCRIPTION

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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http://www.imgt.org

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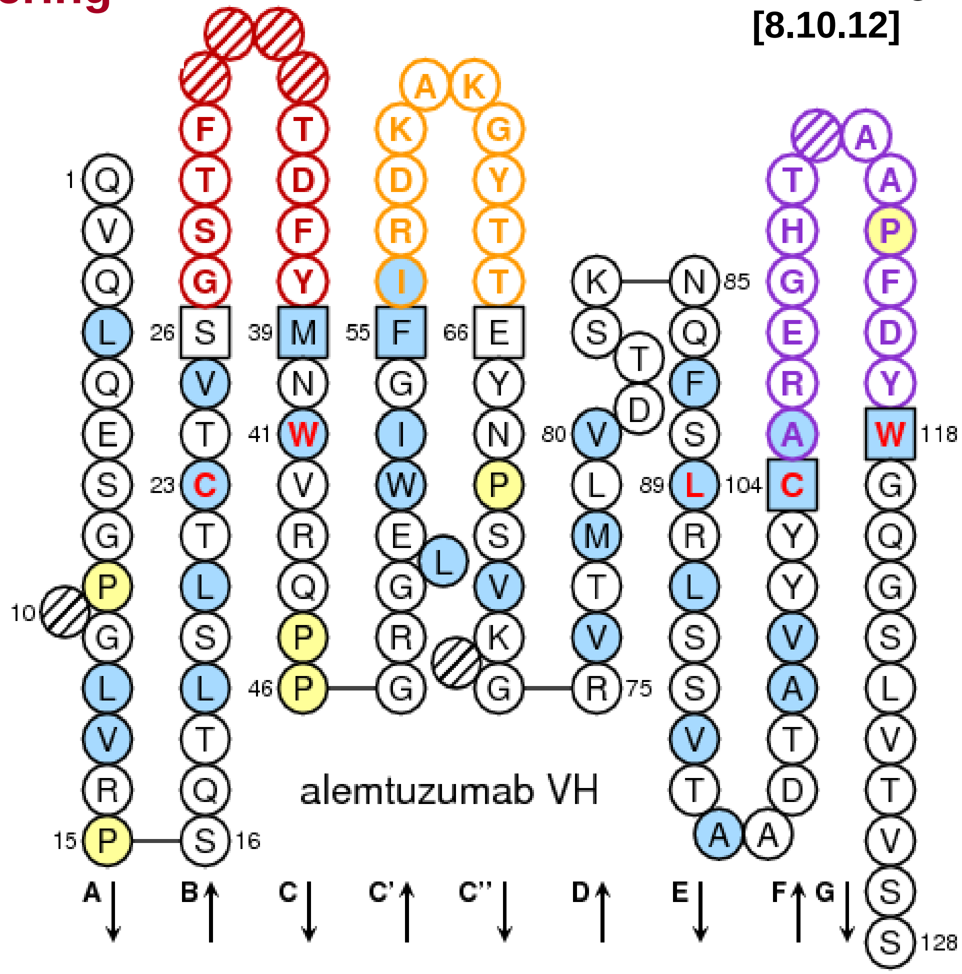
NUMEROTATION axiom

http://www.imgt.org

IMGT Collier de Perles

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



CDR-IMGT lengths
[8.10.12]

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

NUMEROTATION axiom

http://www.imgt.org

IMGT Collier de Perles

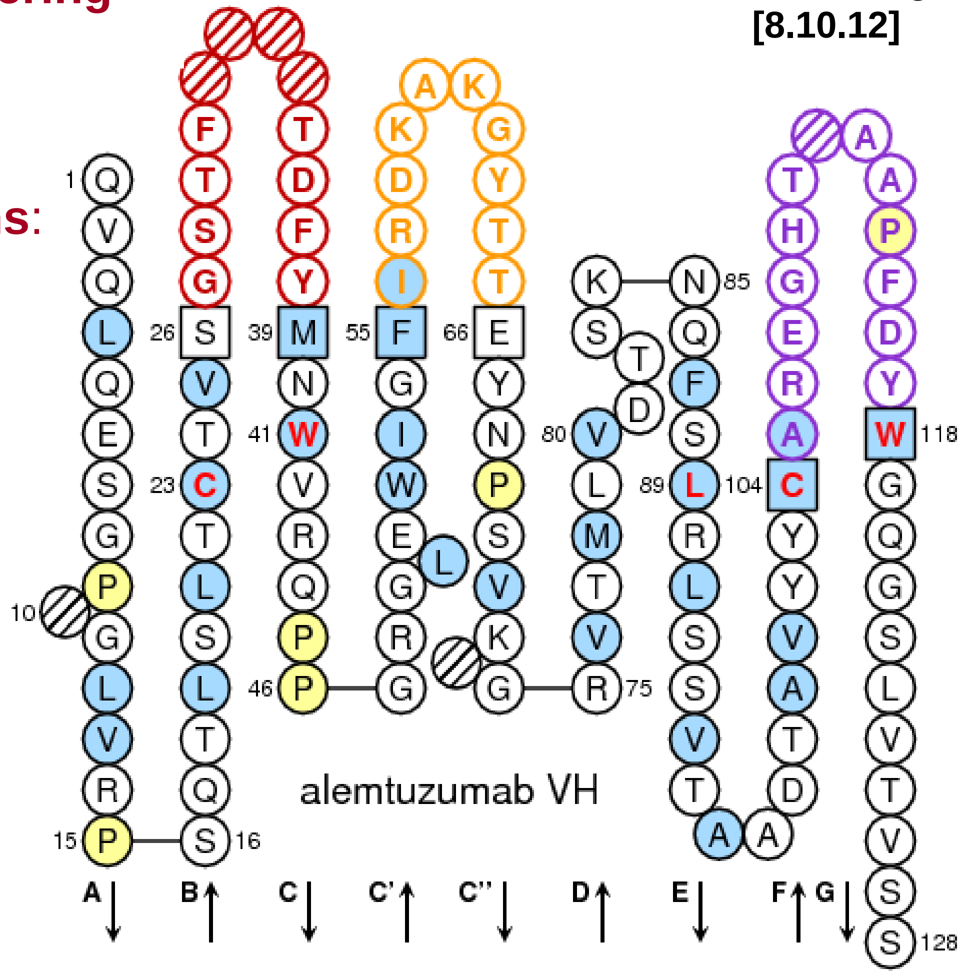
Based on the **IMGT unique numbering** (first one in **1997**)

- 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



CDR-IMGT lengths [8.10.12]

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

Concepts of NUMEROTATION

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 and V-LIKE-DOMAIN)
- the constant domains (C-DOMAIN and C-LIKE-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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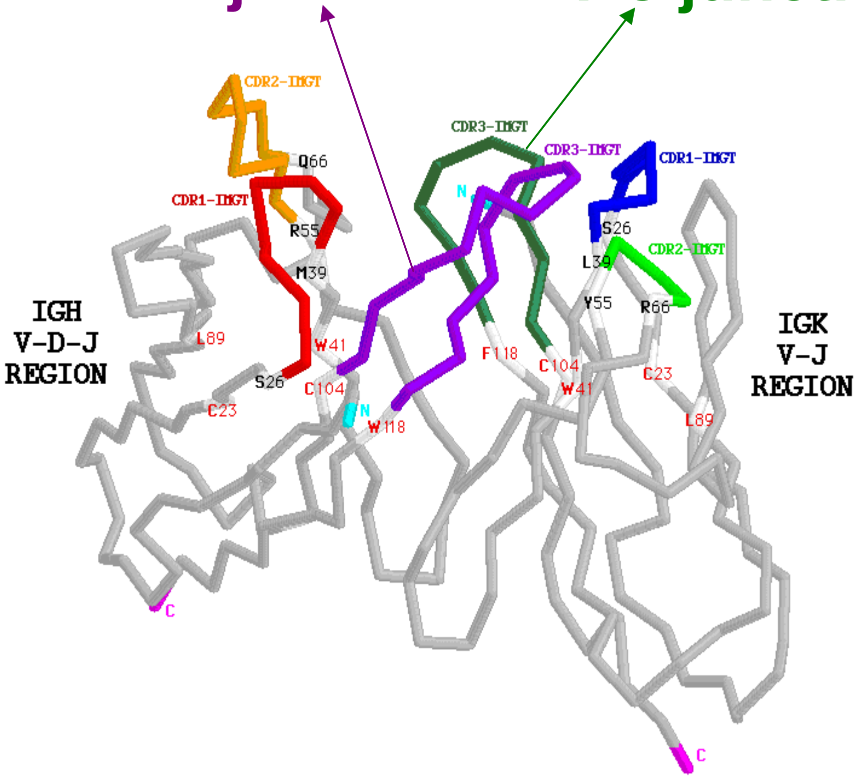
V-DOMAIN: VH and V-KAPPA

http://www.imgt.org

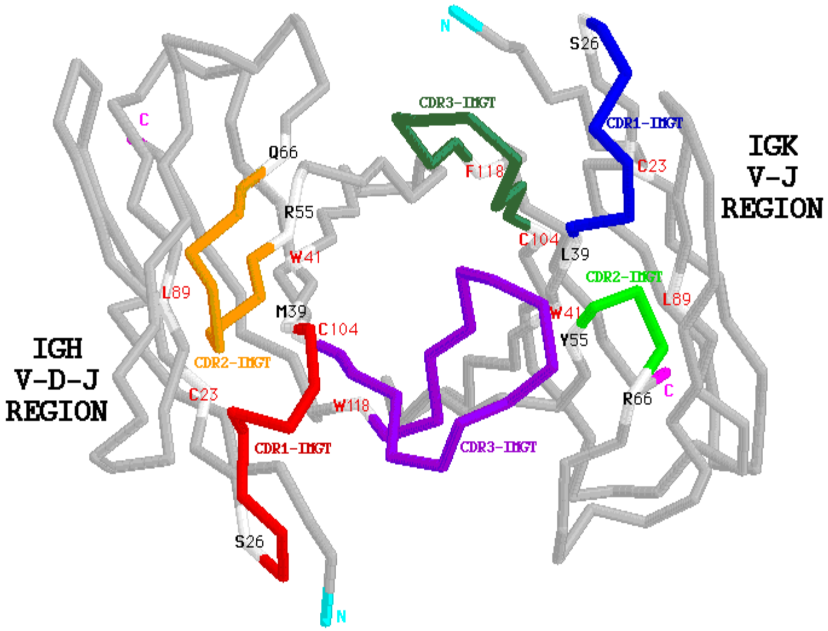
VH **V-KAPPA**

V-D-J junction **V-J junction**



Side view of the V-DOMAIN

VH **V-KAPPA**



View from above the CDR-IMGT

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

IMGT® http://www.imgt.org

Immunoglobulin V-D-J generation of sequence diversity

http://www.imgt.org

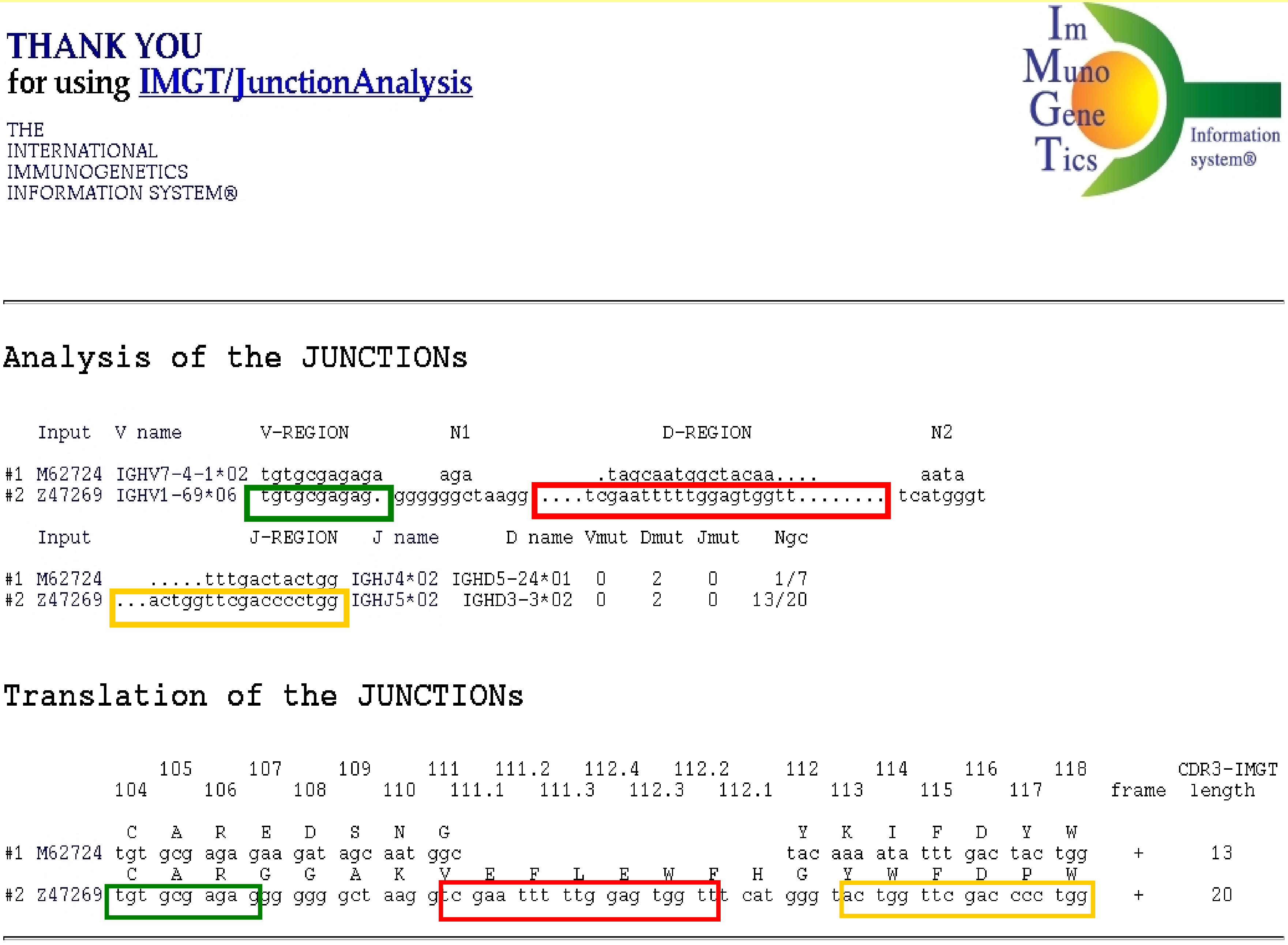
3’V-REGION N-REGION D-REGION N-REGION 5’J-REGION

tgtgcgaaaga tacc agcatattgtggtggtgactgctattcc gat acaactggttcgactcc**tgg**

JUNCTION

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. gggggctaagg ....tcgaattttggagtggtt........ 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
```

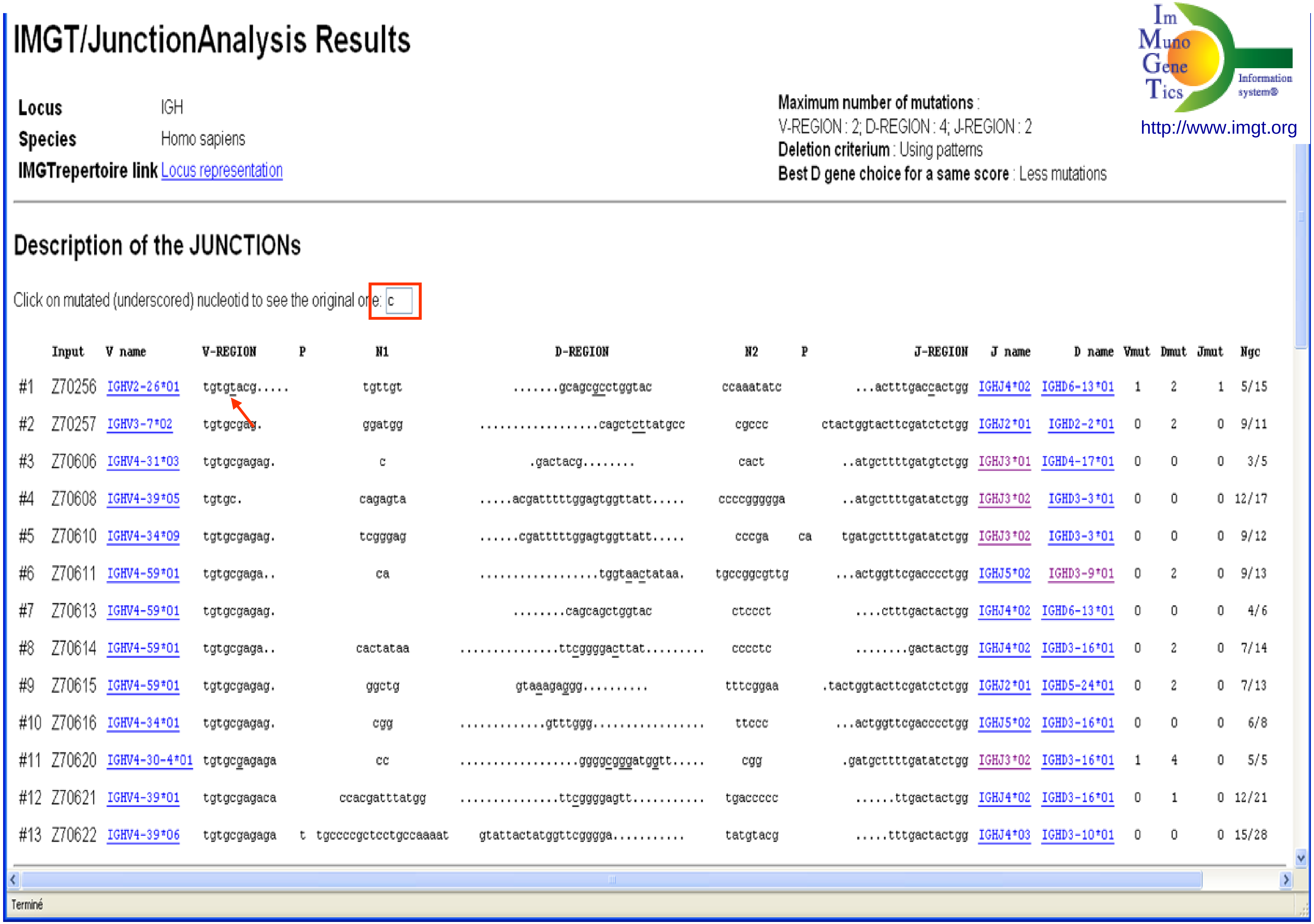
Translation of the JUNCTIONs

```
              105     107     109     111   111.2   112.4   112.2     112     114     116     118         CDR3-IMGT
          104     106     108     110   111.1   111.3   112.3   112.1     113     115     117       frame  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

http://www.imgt.org



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

Description of the JUNCTIONs

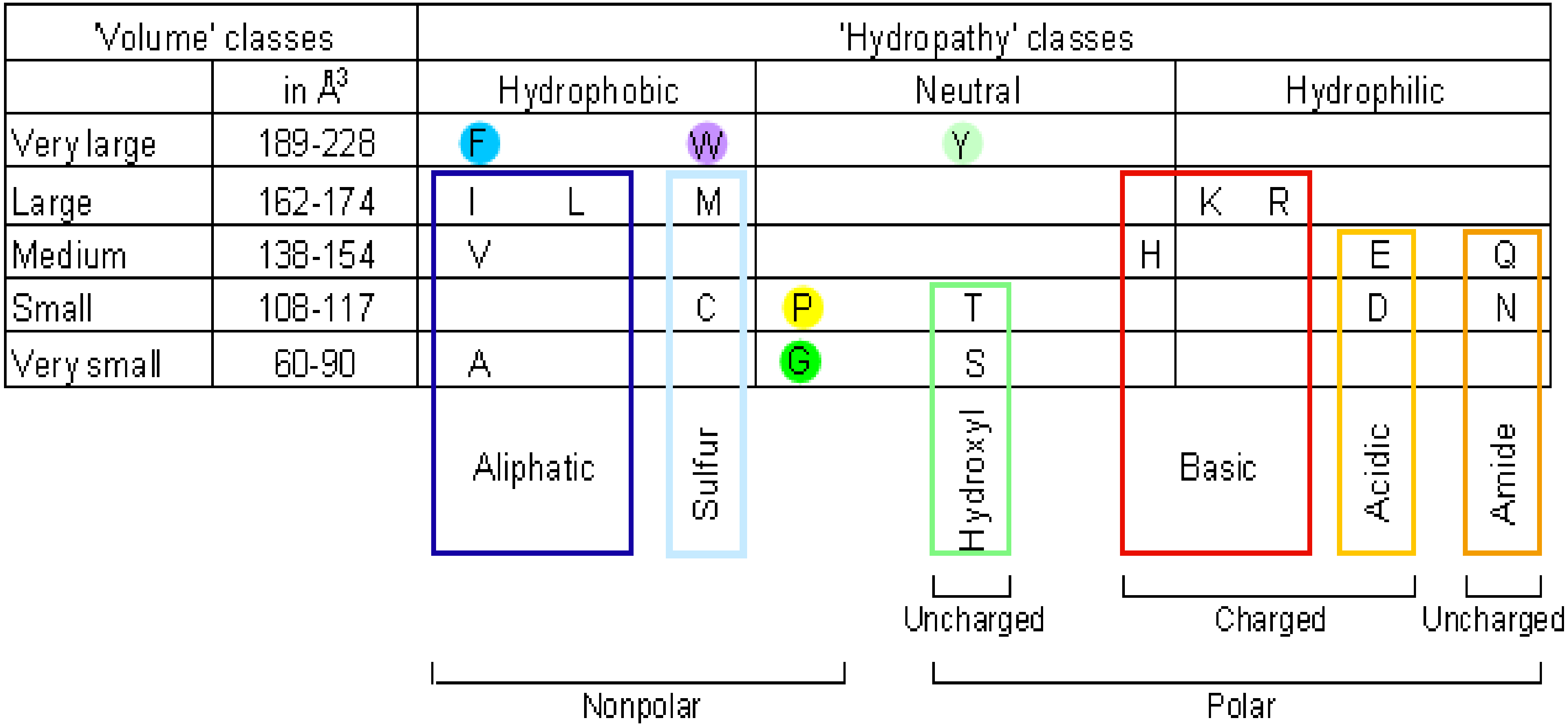
Click on mutated (underscored) nucleotid to see the original one: c

	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	.....acgattttggagtggttatt.....	ccccgggga		..atgcttttgatatctgg	IGHJ3*02	IGHD3-3*01	0	0	0	12/17
#5	Z70610	IGHV4-34*09	tgtgcgagag.		tcgggag	......cgattttggagtggttatt.....	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...........	tgacccc		......ttgactactgg	IGHJ4*02	IGHD3-16*01	0	1	0	12/21
#13	Z70622	IGHV4-39*06	tgtgcgagaga	t	tgccccgctcctgccaaaat	gtattactatggttcggggga...........	tatgtacg		.....tttgactactgg	IGHJ4*03	IGHD3-10*01	0	0	0	15/28

Terminé

The 11 IMGT physicochemical AA classes

http://www.imgt.org



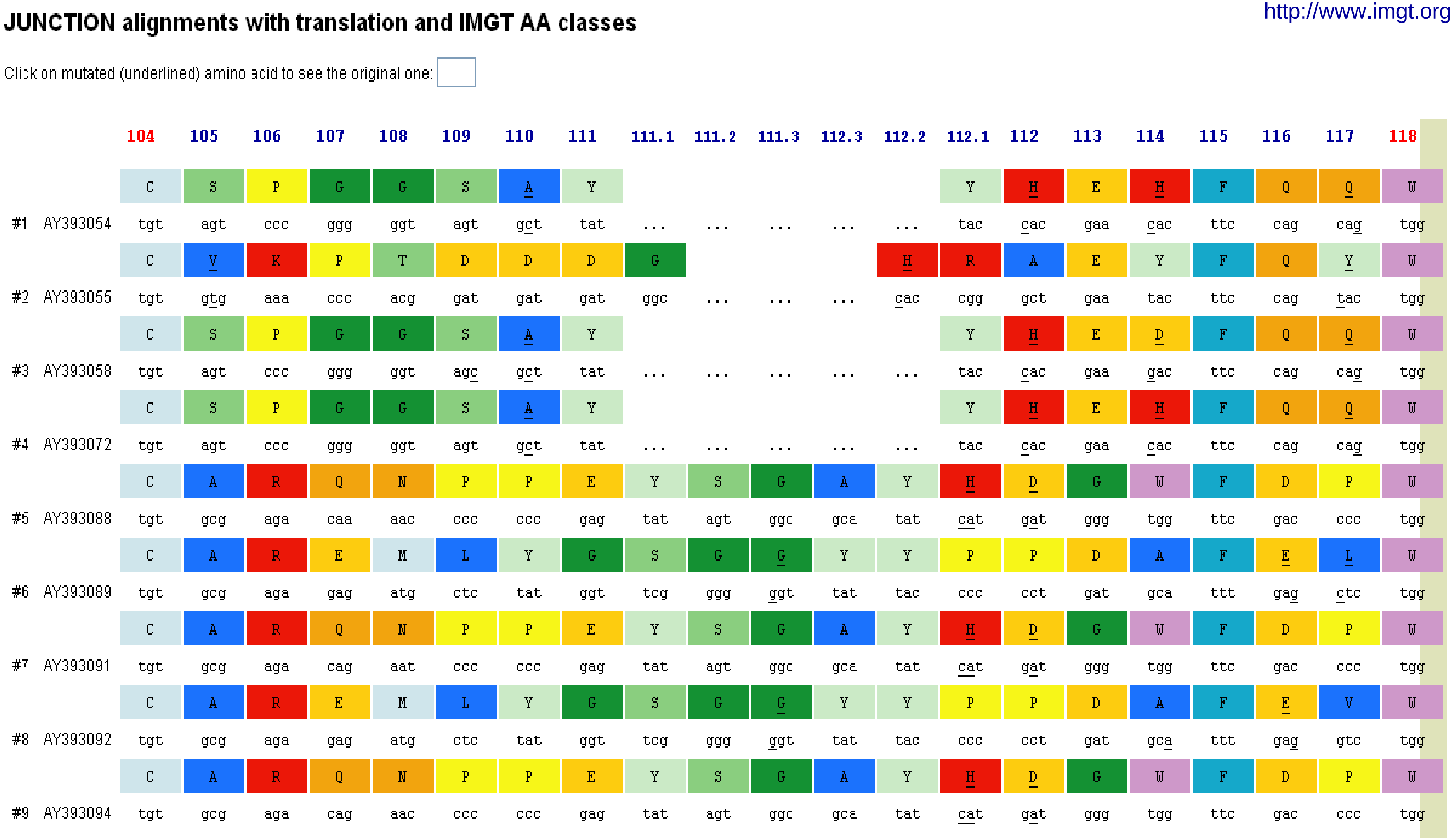
'Volume' classes		'Hydropathy' classes		
	in Å³	Hydrophobic	Neutral	Hydrophilic
Very large	189-228	F W	Y	
Large	162-174	I L M		K R
Medium	138-154	V	H	E Q
Small	108-117	C	P T	D N
Very small	60-90	A	G S	

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

IMGT/JunctionAnalysis

Analysis of the IG and TR junctions

http://www.imgt.org



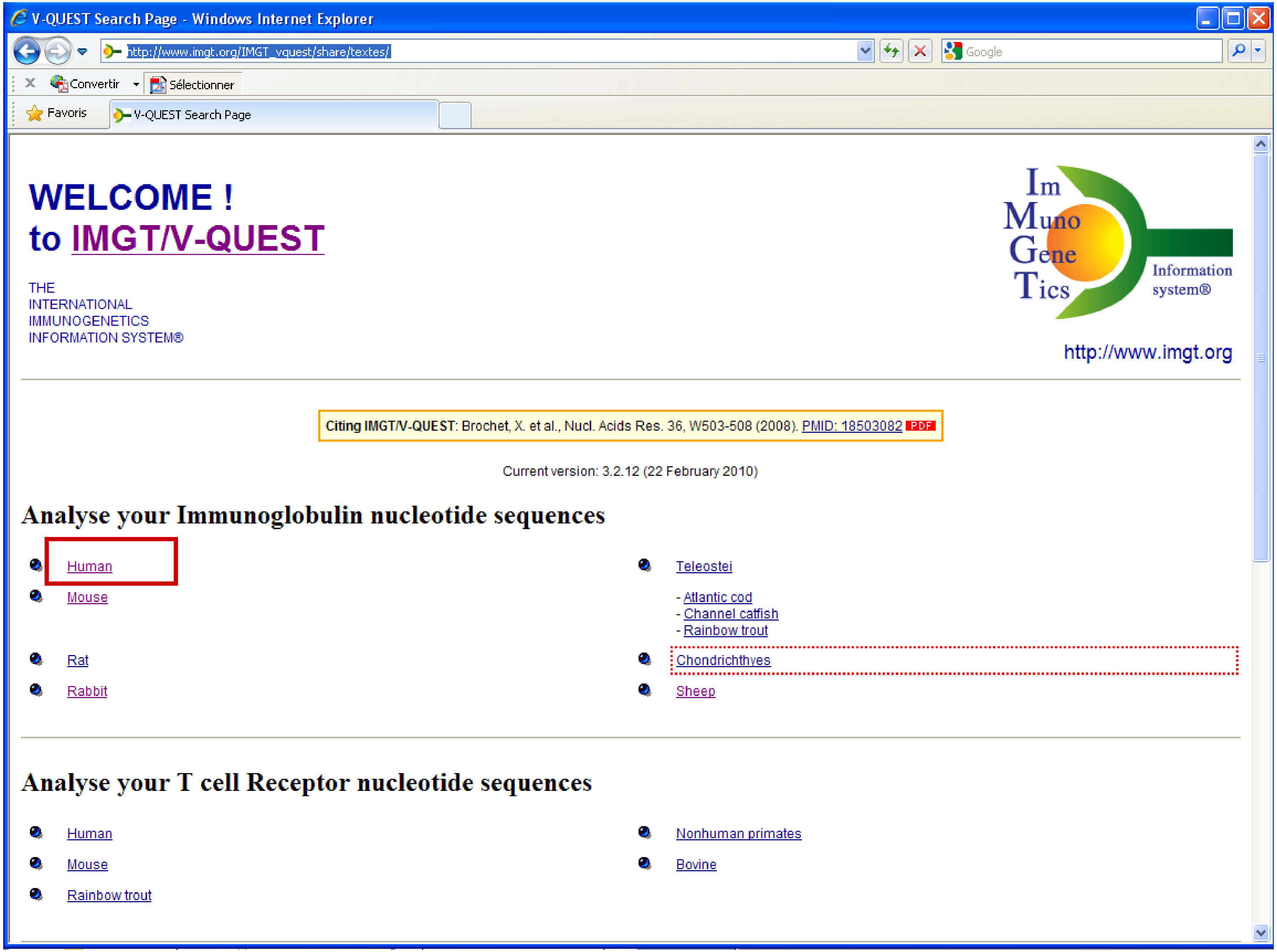
JUNCTION alignments with translation and IMGT AA classes

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	A	Y						Y	H	E	H	F	Q	Q	W
#1	AY393054	tgt	agt	ccc	ggg	ggt	agt	gct	tat	...	...	...	...	...	tac	cac	gaa	cac	ttc	cag	cag	tgg
		C	V	K	P	T	D	D	D	G				H	R	A	E	Y	F	Q	Y	W
#2	AY393055	tgt	gtg	aaa	ccc	acg	gat	gat	gat	ggc	...	...	...	cac	cgg	gct	gaa	tac	ttc	cag	tac	tgg
		C	S	P	G	G	S	A	Y						Y	H	E	D	F	Q	Q	W
#3	AY393058	tgt	agt	ccc	ggg	ggt	agc	gct	tat	...	...	...	...	...	tac	cac	gaa	gac	ttc	cag	cag	tgg
		C	S	P	G	G	S	A	Y						Y	H	E	H	F	Q	Q	W
#4	AY393072	tgt	agt	ccc	ggg	ggt	agt	gct	tat	...	...	...	...	...	tac	cac	gaa	cac	ttc	cag	cag	tgg
		C	A	R	Q	N	P	P	E	Y	S	G	A	Y	H	D	G	W	F	D	P	W
#5	AY393088	tgt	gcg	aga	caa	aac	ccc	ccc	gag	tat	agt	ggc	gca	tat	cat	gat	ggg	tgg	ttc	gac	ccc	tgg
		C	A	R	E	M	L	Y	G	S	G	G	Y	Y	P	P	D	A	F	E	L	W
#6	AY393089	tgt	gcg	aga	gag	atg	ctc	tat	ggt	tcg	ggg	ggt	tat	tac	ccc	cct	gat	gca	ttt	gag	ctc	tgg
		C	A	R	Q	N	P	P	E	Y	S	G	A	Y	H	D	G	W	F	D	P	W
#7	AY393091	tgt	gcg	aga	cag	aat	ccc	ccc	gag	tat	agt	ggc	gca	tat	cat	gat	ggg	tgg	ttc	gac	ccc	tgg
		C	A	R	E	M	L	Y	G	S	G	G	Y	Y	P	P	D	A	F	E	V	W
#8	AY393092	tgt	gcg	aga	gag	atg	ctc	tat	ggt	tcg	ggg	ggt	tat	tac	ccc	cct	gat	gca	ttt	gag	gtc	tgg
		C	A	R	Q	N	P	P	E	Y	S	G	A	Y	H	D	G	W	F	D	P	W
#9	AY393094	tgt	gcg	aga	cag	aac	ccc	ccc	gag	tat	agt	ggc	gca	tat	cat	gat	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)

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



WELCOME !
to IMGT/V-QUEST

THE
INTERNATIONAL
IMMUNOGENETICS
INFORMATION SYSTEM®

http://www.imgt.org

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

Current version: 3.2.12 (22 February 2010)

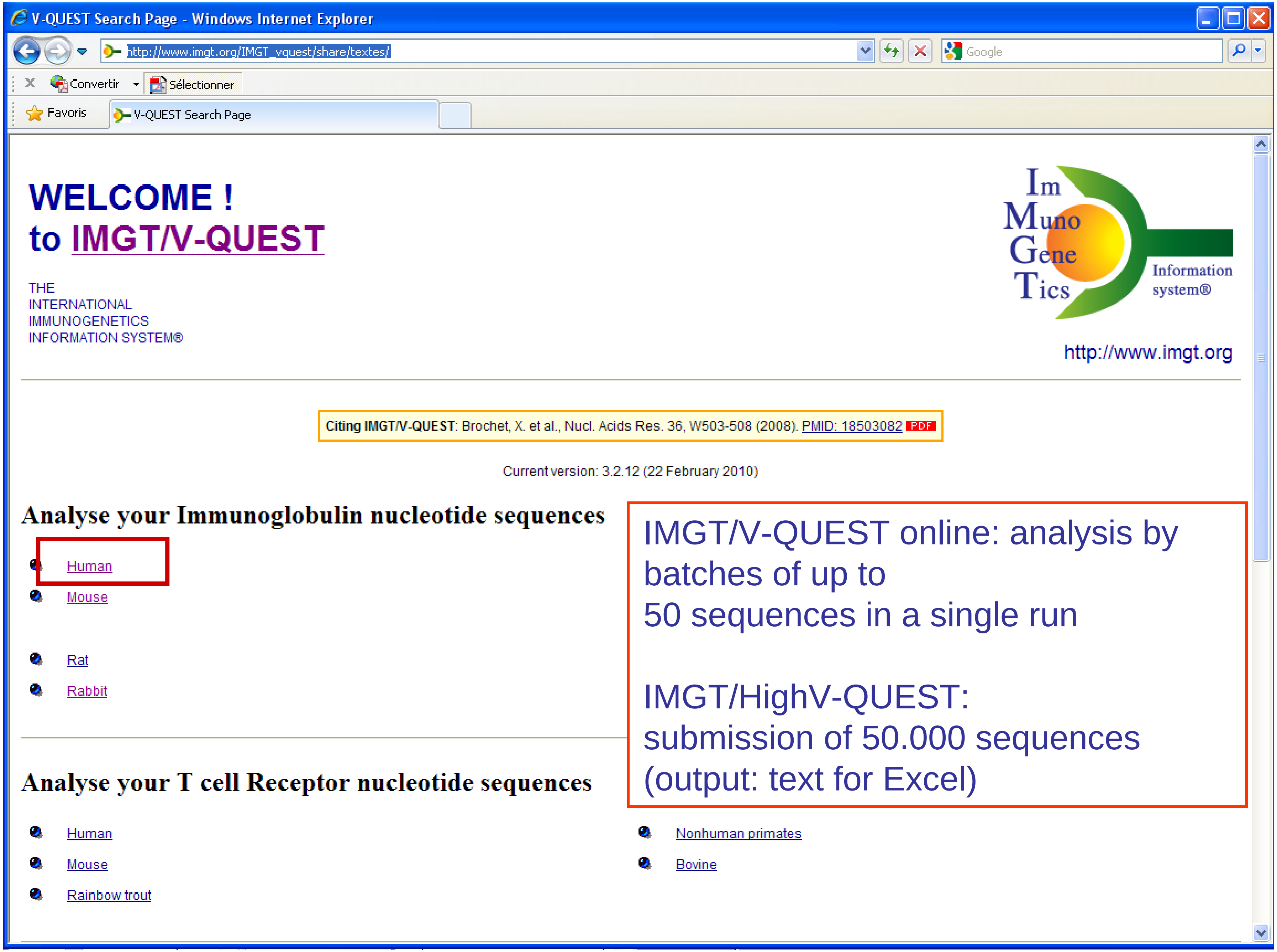
Analyse your Immunoglobulin nucleotide sequences

- Human
- Mouse
- Rat
- Rabbit
- Teleostei
  - Atlantic cod
  - Channel catfish
  - Rainbow trout
- Chondrichthyes
- Sheep

Analyse your T cell Receptor nucleotide sequences

- Human
- Mouse
- Rainbow trout
- Nonhuman primates
- Bovine

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



WELCOME !
to IMGT/V-QUEST

THE
INTERNATIONAL
IMMUNOGENETICS
INFORMATION SYSTEM®

http://www.imgt.org

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

Current version: 3.2.12 (22 February 2010)

Analyse your Immunoglobulin nucleotide sequences

- Human
- Mouse
- Rat
- Rabbit

Analyse your T cell Receptor nucleotide sequences

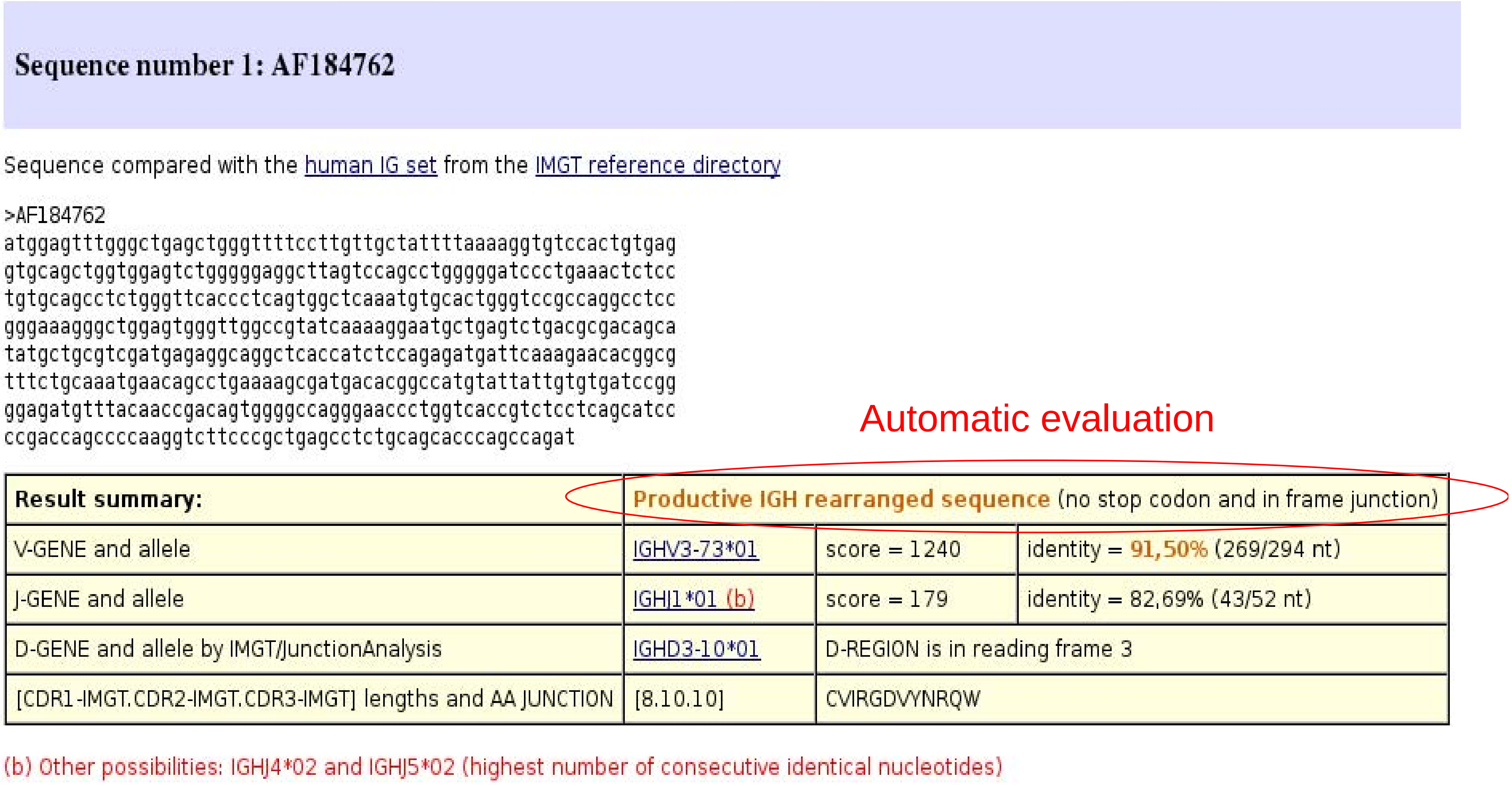
- Human
- Mouse
- Rainbow trout
- Nonhuman primates
- Bovine

IMGT/V-QUEST online: analysis by batches of up to
50 sequences in a single run

IMGT/HighV-QUEST:
submission of 50.000 sequences
(output: text for Excel)

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
gtgcagctggtggagtctgggggaggcttagtccagcctggggggatccctgaaactctcc
tgtgcagcctctgggttcaccctcagtggctcaaatgtgcactgggtccgccaggcctcc
gggaaagggctggagtgggttggccgtatcaaaaggaatgctgagtctgacgcgacagca
tatgctgcgtcgatgagaggcaggctcaccatctccagagatgattcaaagaacacggcg
tttctgcaaatgaacagcctgaaaagcgatgacacggccatgtattattgtgtgatccgg
ggagatgtttacaaccgacagtggggccagggaaccctggtcaccgtctcctcagcatcc
ccgaccagccccaaggtcttcccgctgagcctctgcagcacccagccagat
```

Automatic evaluation

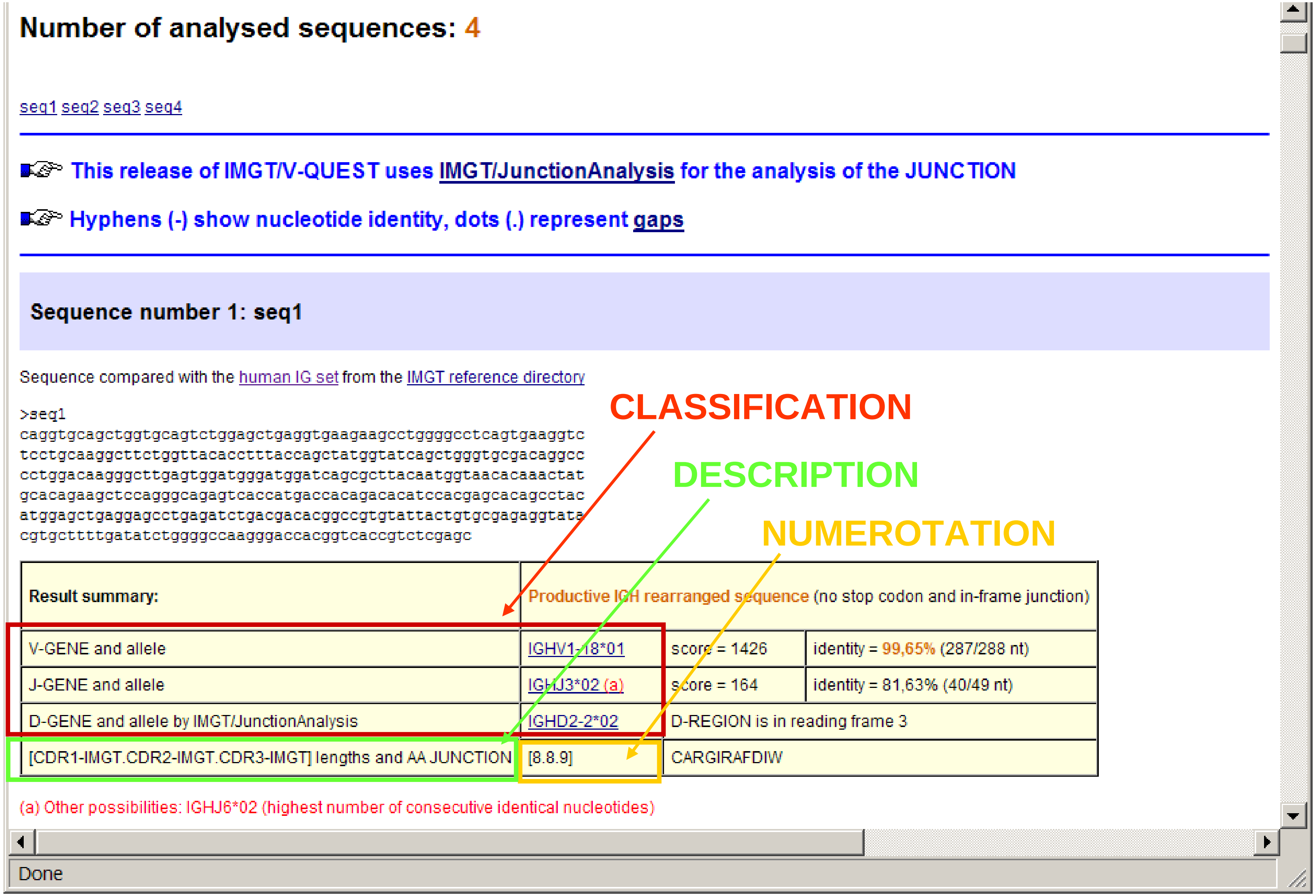
Result summary:	**Productive IGH rearranged sequence** (no stop codon and in frame junction)		
V-GENE and allele	IGHV3-73*01	score = 1240	identity = **91,50%** (269/294 nt)
J-GENE and allele	IGHJ1*01 (b)	score = 179	identity = 82,69% (43/52 nt)
D-GENE and allele by IMGT/JunctionAnalysis	IGHD3-10*01	D-REGION 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
```

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

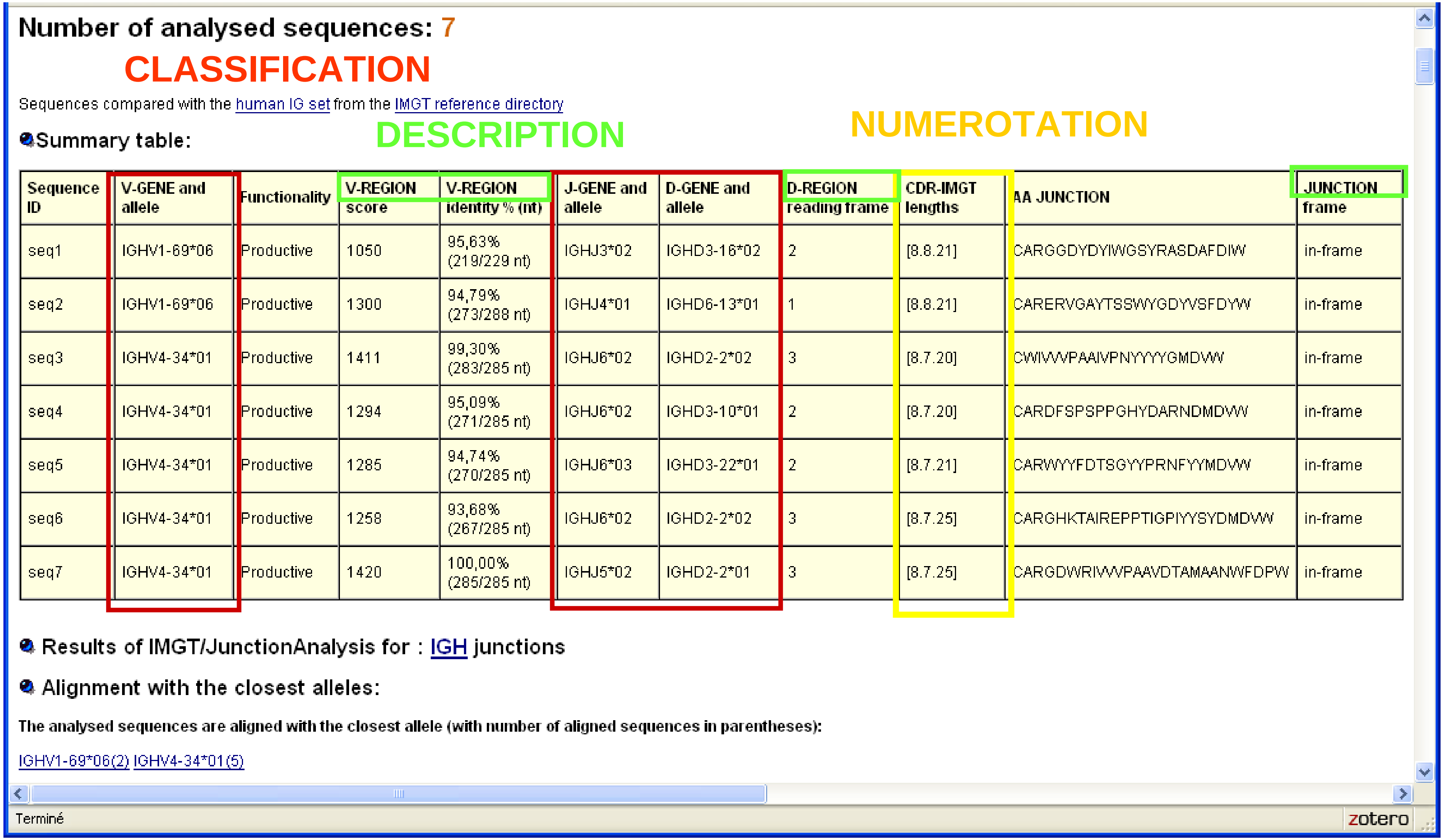
CLASSIFICATION

DESCRIPTION

NUMEROTATION

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

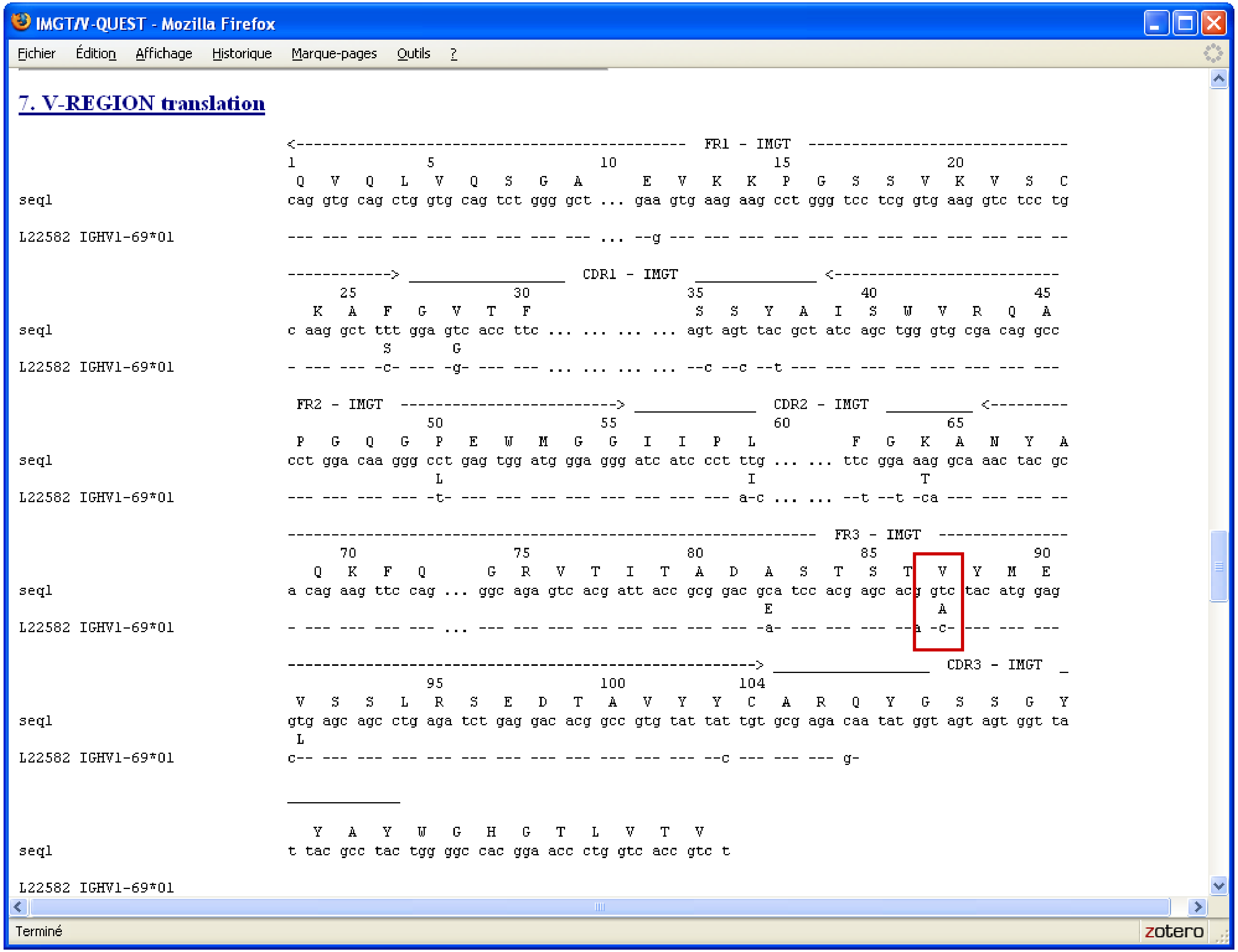
Alignment with the closest alleles:

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

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

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

http://www.imgt.org



7. V-REGION translation

```
                               <---------------------------------------------  FR1 - IMGT  ------------------------------
                               1               5                   10                  15                  20
                                Q   V   Q   L   V   Q   S   G   A       E   V   K   K   P   G   S   S   V   K   V   S   C
seql                           cag gtg cag ctg gtg cag tct ggg gct ... gaa gtg aag aag cct ggg tcc tcg gtg aag gtc tcc tg

L22582 IGHV1-69*01             --- --- --- --- --- --- --- --- --- ... --g --- --- --- --- --- --- --- --- --- --- --- --

                               ------------> ___________________ CDR1 - IMGT  _______________<--------------------------
                                     25                  30                  35                  40                  45
                                  K   A   F   G   V   T   F                   S   S   Y   A   I   S   W   V   R   Q   A
seql                           c aag gct ttt gga gtc acc ttc ... ... ... ... agt agt tac gct atc agc tgg gtg cga cag gcc
                                          S       G
L22582 IGHV1-69*01             - --- --- -c- --- -g- --- --- ... ... ... ... --c --c --t --- --- --- --- --- --- --- ---

                                FR2 - IMGT  ------------------------->  ______________  CDR2 - IMGT  __________ <---------
                                               50                  55                  60                  65
                                P   G   Q   G   P   E   W   M   G   G   I   I   P   L           F   G   K   A   N   Y   A
seql                           cct gga caa ggg cct gag tgg atg gga ggg atc atc cct ttg ... ... ttc gga aag gca aac tac gc
                                                L                                   I                   T
L22582 IGHV1-69*01             --- --- --- --- -t- --- --- --- --- --- --- --- --- a-c ... ... --t --t -ca --- --- --- --

                               -------------------------------------------------------------  FR3 - IMGT  ---------------
                                     70                  75                  80                  85                  90
                                  Q   K   F   Q       G   R   V   T   I   T   A   D   A   S   T   S   T   V   Y   M   E
seql                           a cag aag ttc cag ... ggc aga gtc acg att acc gcg gac gca tcc acg agc acg gtc tac atg gag
                                                                      E                   A
L22582 IGHV1-69*01             - --- --- --- --- ... --- --- --- --- --- --- --- --- -a- --- --- --- --a -c- --- --- ---

                               ------------------------------------------------------> __________________  CDR3 - IMGT  _
                                               95                  100          104
                                V   S   S   L   R   S   E   D   T   A   V   Y   Y   C   A   R   Q   Y   G   S   S   G   Y
seql                           gtg agc agc ctg aga tct gag gac acg gcc gtg tat tat tgt gcg aga caa tat ggt agt agt ggt ta
                                L
L22582 IGHV1-69*01             c-- --- --- --- --- --- --- --- --- --- --- --- --c --- --- --- g-

                               _____________

                                  Y   A   Y   W   G   H   G   T   L   V   T   V
seql                           t tac gcc tac tgg ggc cac gga acc ctg gtc acc gtc t

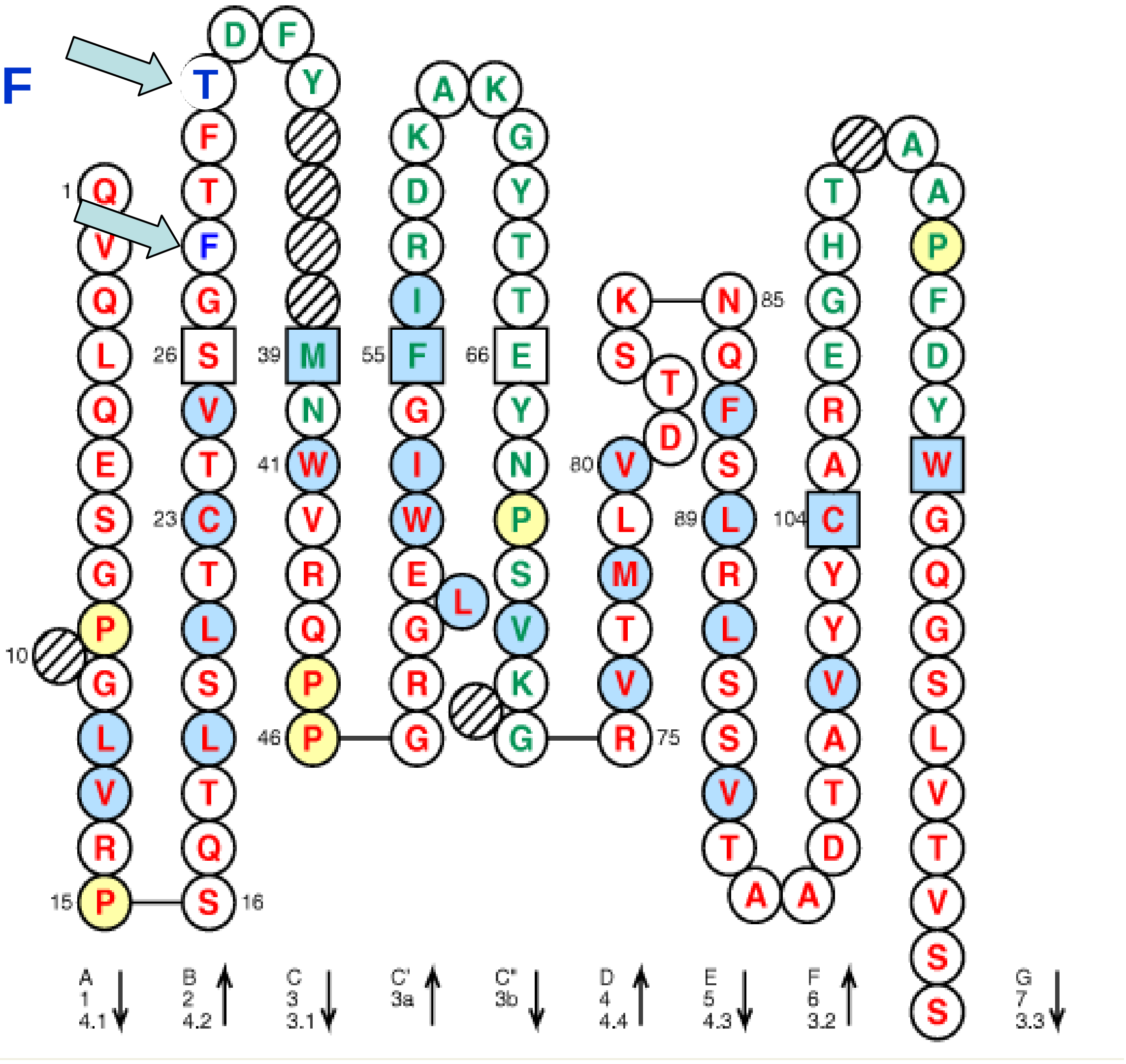
L22582 IGHV1-69*01
```

Antibody humanization and engineering

http://www.imgt.org

Alemtuzumab (CAMPATH®)

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



VH domain
[8.10.12]

🟥 human
🟩 rat

IMGT® http://www.imgt.org

Towards «Potential immunogenicity evaluation»

http://www.imgt.org

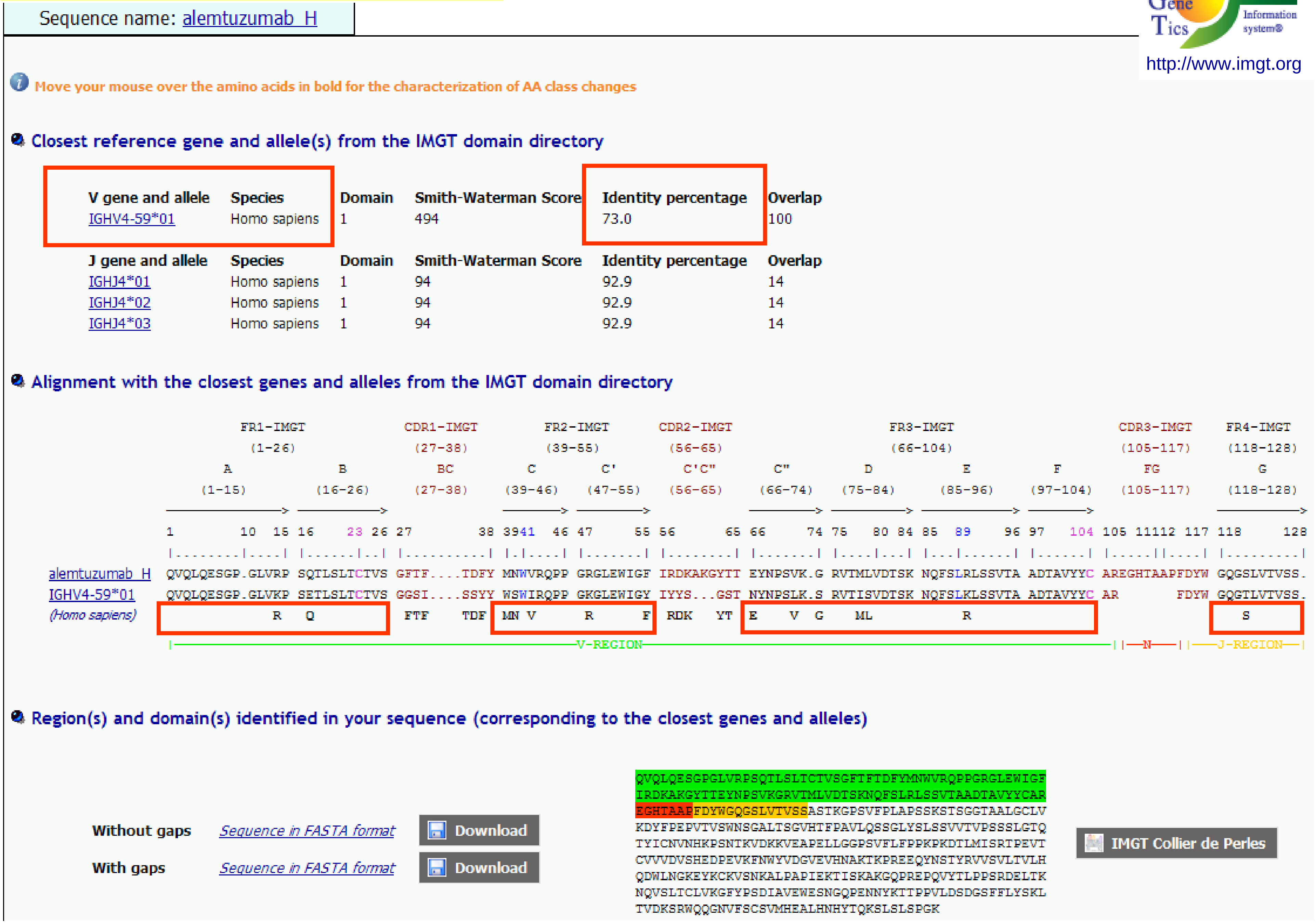
- Comparison with the closest human germline genes and alleles
- Number of different AA in FR-IMGT

		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**

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

IMGT/DomainGapAlign

http://www.imgt.org



Sequence name: alemtuzumab_H

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
              |------------------------------------------V-REGION------------------------------------------------| |---N---| |---J-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/DomainGapAlign

Towards «Potential immunogenicity evaluation»

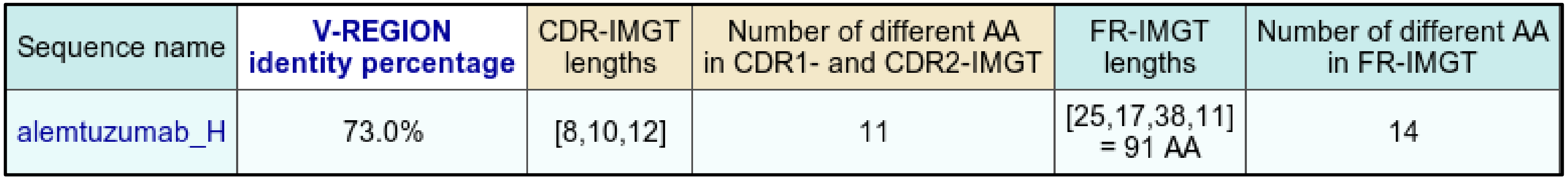
http://www.imgt.org

V-REGION identity percent

CDR-IMGT lengths

FR-IMGT lengths

Closest human germline
IGHV4-59*01



Sequence name	**V-REGION identity percentage**	CDR-IMGT lengths	Number of different AA in CDR1- and CDR2-IMGT	FR-IMGT lengths	Number of different AA in FR-IMGT
alemtuzumab_H	73.0%	[8,10,12]	11	[25,17,38,11] = 91 AA	14

11 different AA in CDR1- and CDR2-IMGT

14 different AA in FR-IMGT 14/91

Ehrenmann et al. Nucl. Acids Res. 38, D301-307 (2010)

IMGT/DomainGapAlign

Towards «Potential immunogenicity evaluation»

http://www.imgt.org

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 (- - -)**

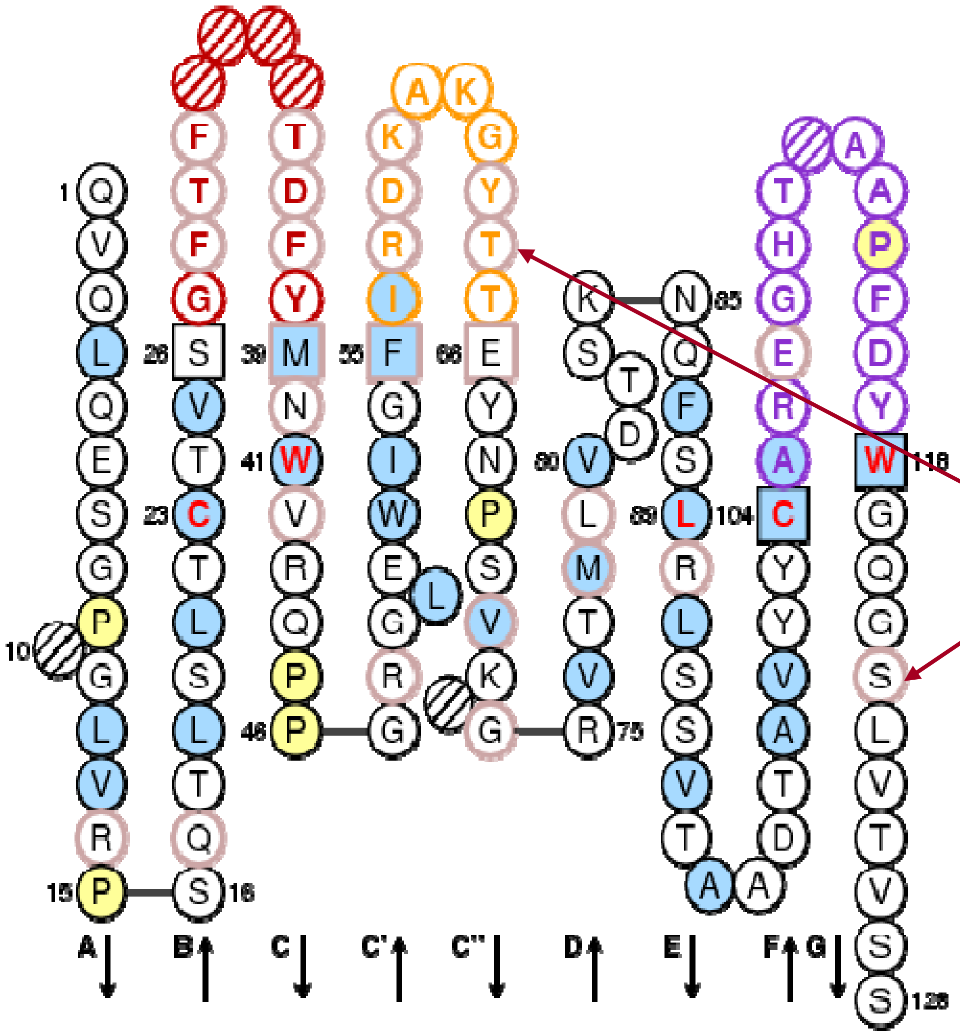
Ehrenmann et al. Nucl. Acids Res. 38, D301-307 (2010)

IMGT/DomainGapAlign:

Towards «Potential immunogenicity evaluation»

http://www.imgt.org

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)

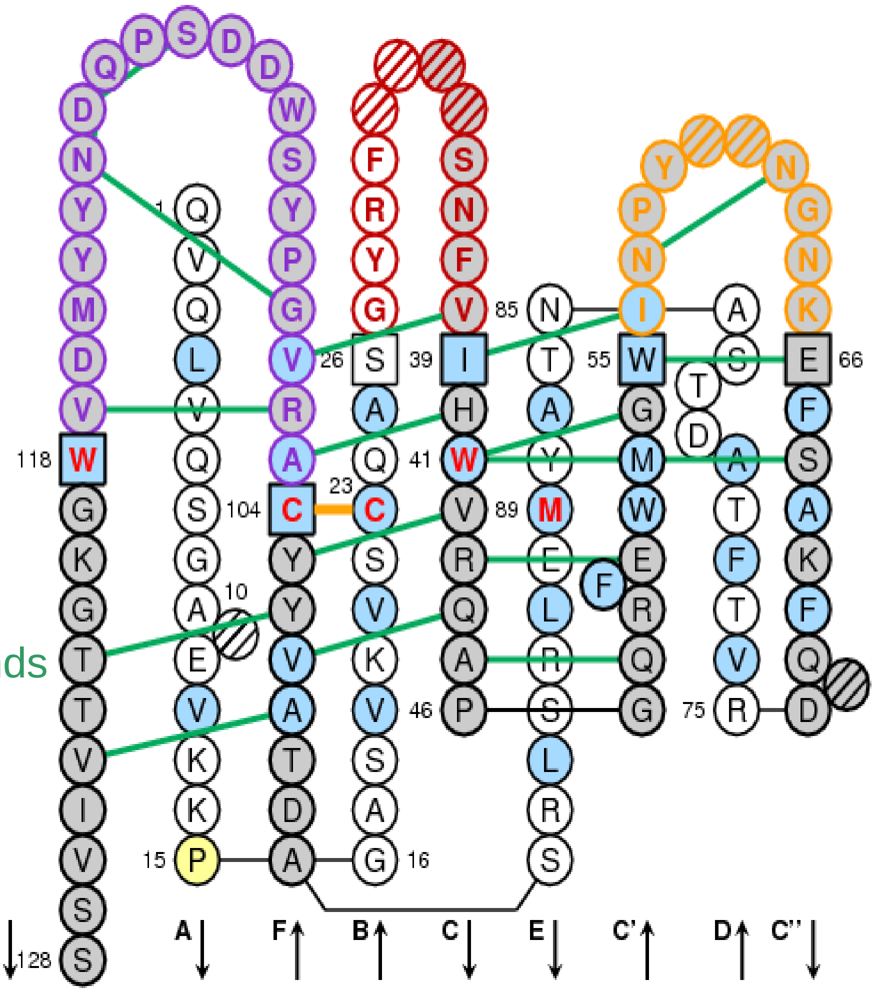
Ehrenmann et al. Nucl. Acids Res. 38, D301-307 (2010)

IMGT/3Dstructure-DB

http://www.imgt.org

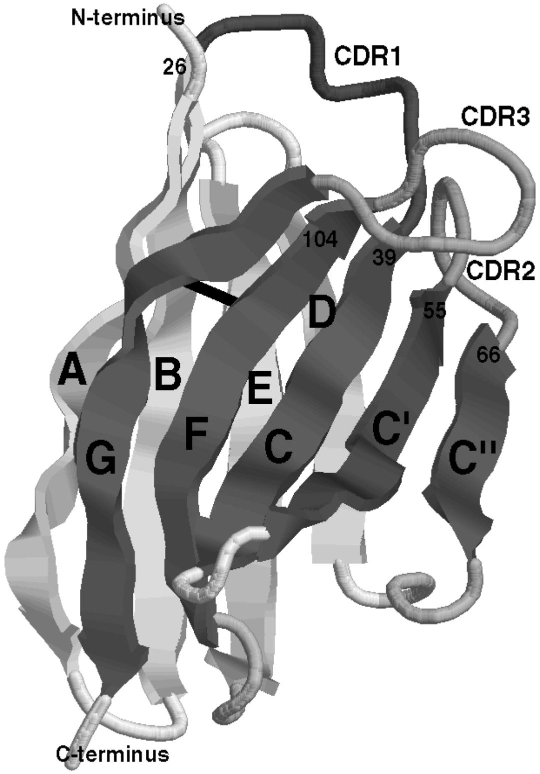
IMGT Collier de Perles : *Homo sapiens* (Human) IGHV V-DOMAIN from b12 (1hzh_H)

CDR-IMGT lengths [8.8.20]



Hydrogen bonds

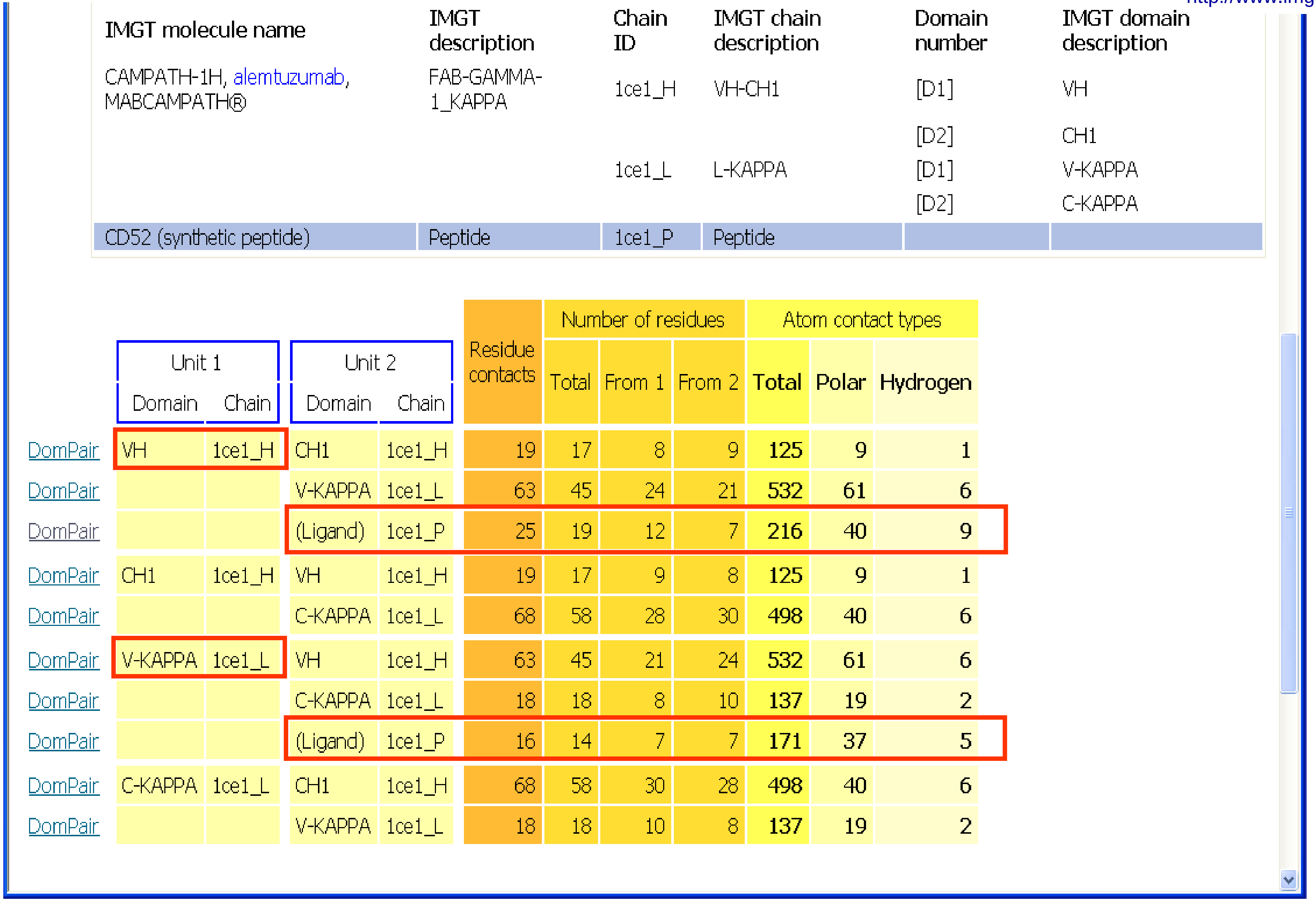
V-DOMAIN



Lefranc et al. Nucl. Acids Res. 37, D1006-1012 (2009)

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

http://www.imgt.org

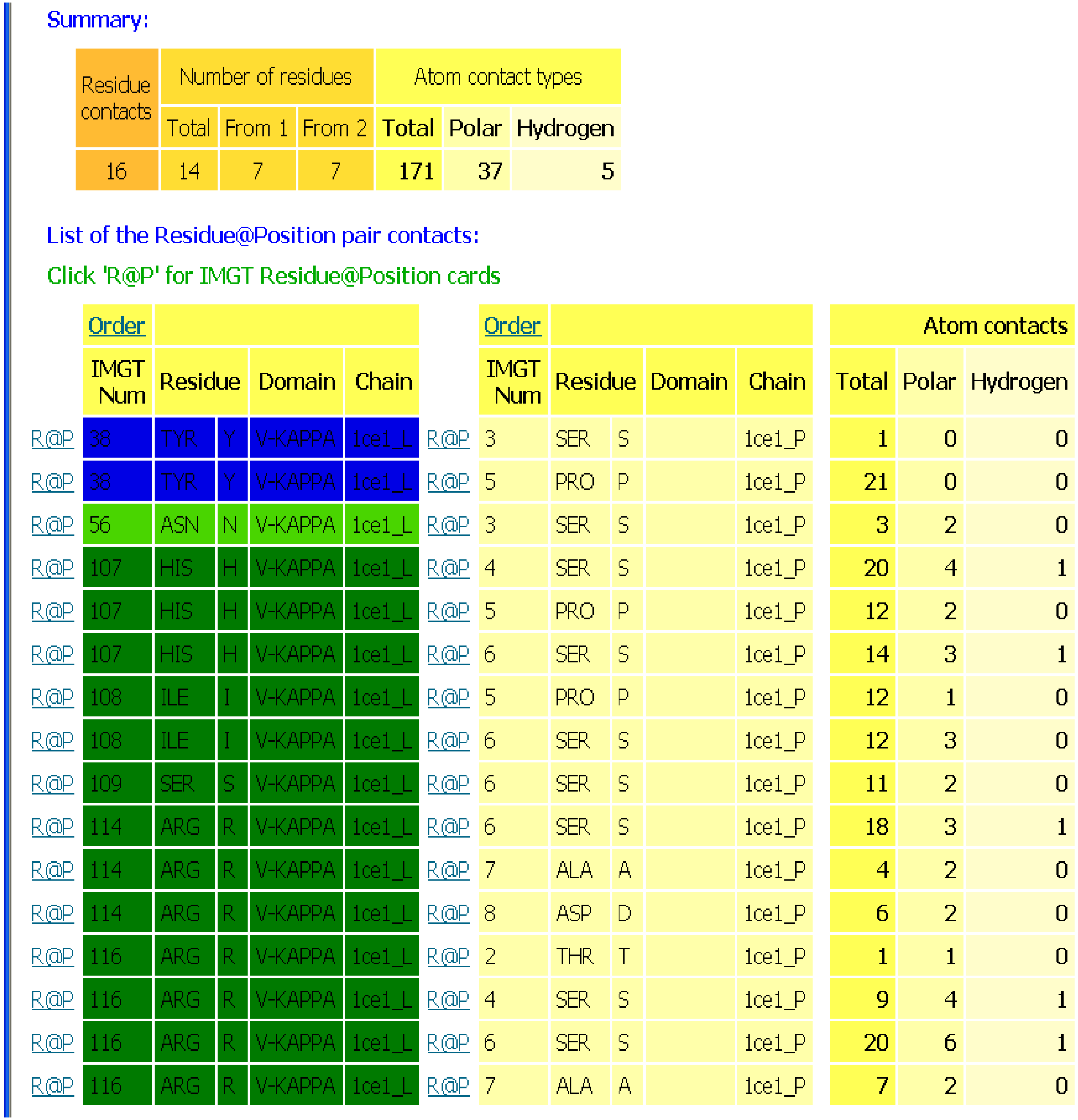


IMGT molecule name	IMGT description	Chain ID	IMGT chain description	Domain number	IMGT domain description
CAMPATH-1H, alemtuzumab, MABCAMPATH®	FAB-GAMMA-1_KAPPA	1ce1_H	VH-CH1	[D1]	VH
				[D2]	CH1
		1ce1_L	L-KAPPA	[D1]	V-KAPPA
				[D2]	C-KAPPA
CD52 (synthetic peptide)	Peptide	1ce1_P	Peptide		

	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



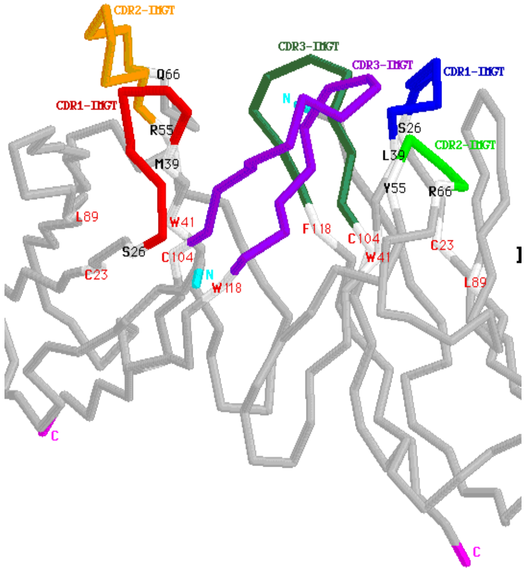
Summary:

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

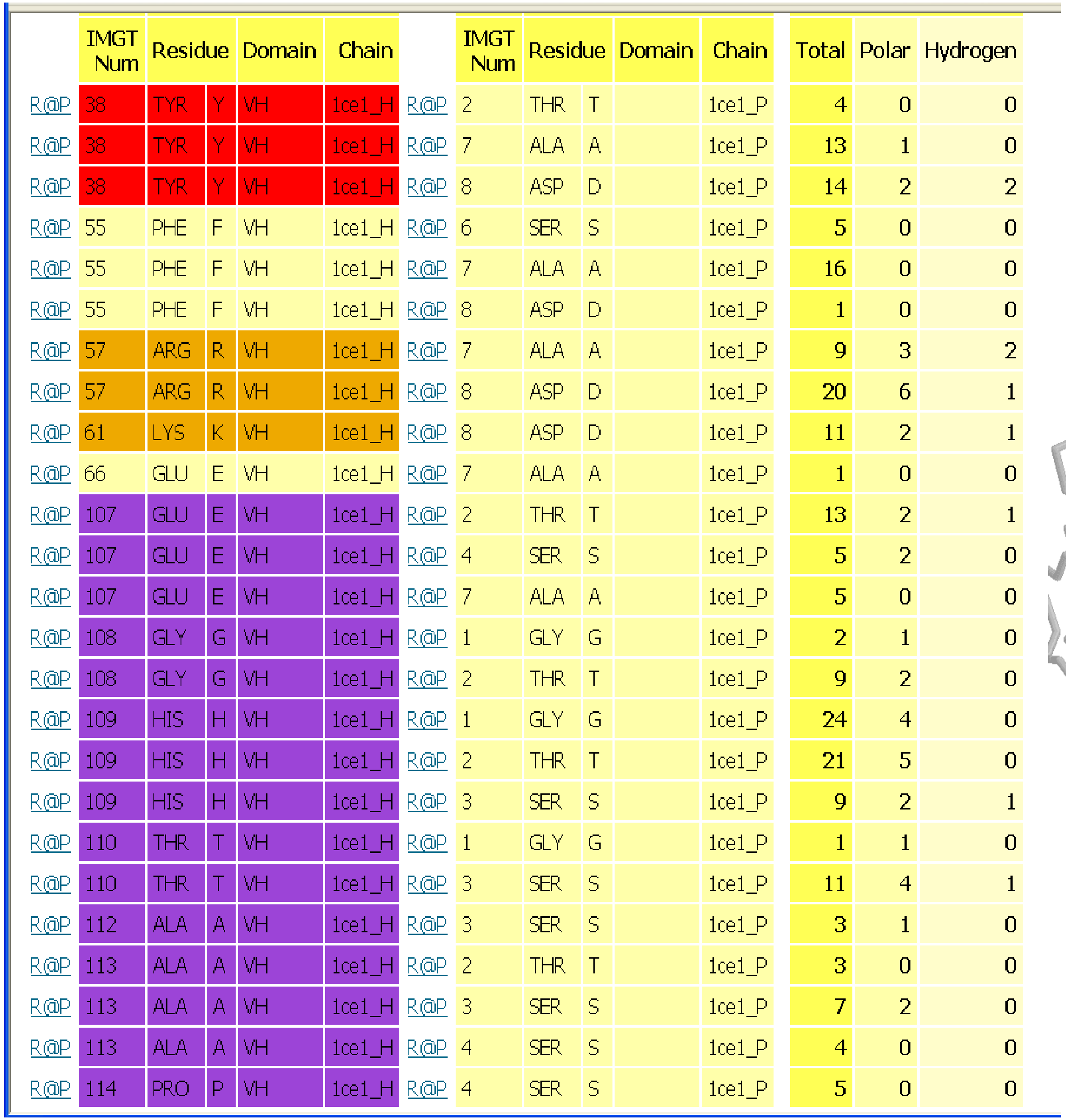
	Order						Order					Atom contacts		
	IMGT Num	Residue		Domain	Chain		IMGT Num	Residue		Domain	Chain	Total	Polar	Hydrogen
R@P	38	TYR	Y	V-KAPPA	1ce1_L	R@P	3	SER	S		1ce1_P	1	0	0
R@P	38	TYR	Y	V-KAPPA	1ce1_L	R@P	5	PRO	P		1ce1_P	21	0	0
R@P	56	ASN	N	V-KAPPA	1ce1_L	R@P	3	SER	S		1ce1_P	3	2	0
R@P	107	HIS	H	V-KAPPA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



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

Contacts VH-(Ligand)

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
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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
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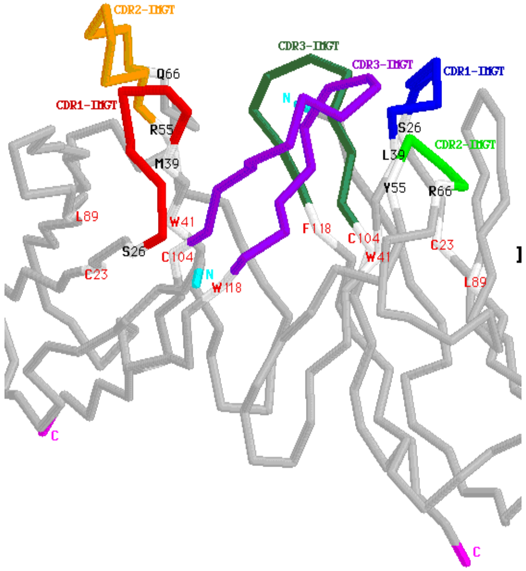

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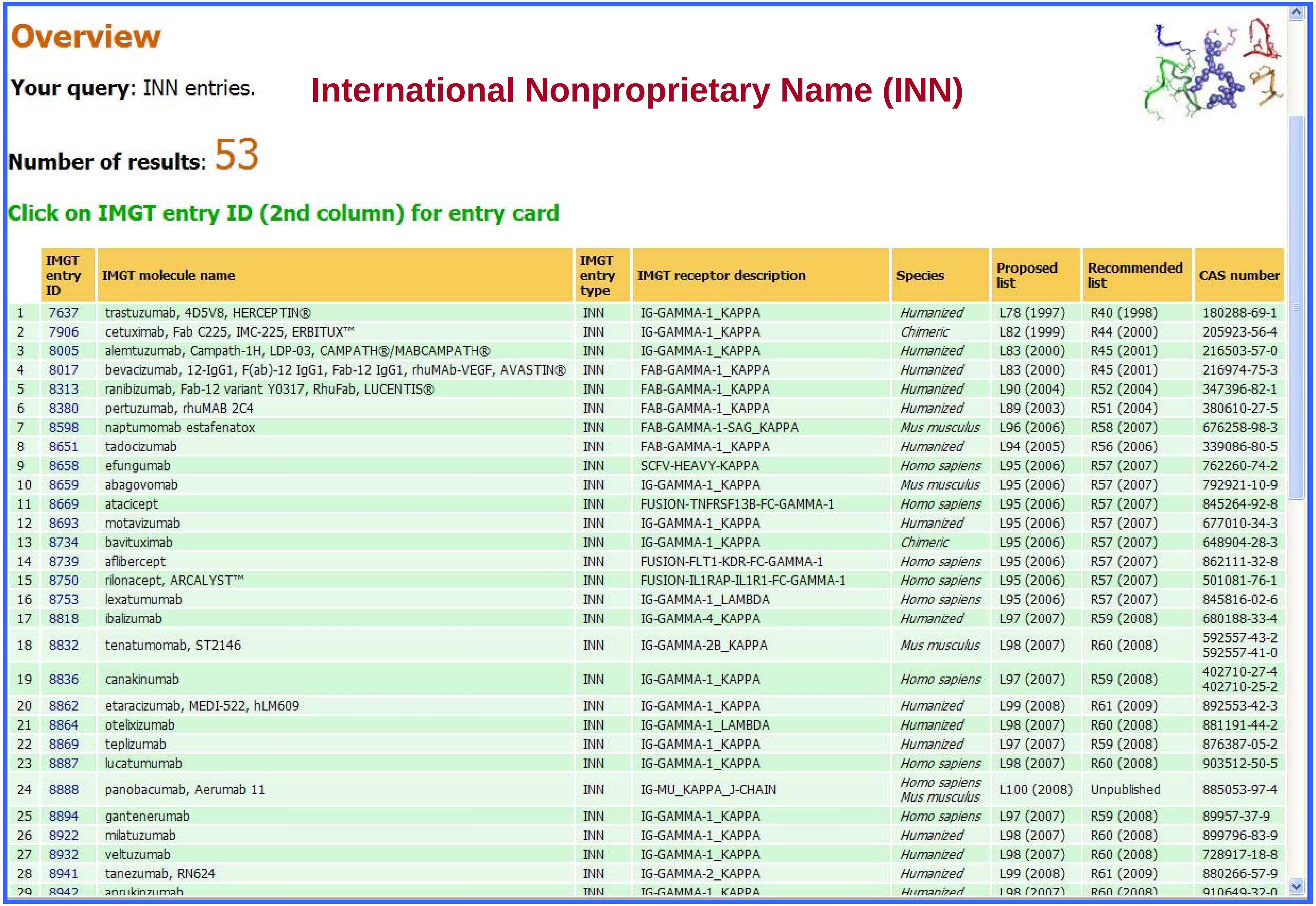
IMGT/2Dstructure-DB



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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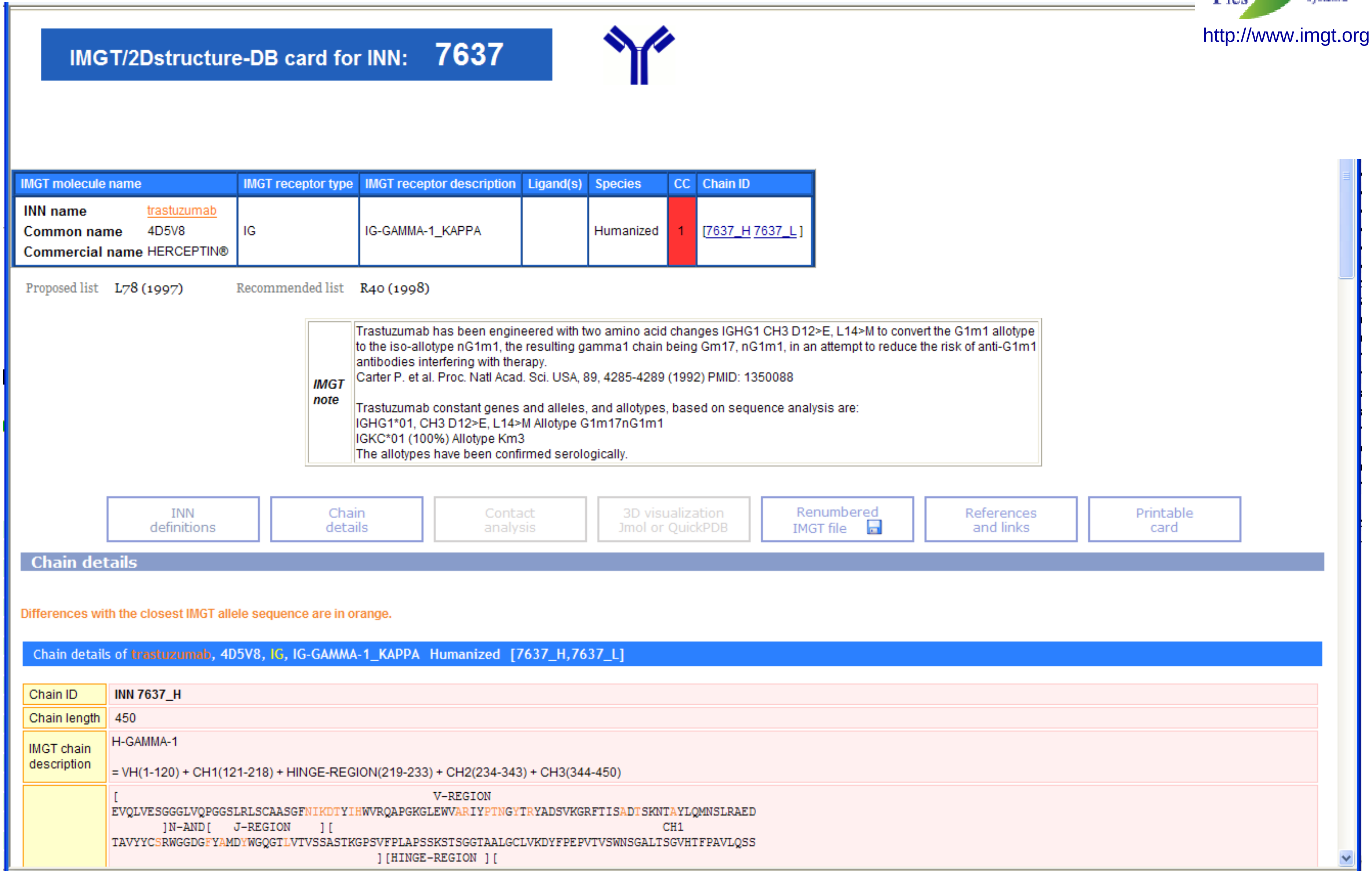

IMGT/2Dstructure-DB card for INN: 7637

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

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.

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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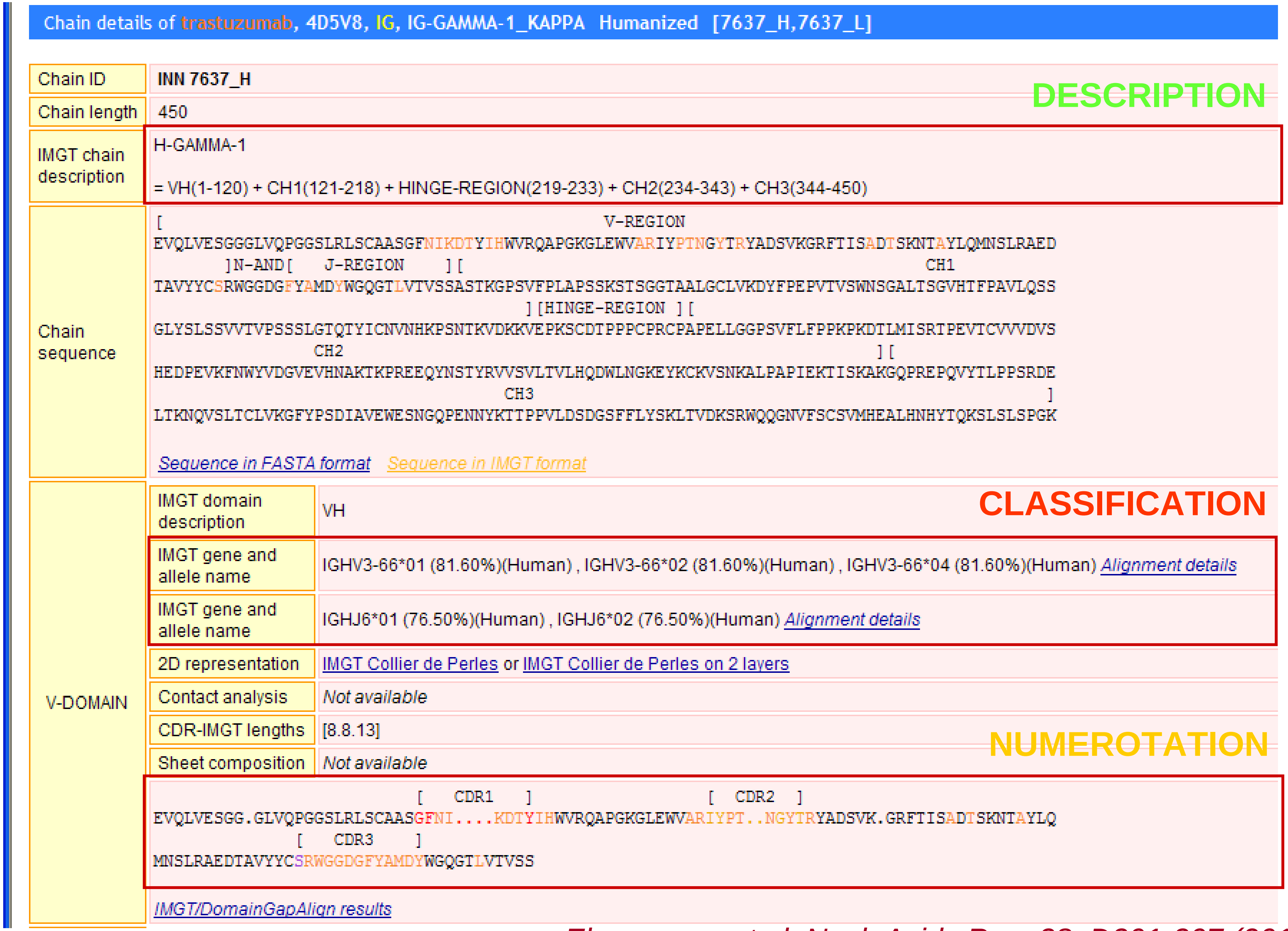
IMGT/2Dstructure-DB



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

DESCRIPTION

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

CLASSIFICATION

NUMEROTATION

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
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IMGT/DomainGapAlign results

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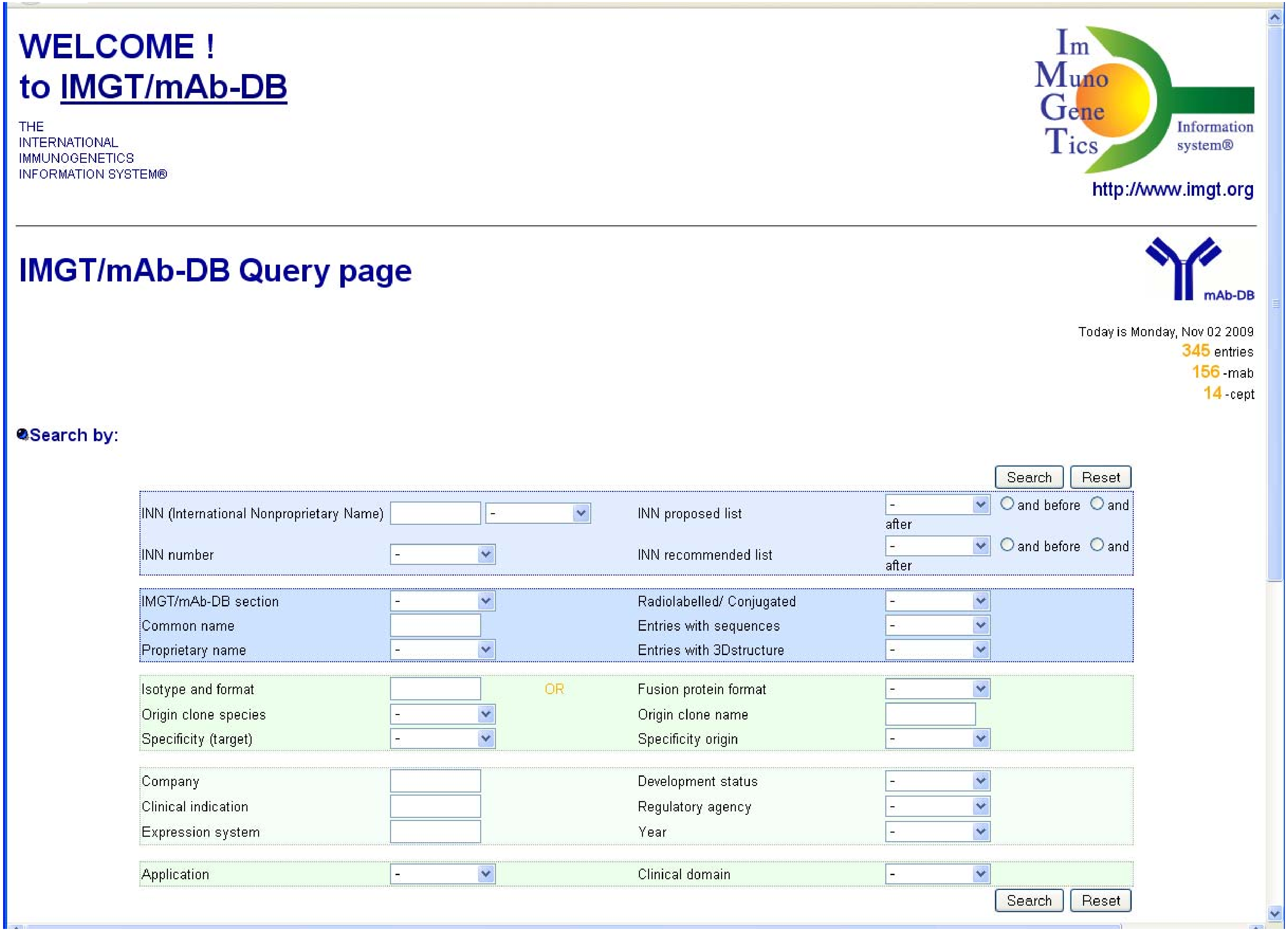

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IMGT/mAb-DB Query page

mAb-DB

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

Search by:

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 -

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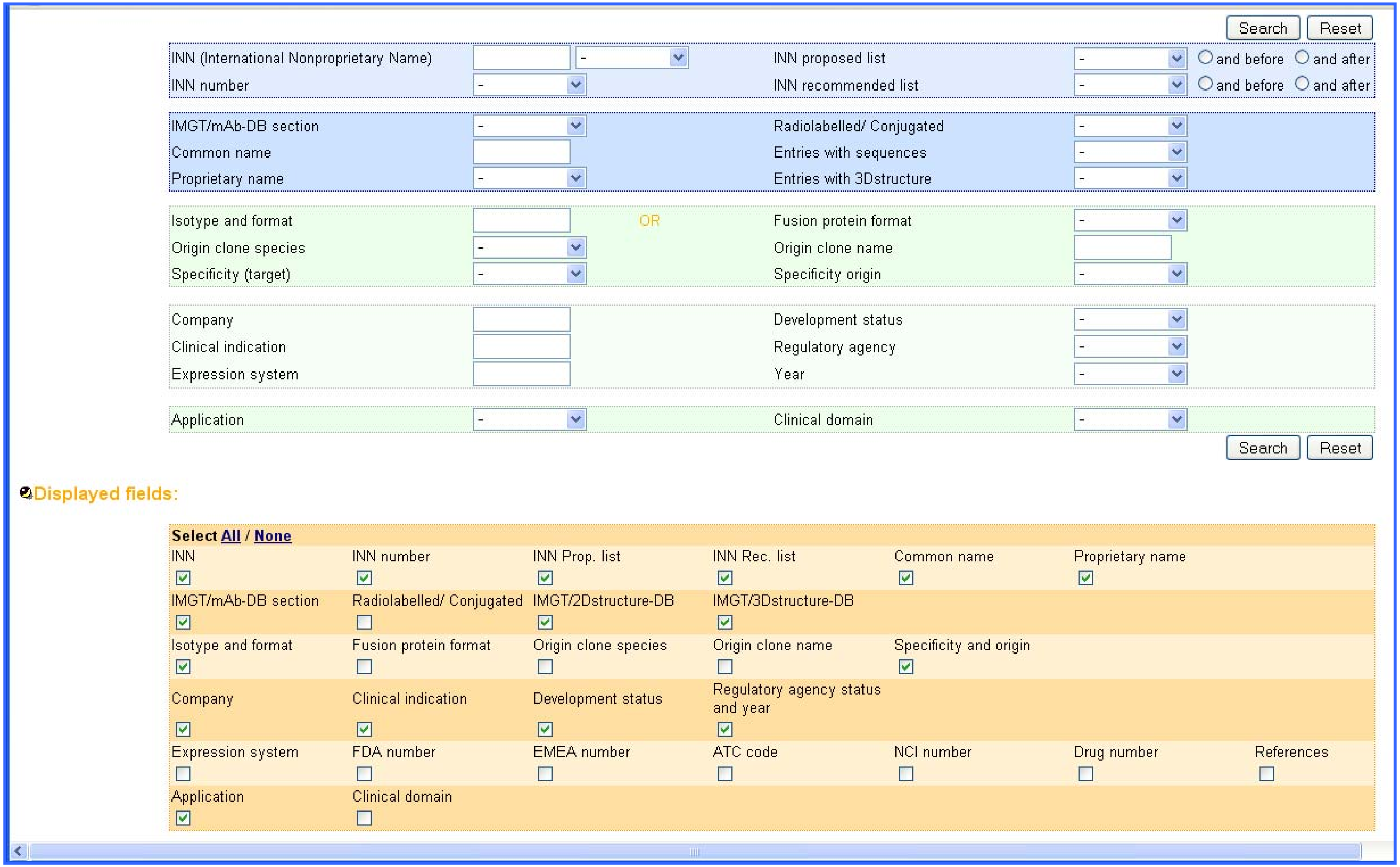
IMGT/mAb-DB



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	-

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INN ☑	INN number ☑	INN Prop. list ☑	INN Rec. list ☑	Common name ☑	Proprietary name ☑	
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Isotype and format ☑	Fusion protein format ☐	Origin clone species ☐	Origin clone name ☐	Specificity and origin ☑		
Company ☑	Clinical indication ☑	Development status ☑	Regulatory agency status and year ☑			
Expression system ☐	FDA number ☐	EMEA number ☐	ATC code ☐	NCI number ☐	Drug number ☐	References ☐
Application ☑	Clinical domain ☐					

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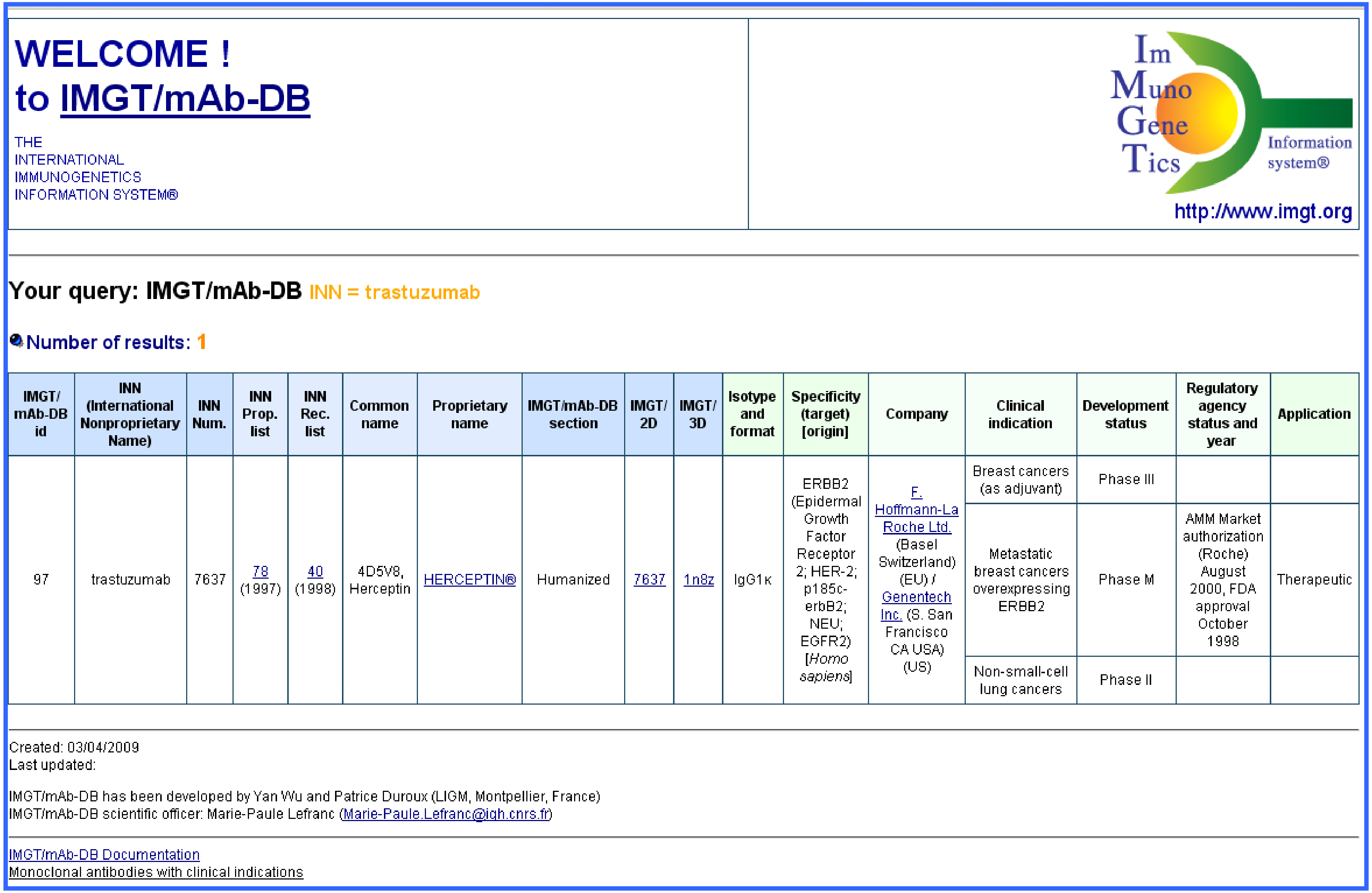

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Number of results: 1

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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- Bridge the gap between sequences and 3D structures and vice versa
    - IMGT/2Dstructure-DB cards (INN)

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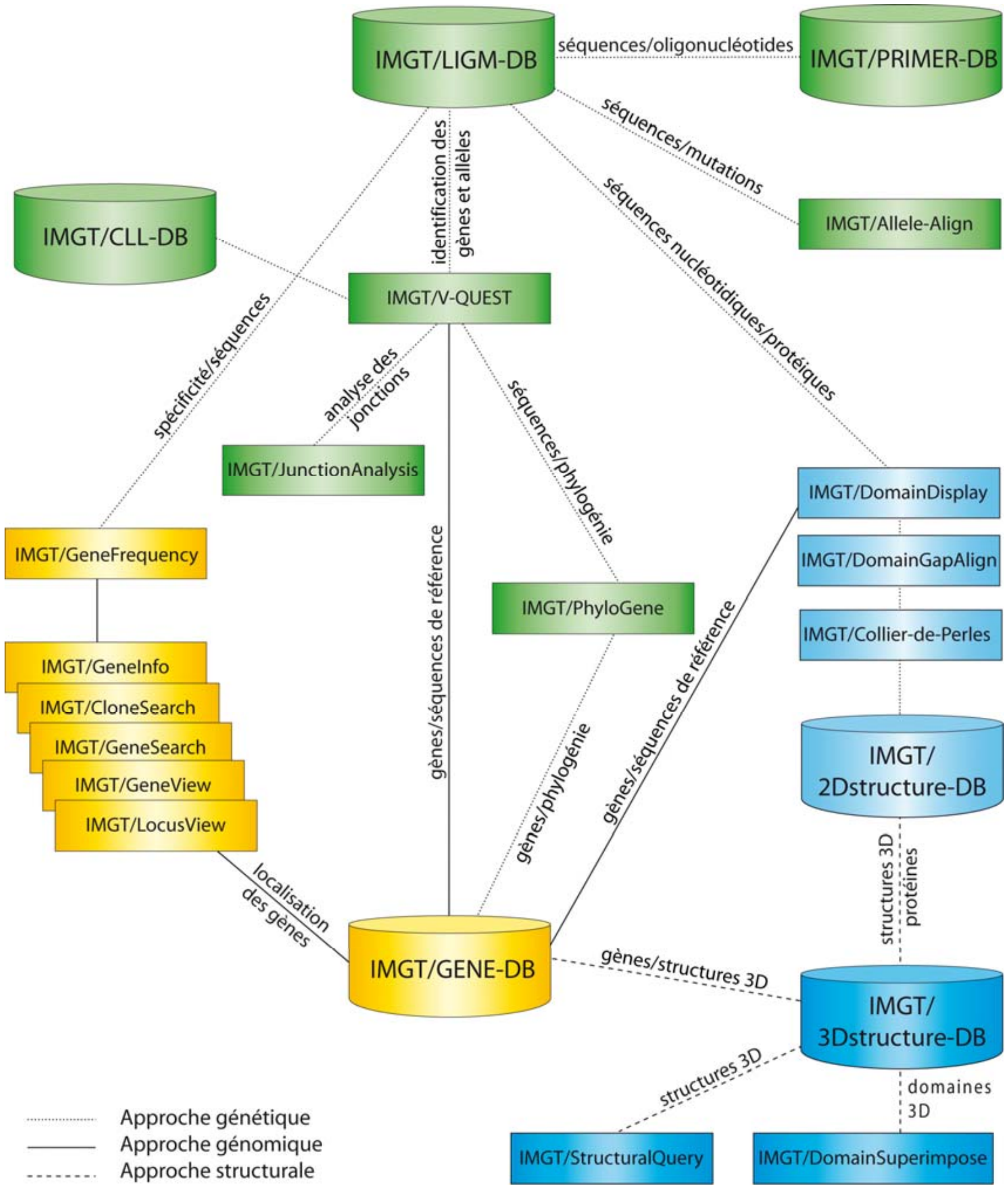
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IMGT/PRIMER-DB
séquences/mutations
IMGT/Allele-Align
séquences nucléotidiques/protéiques
identification des gènes et allèles
IMGT/CLL-DB
IMGT/V-QUEST
spécificité/séquences
analyse des jonctions
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localisation des gènes
IMGT/GENE-DB
gènes/structures 3D
IMGT/3Dstructure-DB
structures 3D
domaines 3D
IMGT/StructuralQuery
IMGT/DomainSuperimpose

Approche génétique
Approche génomique
Approche structurale

- 6 databases
- 15 online tools

- Sequences
- Genes
- Structures

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

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