Immunoinformatique

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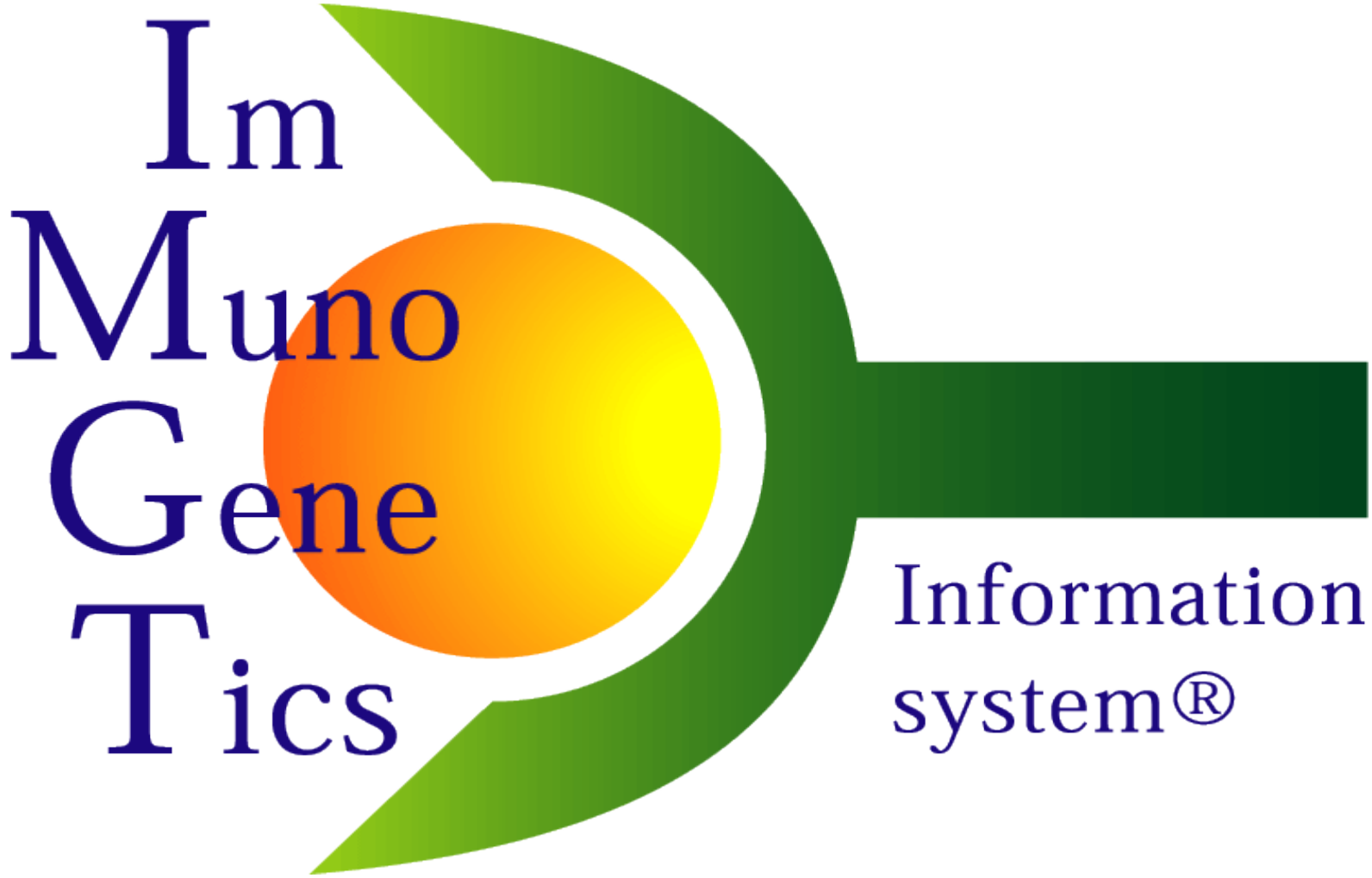
FMBS312, Master recherche 2 Bio-Med, TC3,
Universités Montpellier 1 et 2, ENSCM, 1 octobre 2009

IMGT®, the international ImMunoGeneTics information system®

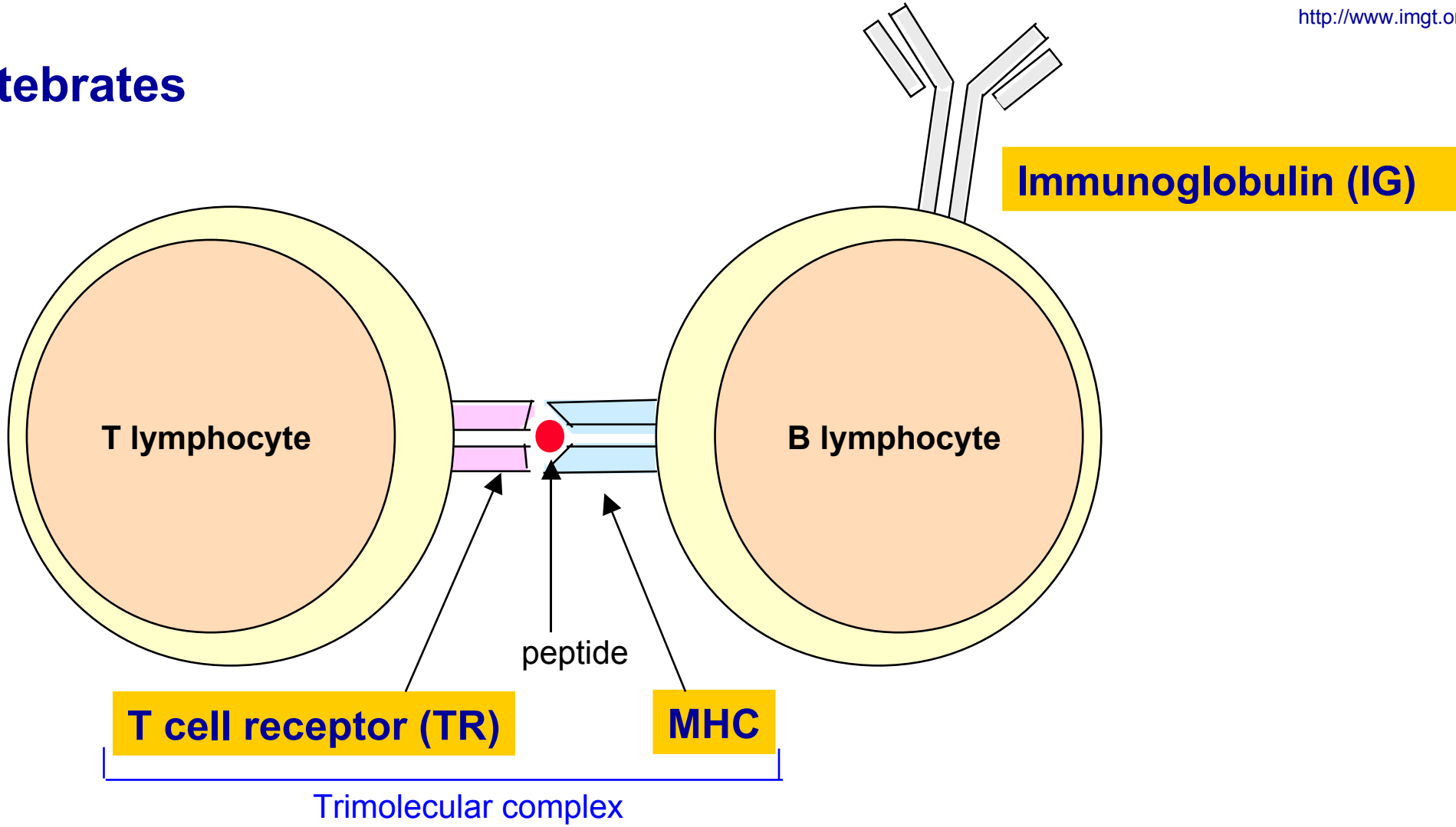
http://www.imgt.org



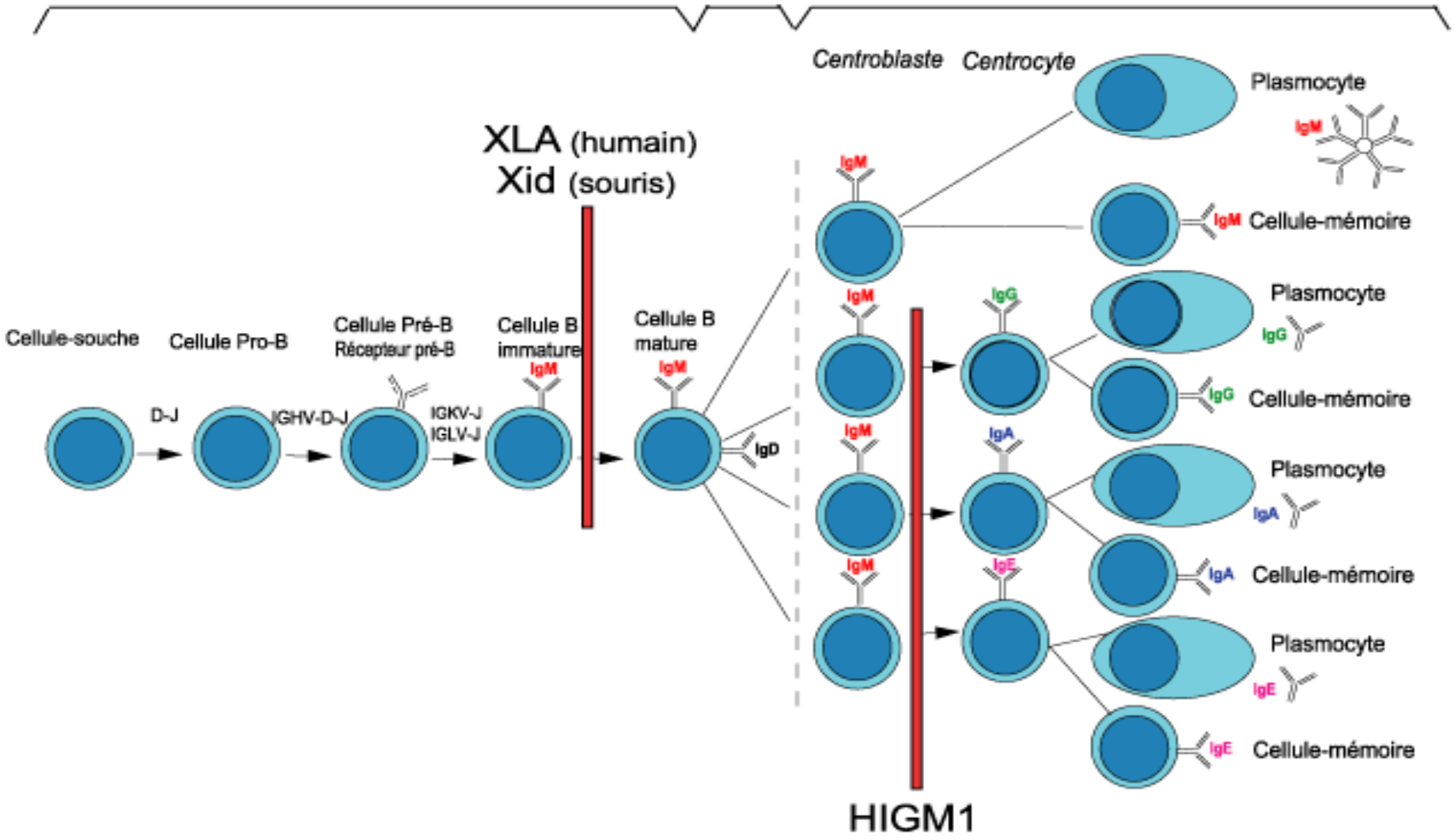
IMGT® domain: the adaptive immune response

http://www.imgt.org

Vertebrates



Bone marrow **Blood** **Lymph nodes, spleen**



V-D-J and V-J rearrangements

Hypermutations, selection

When and why was IMGT created?

IMGT birth and objectives

IMGT was created in June 1989, following the Human Genome Meeting HGM, at New Haven, USA.

* ***Thomas Shows and Ken Kidd, meeting organizers***
* ***Lap Chee Tsui, chromosome 7 responsable***
* ***Claude Boucheix (CD nomenclature)***

1. At New haven, entry of the 16 human T cell receptor gamma genes (TRG) in the genome database, Genome Database (GDB).

2. IMGT was created to answer the need to manage the T cell receptor (TR) and immunoglobulin (IG) genes and to enter them in the generalist databases.

Why was IMGT necessary?

1. Unique structure of the immunoglobulin (IG) and T cell receptor (TR) genes.

Genomic DNA in germline configuration

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

V-GENE

>X62106.0|HSVI2|*Homo sapiens* VI-2 gene for immunoglobulin heavy chain

```
tgagagctcc gttcctcacc atggactgga cctggaggat cctcttcttg gtggcagcag      60
ccacaggtaa gaggctccct agtcccagtg atgagaaaga gattgagtcc agtccaggga     120
gatctcatcc acttctgtgt tctctccaca ggagcccact cccaggtgca gctggtgcag     180
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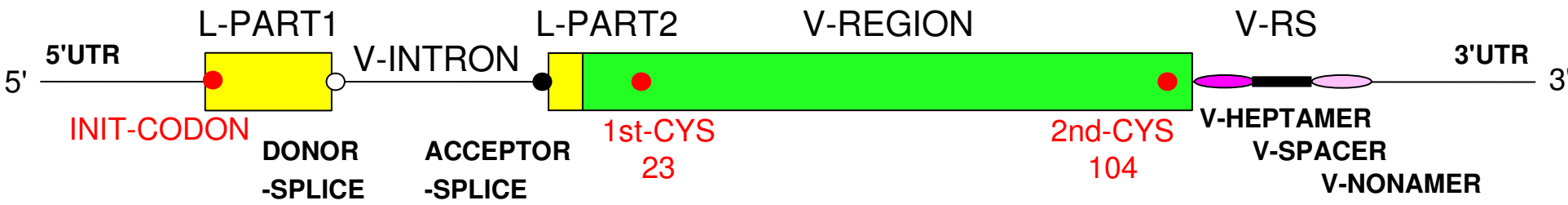

Genomic DNA in germline configuration

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D-GENE

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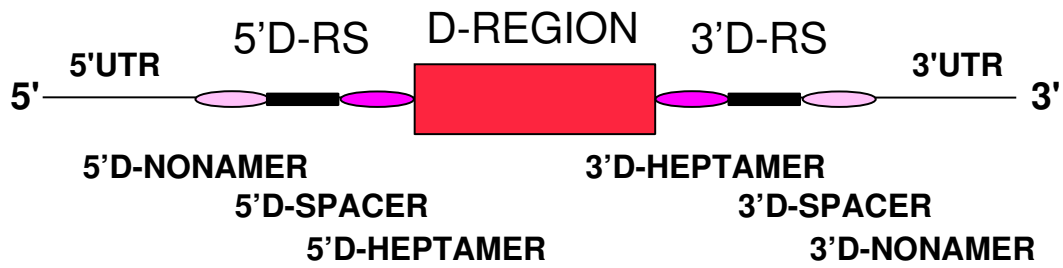
ggcagctcta caaaaacc



J-GENE

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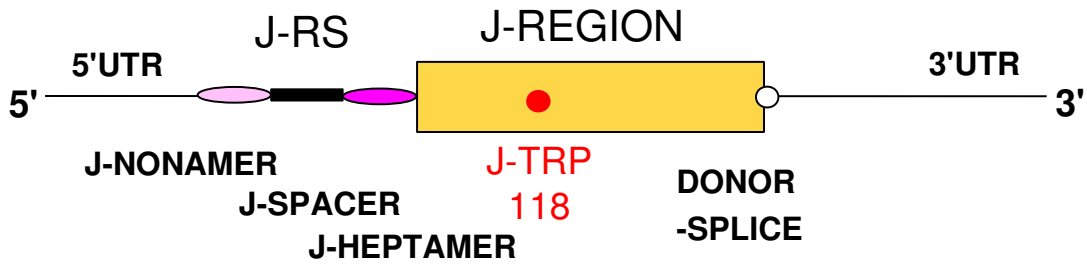

Why was IMGT necessary?

2. Huge diversity of the immunoglobulin and T cell receptor repertoires.

Spacefill 3D representation of an IgG

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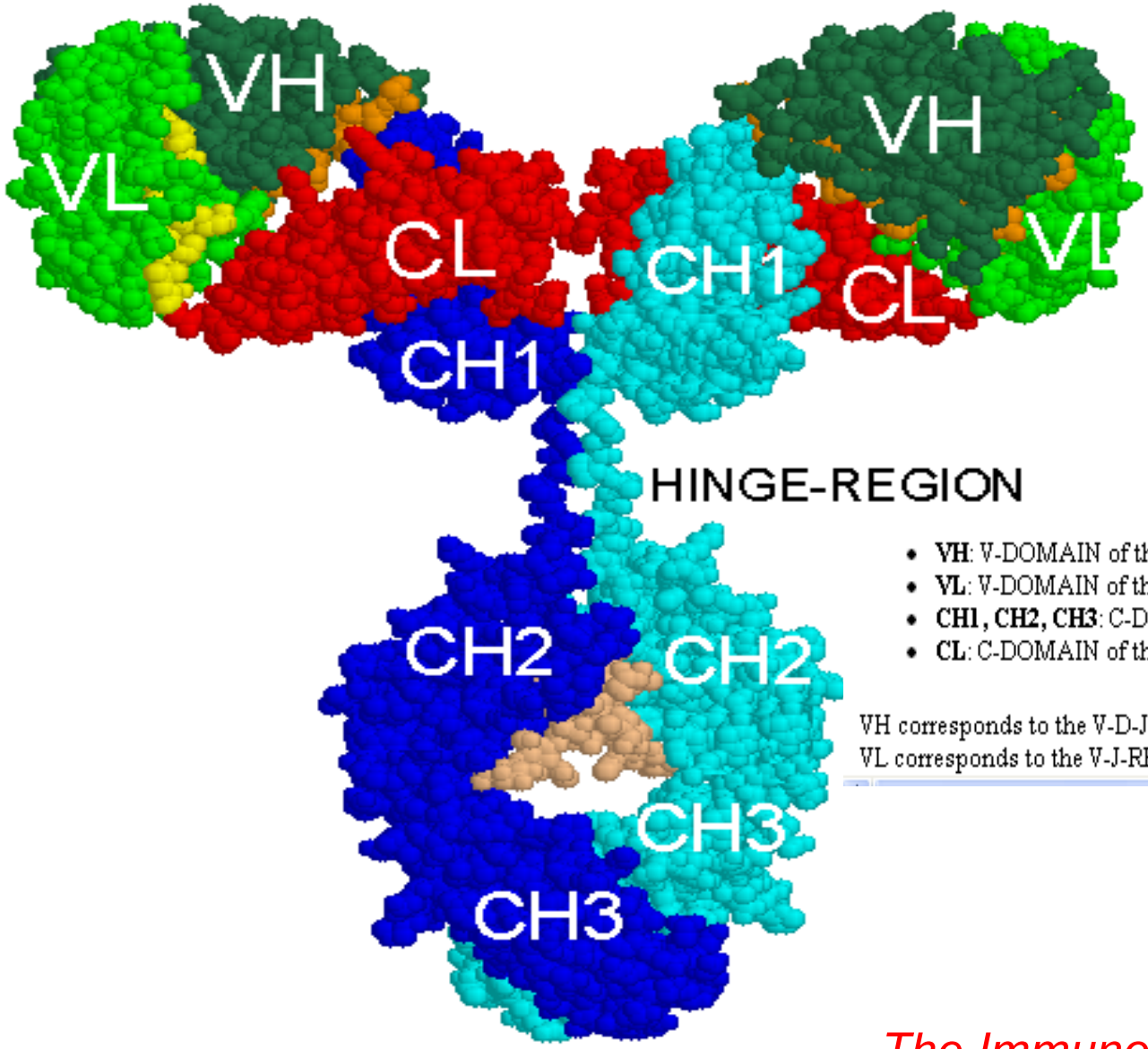


- **VH**: V-DOMAIN of the immunoglobulin heavy chain
- **VL**: V-DOMAIN of the immunoglobulin light chain
- **CH1, CH2, CH3**: C-DOMAIN of the immunoglobulin heavy chain
- **CL**: C-DOMAIN of the immunoglobulin light chain

VH corresponds to the V-D-J-REGION (in green (V), orange (DJ)) of the heavy chain.
VL corresponds to the V-J-REGION (in green (V) and yellow (J)) of the light chain.

The Immunoglobulin FactsBook, 2001

Immunoglobulin (IG)

T cell receptor (TR)

http://www.imgt.org

V-DOMAIN

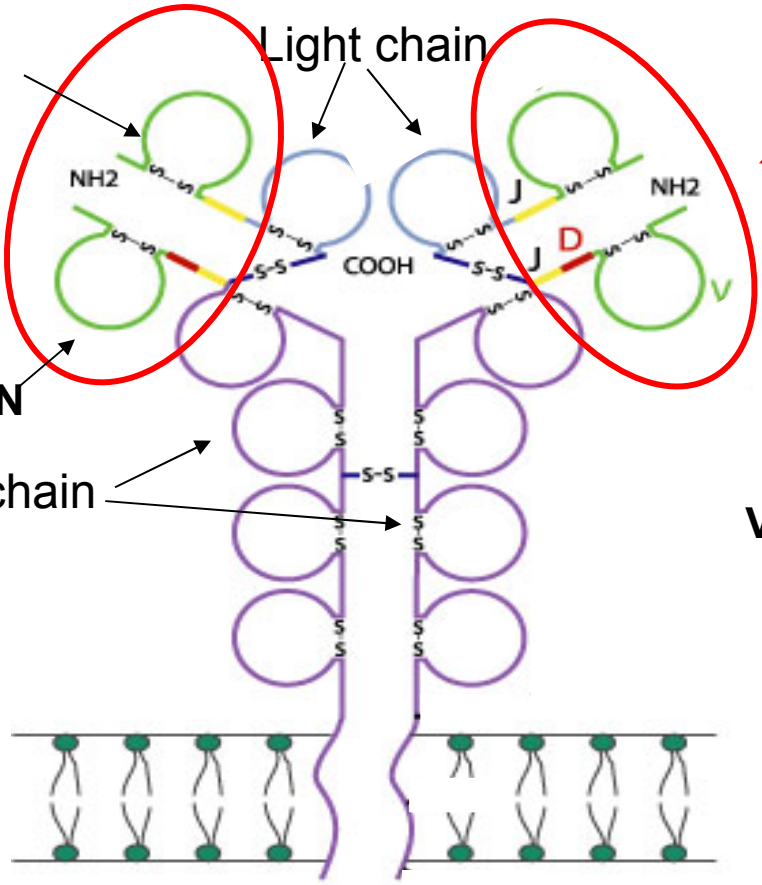
V-J-REGION

V-DOMAIN

V-D-J-REGION

Light chain

Heavy chain



Membrane IgM

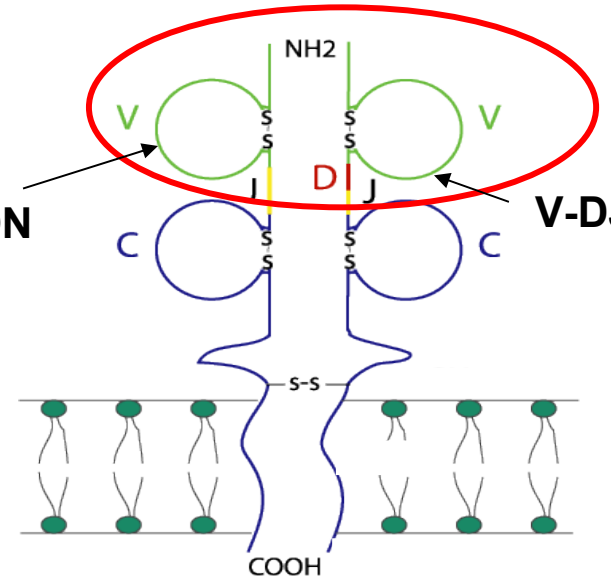
Contribution of the
2 V-DOMAINs
to the antigen binding site

Alpha - Beta

Gamma - Delta

V-J-REGION

V-DJ-REGION



T cell receptor

The Immunoglobulin FactsBook, 2001

Immunoglobulin IgG

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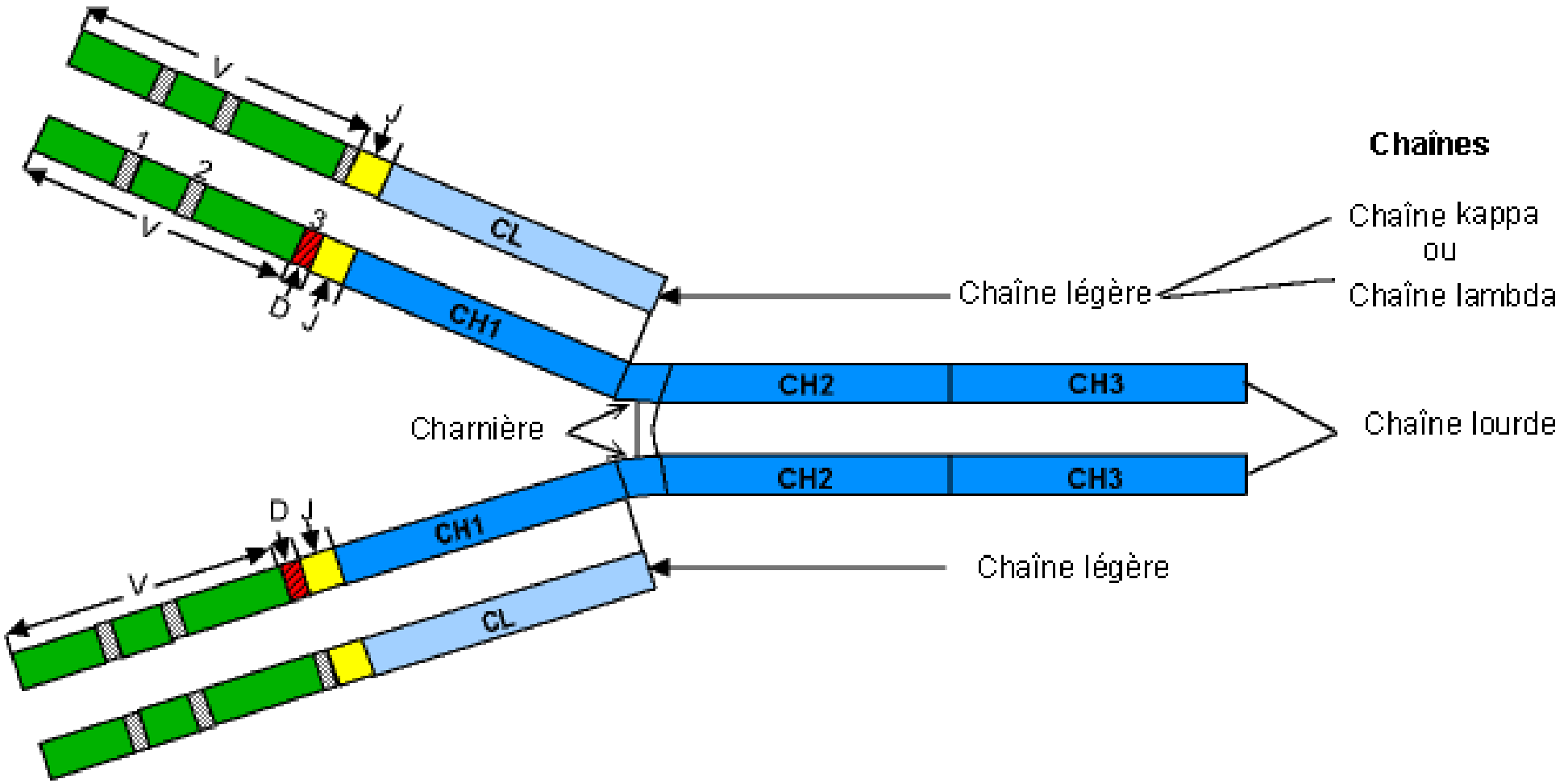
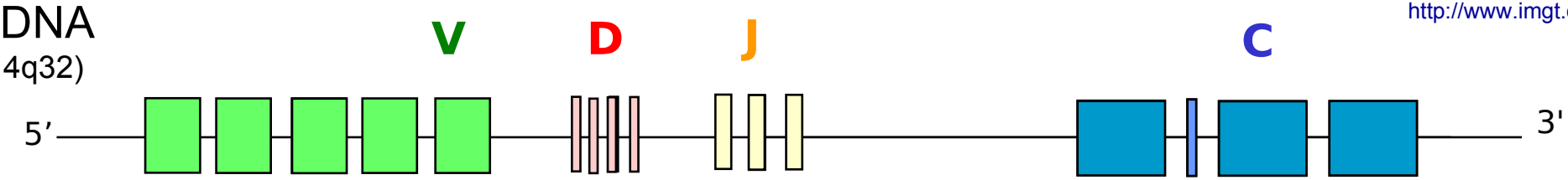


Immunoglobulin (IG) synthesis

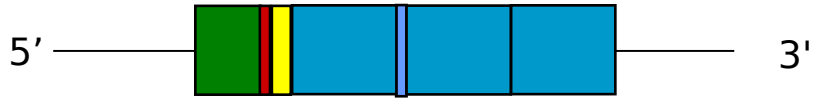
http://www.imgt.org

genomic DNA
(IGH Locus 14q32)

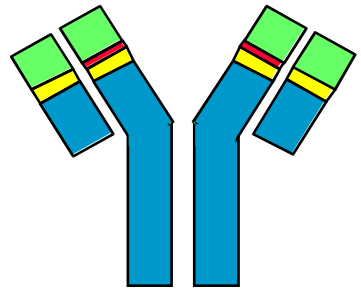


rearranged DNA

mRNA



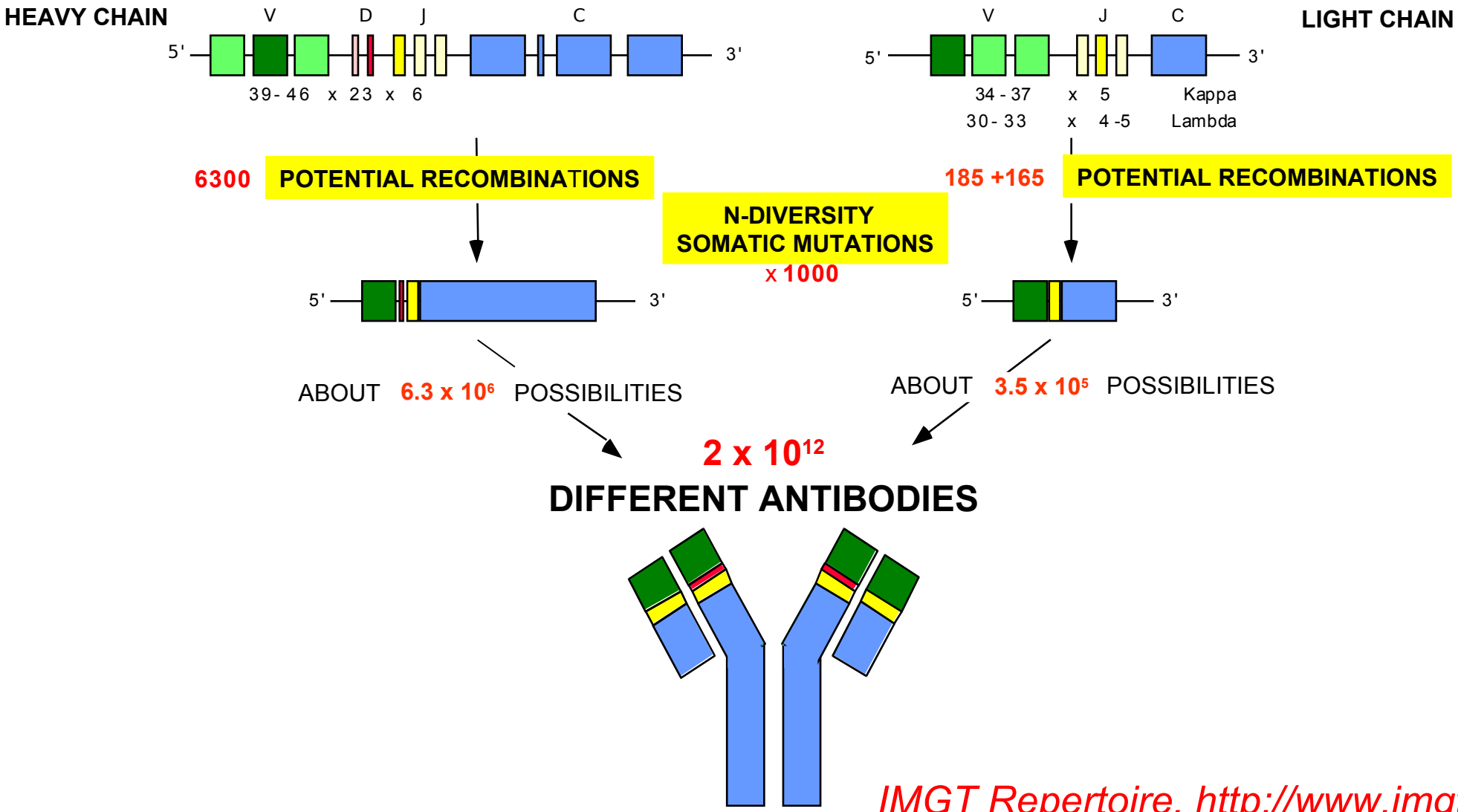
2×10^{12} different IG per individual



Immunoglobulin (IG) synthesis

http://www.imgt.org

150
FUNCTIONAL IG GENES



What was the first goal?

http://www.imgt.org

CONTENT

1. Immunoglobulins AND T cell receptors
2. Human AND other vertebrate species

DATA

1. Genes AND alleles
2. Sequences (germline AND rearranged)
3. Polymorphisms: genomic AND somatic hypermutations
4. 3D structures

IMGT® Web resources

http://www.imgt.org

IMGT Repertoire — 10,000 pages HTML

- Chromosomal localizations
- Locus representations
- Genes tables
- Potential repertoire
- Alignments of alleles
- Protein displays
- IMGT Colliers de Perles…

IMGT Index

IMGT Bloc-notes

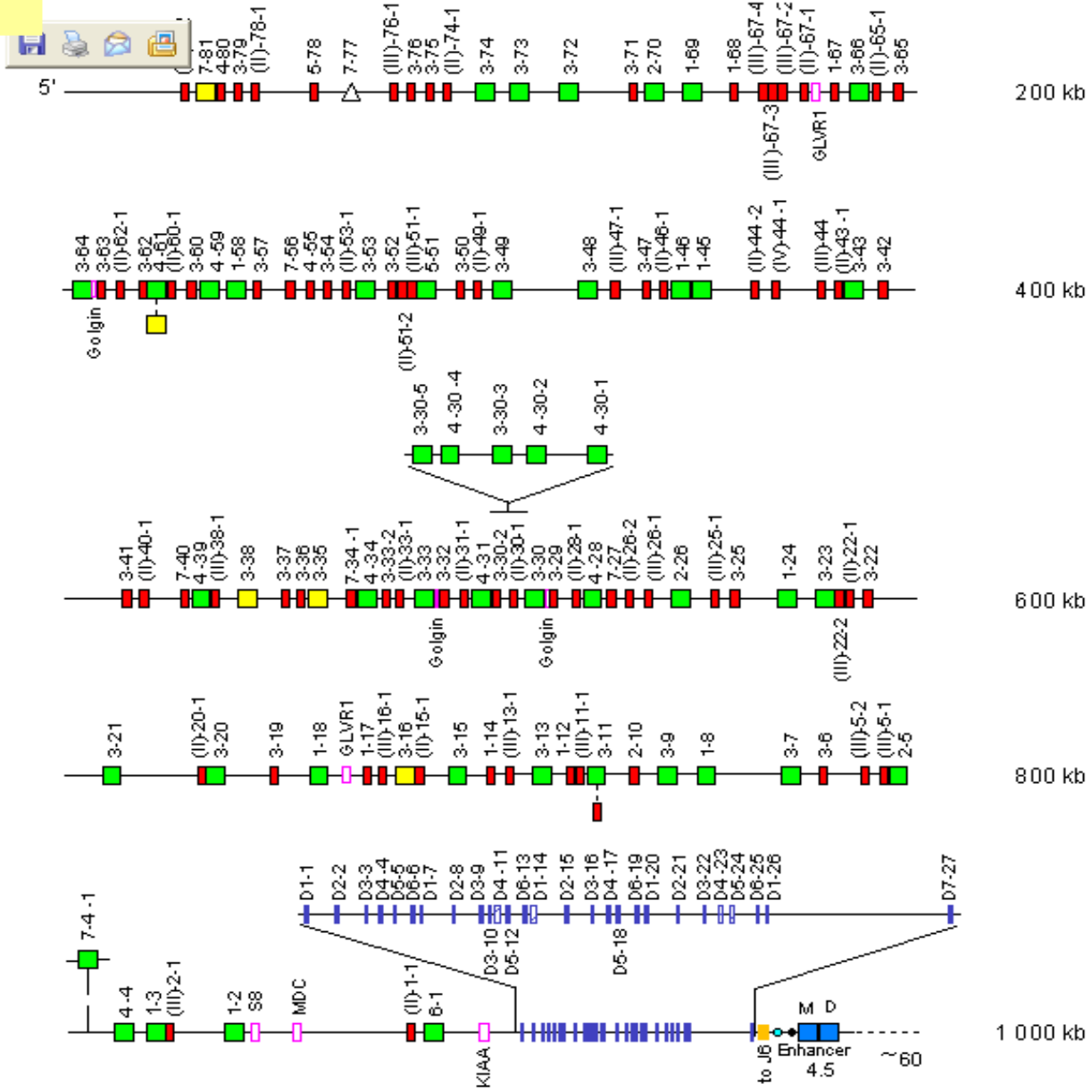
- Interesting links, PubMed,
- Meeting announcements
- IMGT Immunoinformatics page,…

IMGT Education

- Tutorials, IMGT Lexique, …

Human IGH locus

Chromosome 14q32.33



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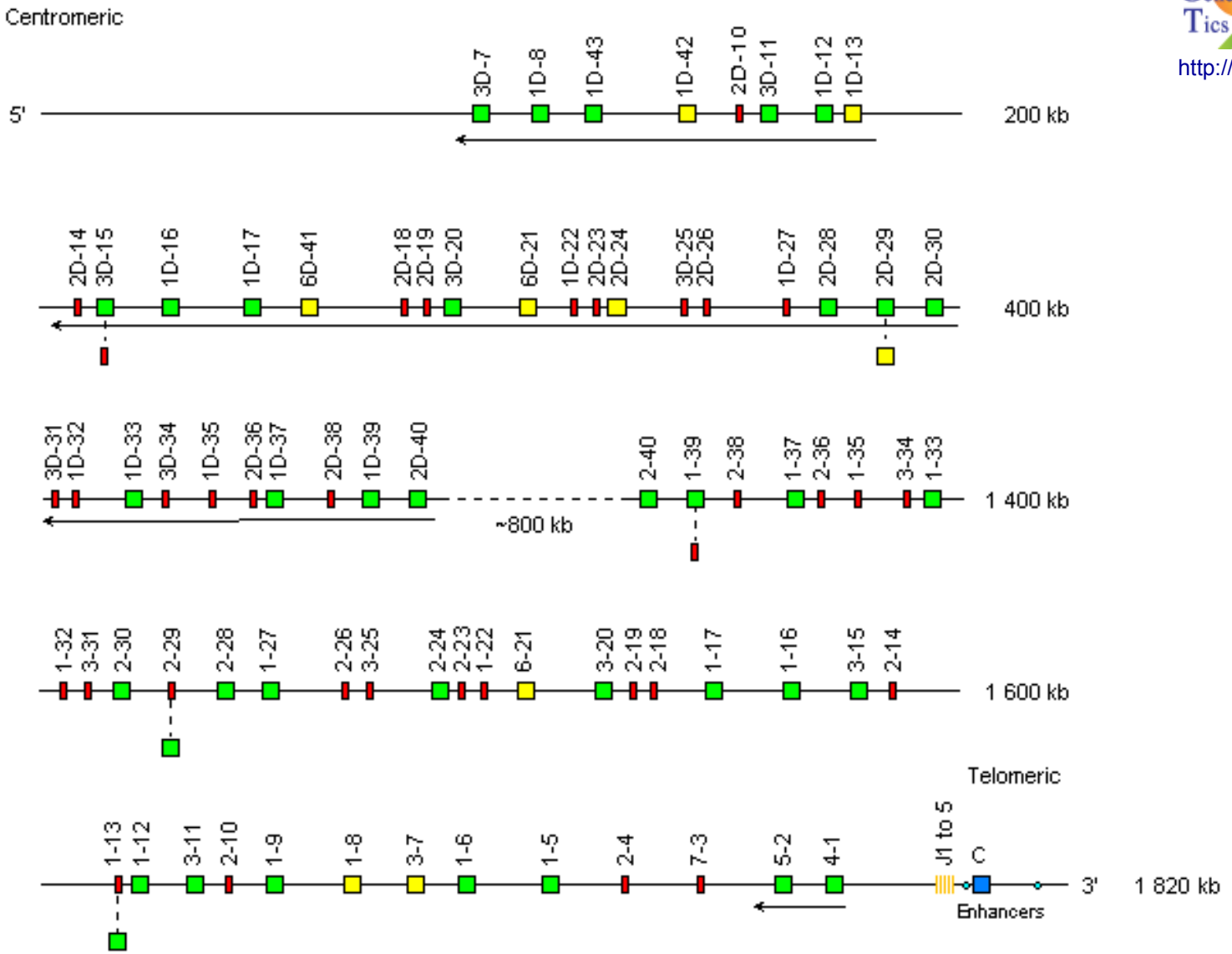
Human IGK locus

Chromosome 2p11.2



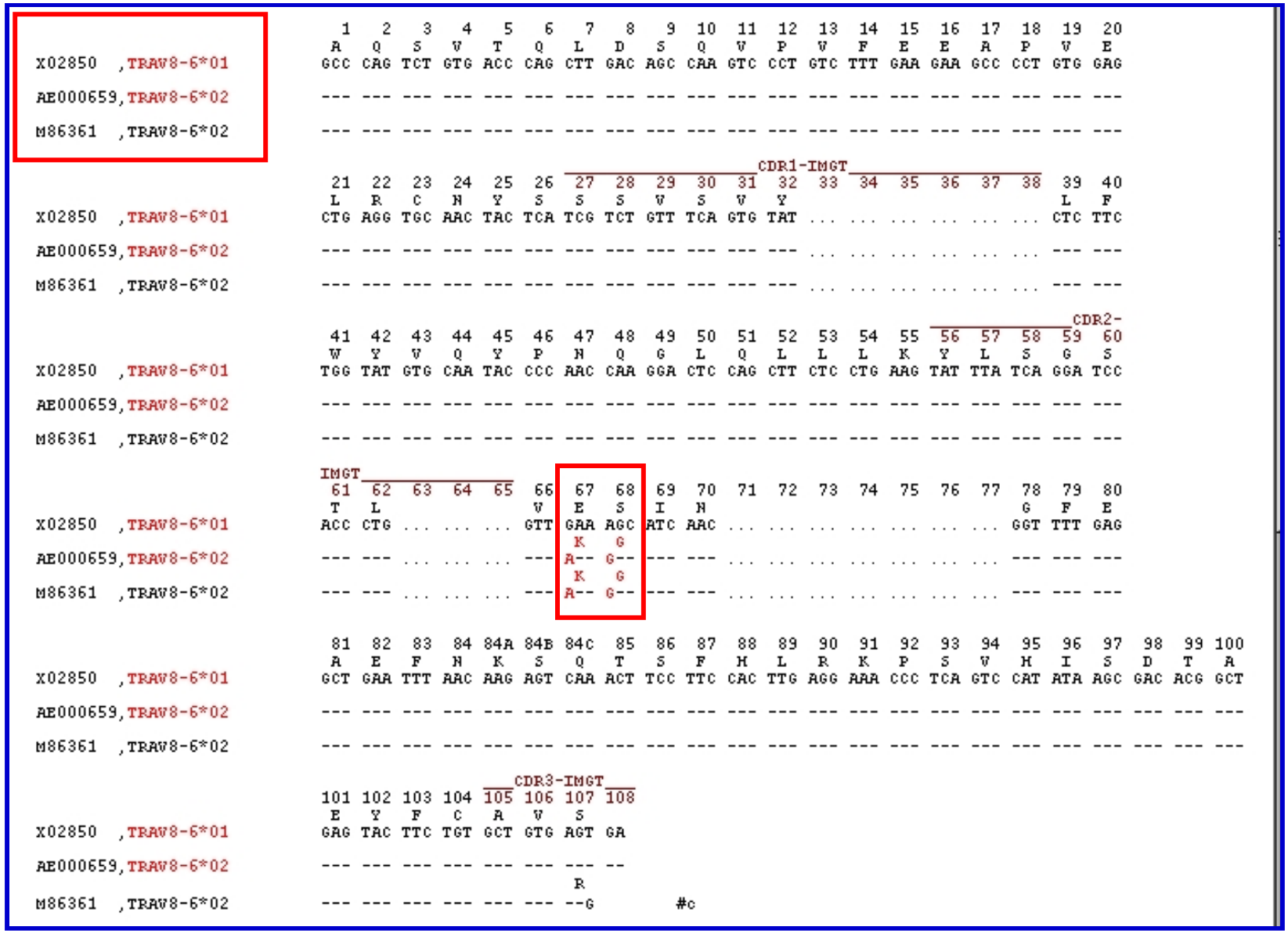
IMGT Repertoire, http://www.imgt.org

Human IGHV genes on chromosome 14 at 14q32.33

http://www.imgt.org

Subgroup	Functional	ORF	Pseudogene	Total
IGHV1	9	-	5	14
IGHV2	3	-	1	4
IGHV3	18-20**(+1)*	3	25(+1)*	47-49**
IGHV4	6-9**(+1)*	(+1)*	2	9-12**
IGHV5	1	-	1	2
IGHV6	1	-	-	1
IGHV7	0-1**	1	4	5-6**
IGHV(II)	-	-	22	22
IGHV(III)	-	-	18	18
IGHV(IV)	-	-	1	1
Total	38-44(+2)*	4(+1)*	79(+2)*	123-129**

IMGT Alignment of alleles



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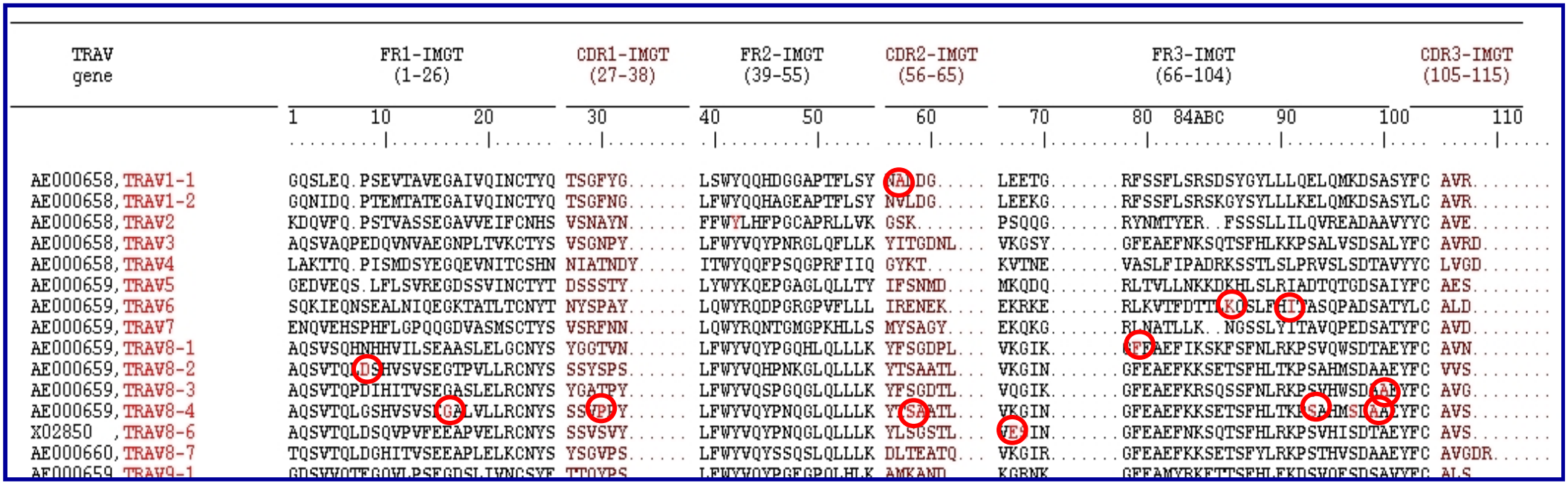
http://www.imgt.org

IMGT Protein display

http://www.imgt.org



TRAV gene	FR1-IMGT (1-26)	CDR1-IMGT (27-38)	FR2-IMGT (39-55)	CDR2-IMGT (56-65)	FR3-IMGT (66-104)	CDR3-IMGT (105-115)
	1 10 20	30	40 50	60	70 80 84ABC 90 100	110
AE000658,TRAV1-1	GQSLEQ.PSEVTAVEGAIVQINCTYQ	TSGFYG.....	LSWYQQHDGGAPTFLSY	NALDG.....	LEETG.....RFSSFLSRSDSYGYLLLQELQMKDSASYFC	AVR.....
AE000658,TRAV1-2	GQNIDQ.PTEMTATEGAIVQINCTYQ	TSGFNG.....	LFWYQQHAGEAPTFLSY	NVLDG.....	LEEKG.....RFSSFLSRSKGYSYLLLKELQMKDSASYLC	AVR.....
AE000658,TRAV2	KDQVFQ.PSTVASSEGAVVEIFCNHS	VSNAYN.....	FFWYLHFPGCAPRLLVK	GSK.....	PSQQG.....RYNMTYER..FSSSLLILQVREADAAVYYC	AVE.....
AE000658,TRAV3	AQSVAQPEDQVNVAEGNPLTVKCTYS	VSGNPY.....	LFWYVQYPNRGLQFLLK	YITGDNL...	VKGSY.....GFEAEFNKSQTSFHLKKPSALVSDSALYFC	AVRD.....
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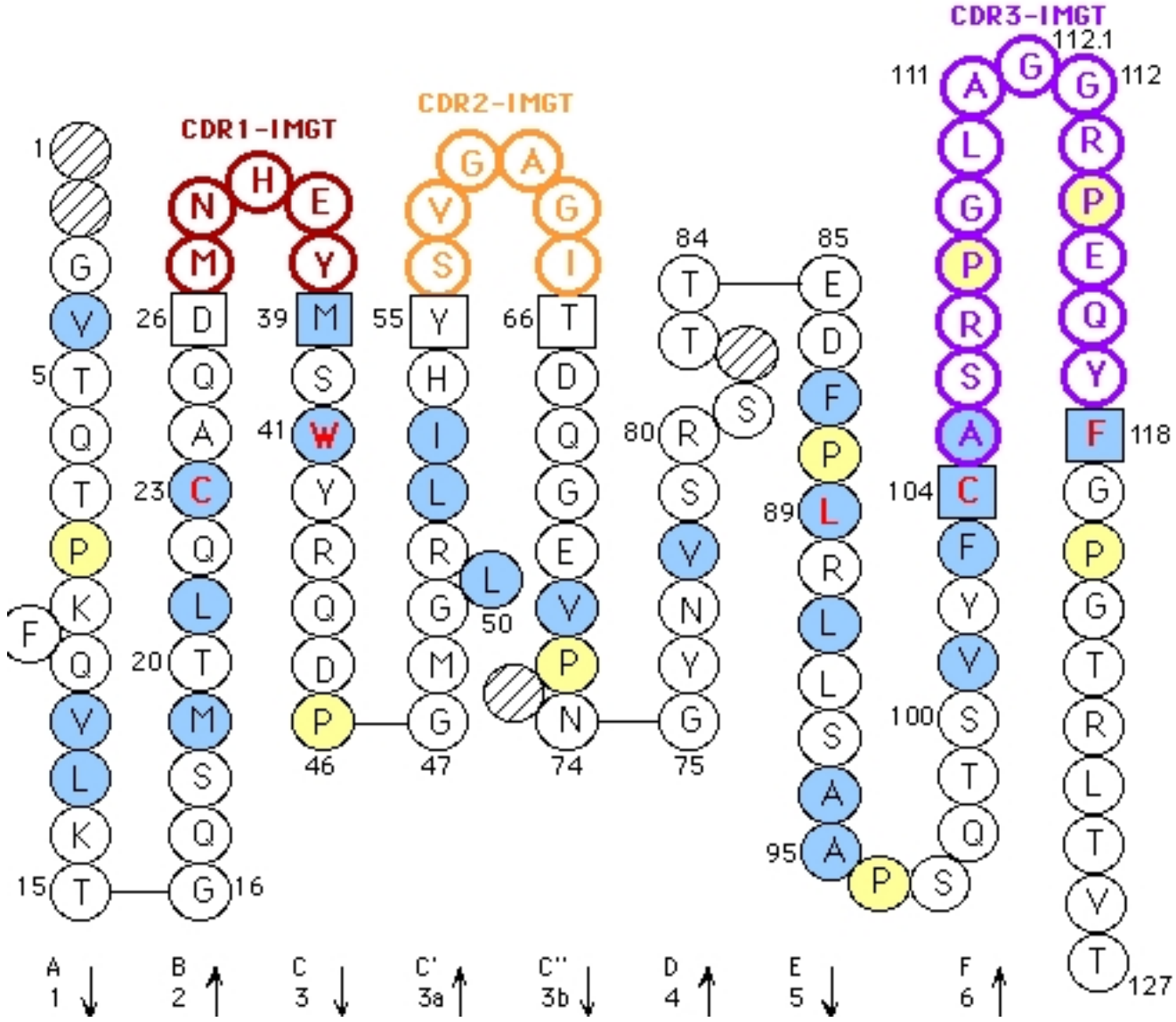
AE000659,TRAV9-1	GDSVVQTEGQVLPSEGDSLIVNCSYE	TTQYPS.....	LFWYVQYPGEGPQLHLK	AMKAND....	KGRNK.....GFEAMYRKETTSFHLEKDSVQESDSAVYFC	ALS.....

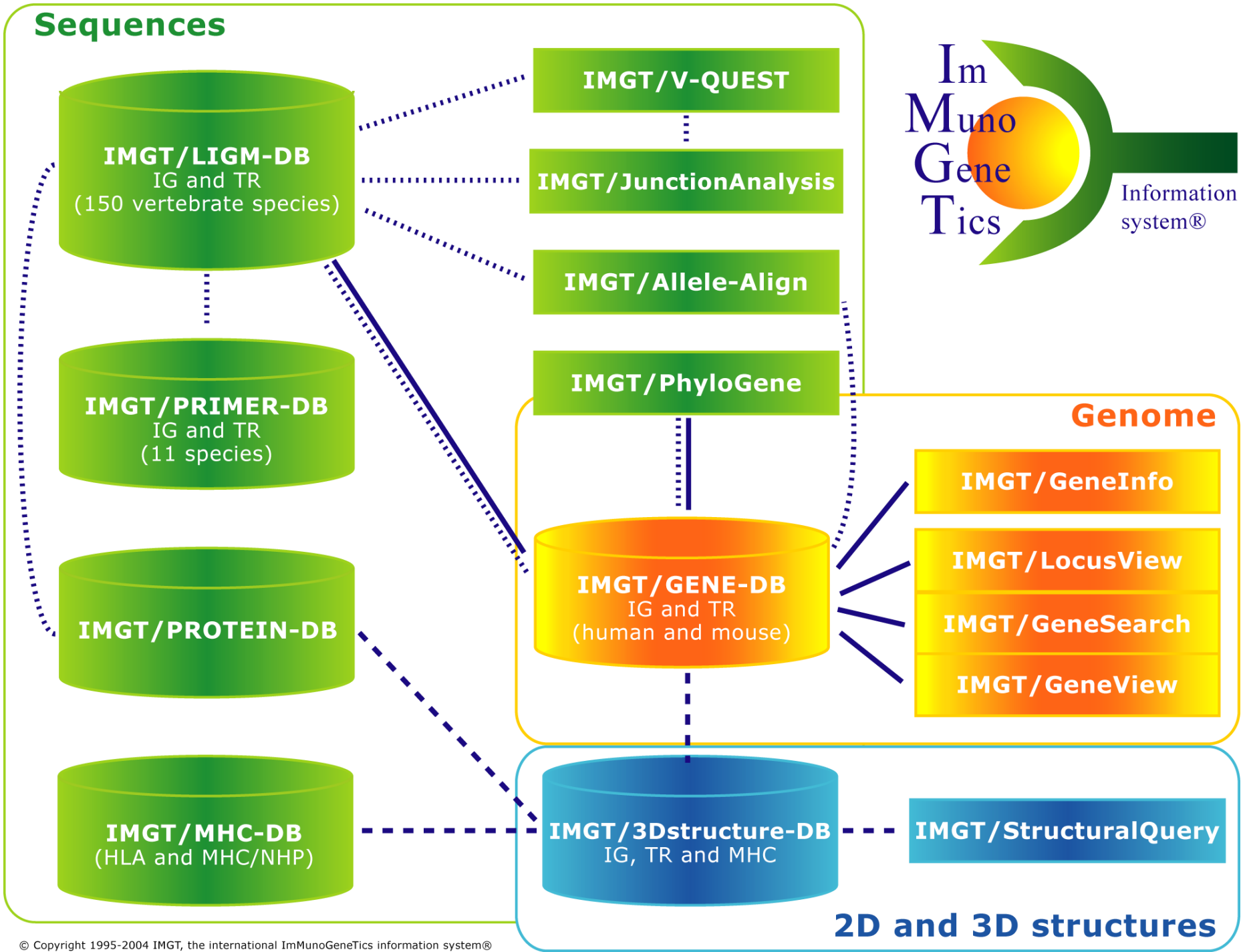
IMGT Repertoire, http://www.imgt.org

IMGT Collier de Perles

http://www.imgt.org



IMGT databases and tools



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IMGT Marie-Paule page: IMGT repertoire - Netscape

Fichier Edition Affichier Aller Communicator Aide

Locus representation: Human IGL

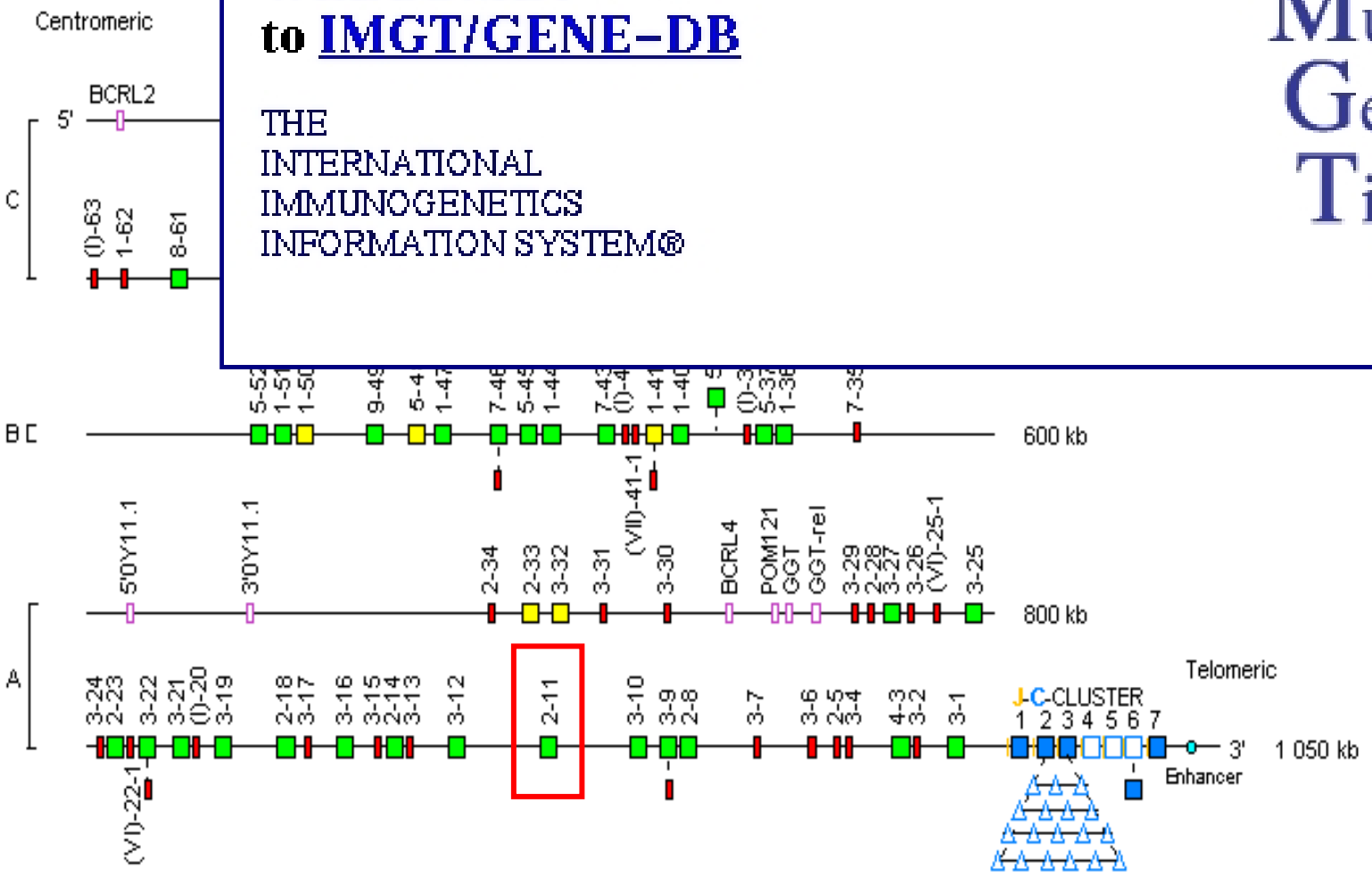
Human IGL 22q11.2

WELCOME !
to IMGT/GENE-DB

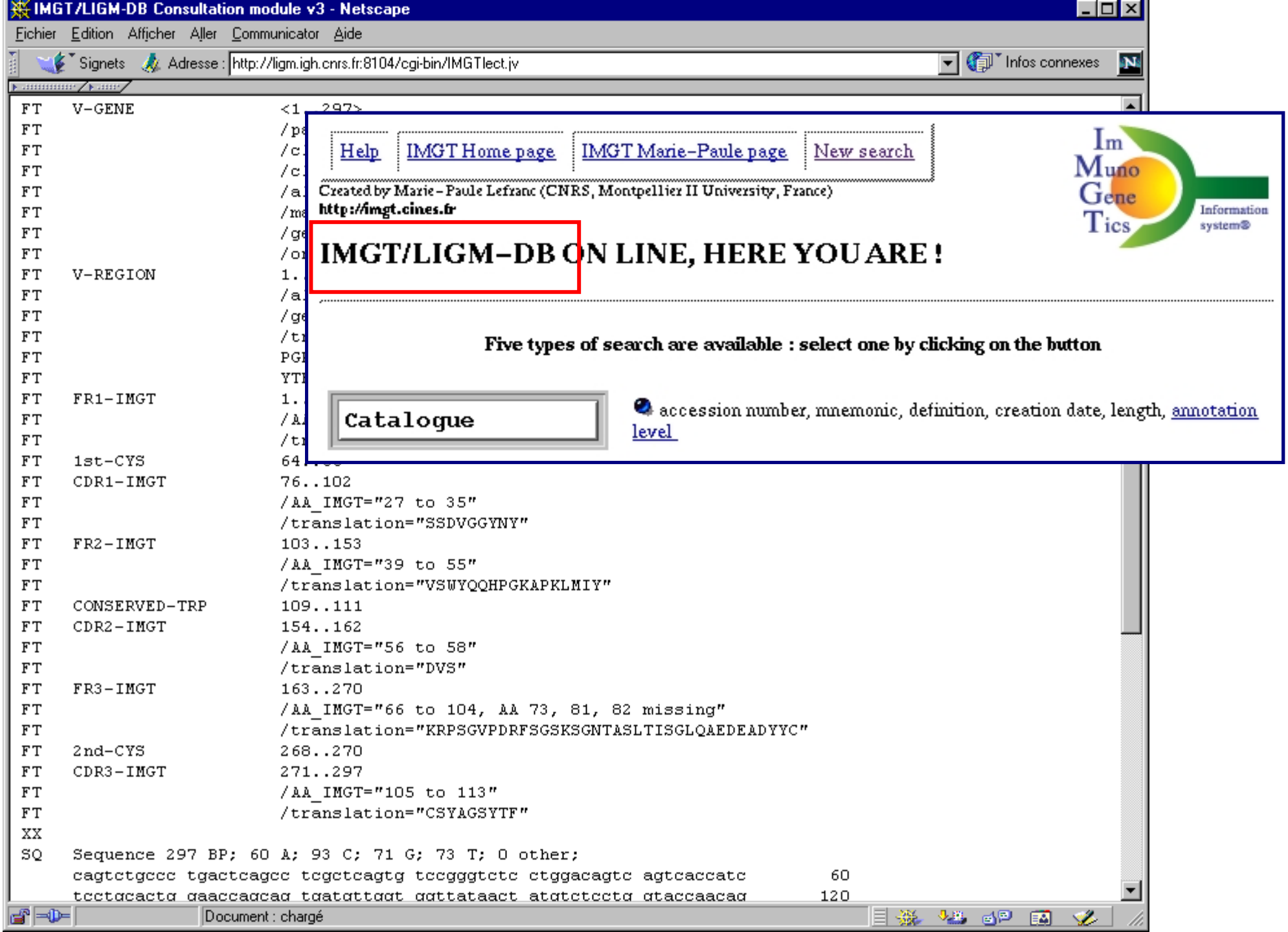
THE
INTERNATIONAL
IMMUNOGENETICS
INFORMATION SYSTEM®

Im Muno Gene Tics

Information system®



Giudicelli V. et al. Nucleic Acids Res. 33, D256-D261 (2005)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Fichier Edition Affiche Aller Communicator Aide
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Infos connexes
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FT /c
FT /a
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Document : chargé
Help
IMGT Home page
IMGT Marie-Paule page
New search
Created by Marie-Paule Lefranc (CNRS, Montpellier II University, France)
http://imgt.cines.fr
IMGT/LIGM-DB ON LINE, HERE YOU ARE !
Five types of search are available : select one by clicking on the button
Catalogue
accession number, mnemonic, definition, creation date, length, annotation level
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Information system®

IMGT/LIGM-DB

http://www.imgt.org

DESCRIPTION

IMGT/LIGM-DB Consultation module v3 - Mozilla Firefox

File Edit View Go Bookmarks Tools Help

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Done

137.963 sequences from 235 species

IMGT-ONTOLOGY:

277 IMGT labels for sequences

285 IMGT labels for 3D structures

SO (Sequence ontology):

67 IMGT labels

cDNA (in databases: mRNA!)

http://www.imgt.org

```
.....gagga ttcaccatgg aactggggct ccgctgggtt ttccttgttg ctttttaga 120
aggtgtccag tgtgaggtgc aactggtgga gtctgggggg ggcctggtca agccgggggg 180
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gctaaccgcc accctctcaa aatccggaaa cacattccgg cccgaggtcc acctgctgcc 1200
gccgccgtcg gaggagctgg ccctgaacga gctggtgacg ctgacgtgcc tggcacgtgg 1260
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taaacccacc catgtcaatg tgtctgttgt catggcggag gtggacggca cctgctactga 1560 .....
```

cDNA

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```
.....gagga ttcaccatgg aactggggct ccgctgggtt ttccttgttg ctttttttaga 120
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gtccctgaga ctctcctgtg cagcctctgg attaagcttc agtacctatg ccatgaactg 240
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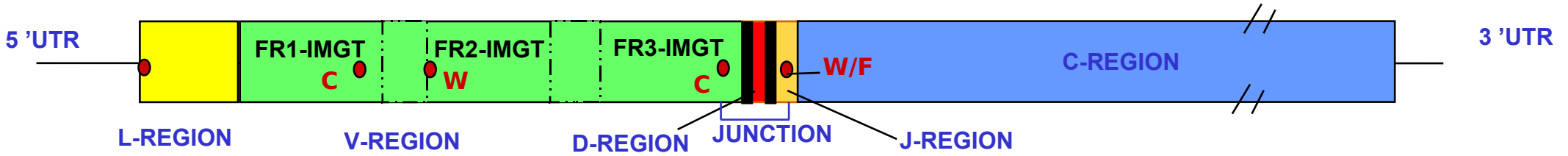

The IMGT-ONTOLOGY concepts

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

IDENTIFICATION

IMGT/LIGM-DB Consultation module v3 - Netscape

Fichier Edition Afficher Aller Communicator Aide

```
ID   HSCOMFRAA IMGT/LIGM annotation : automatic; RNA. HUM; 375 BP.
XX
AC   L39956;
XX
DT   28-SEP-2001 (Rel. 200139-5, arrived in LIGM-DB )
DT   13-NOV-2001 (Rel. 200146-2, Last updated, Version 2)
XX
DE   Homo sapiens monospecific anti-ssDNA antibody heavy chain variable region
DE   mRNA, complementarity determining regions  1-3 and framework regions 1-4.
DE   ;
DE   RNA; rearranged configuration; Ig-Heavy; regular; functionality
DE   productive; group IGHV; subgroup HV3; specificity anti-DNA single-stranded
DE   (ss) [human].
XX
KW   antigen receptor; immunoglobulin superfamily; Ig; Ig-Heavy; variable;
KW   diversity; joining; hybridoma; immunoglobulin.
XX
OS   Homo sapiens (human)
OC   Eukaryota; Metazoa; Chordata; Vertebrata; Mammalia; Eutheria; Primates;
OC   Catarrhini; Hominidae; Homo.
XX
RN   [1]
RP   1-375
RX   MEDLINE; 96195158.
RA   Mitamura K., Suenaga R., Wilson K.B., Abdou N.I.;
RT   "V gene sequences of human anti-ssDNA antibodies secreted by lupus-derived
RT   CD5-negative B cell hybridomas";
RL   Clin. Immunol. Immunopathol. 78(2):152-160(1996).
XX
DR   EMBL; L39956.
XX
FH   Key                 Location/Qualifiers
FH
FT   L-V-D-J-C-SEQUENCE  <1..375>
FT                       /partial
```

Document : chargé

The IMGT-ONTOLOGY concepts

http://www.imgt.org

DESCRIPTION

IMGT/LIGM-DB Consultation module v3 - Mozilla Firefox

File Edit View Go Bookmarks Tools Help

```
FH   Key                  Location/Qualifiers
FH
FT   L-V-D-J-C-SEQUENCE   <1..375>
FT                        /partial
FT                        /db_xref="taxon:9606"
FT                        /cell_type="B-cell hybridoma 2F7"
FT                        /IMGT_note="automatically annotated with IMGT tools"
FT                        /organism="Homo sapiens"
FT   V-D-J-REGION         1..375
FT                        /translation="QVHLVESGGAVFHPGRSLRLSRAASGFTFSSYGMHWVRQAP
FT                        AKGLEWVAVIWYDGSNKYYADSVKGRFTISRDNSKNTLYL
FT                        AKHVTIAAAGRRGAGMDVWGQGTTVTVSS"
FT   V-REGION             1..296
FT                        /allele="IGHV3-33*01, putative"
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FT                        /CDR_length="[8,8,18]"
FT                        /putative_limit="3' side"
FT                        /translation="QVHLVESGGAVFHPGRSLRLSRA
FT                        AKGLEWVAVIWYDGSNKYYADSVKGRFTISRDNSKNT
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

OBTENTION

CLASSIFICATION

NUMEROTATION

IMGT/V-QUEST

IMGT/V-QUEST

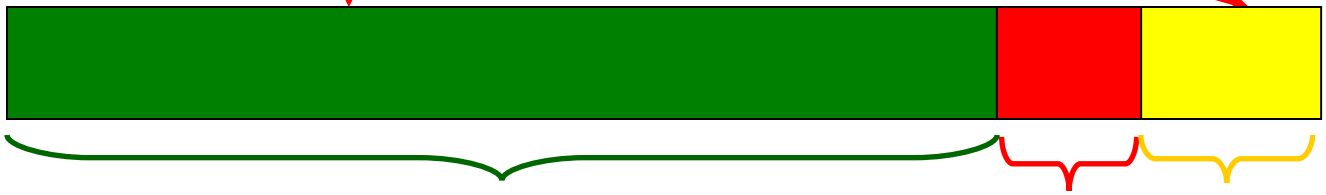
http://www.imgt.org

Alignment for V-GENE

```
AF402940                    score GTGCAGCTGCTCGAGCAGTCTGGGGCT___GAGGTGAGCAAGCCTGGGGCCTCAGTAAAGGTTTCCTGCA
X62109   IGHV1-3*01          1146 CA.GTC.A...T.T............___.......AG.................G.............
X62107   IGHV1-3*02          1110 CA.GTT.A...G.T............___.......AG.................G.............
M99637   IGHV1-8*01           957 CA.GT..A...G.T............___.......AG.................G.....C.......
L06612   IGHV1-46*03          948 CA.GT..A...G.T............___.......AG.................G.............
X92343   IGHV1-46*01          948 CA.GT..A...G.T............___.......AG.................G.............
```

Alignment for J-GENE

```
AF402948                    score CTTCACGGGGCGGGACGCTTTGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTCA
J00256   IGHJ3*01             181 _________________.T.....T..T.................A.T...........T...G
X86355   IGHJ6*02             179 T.A.TACTACTACT...G.A.....................................
X86355   IGHJ3*02             172 _________________.T.....T..TA................A.T...........T...G
```



V-GENE JUNCTION J-GENE

Giudicelli et al. Nucleic Acids Res. 36, W503-W508 (2008)

WELCOME !
to IMGT/V-QUEST

THE
INTERNATIONAL
IMMUNOGENETICS
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**

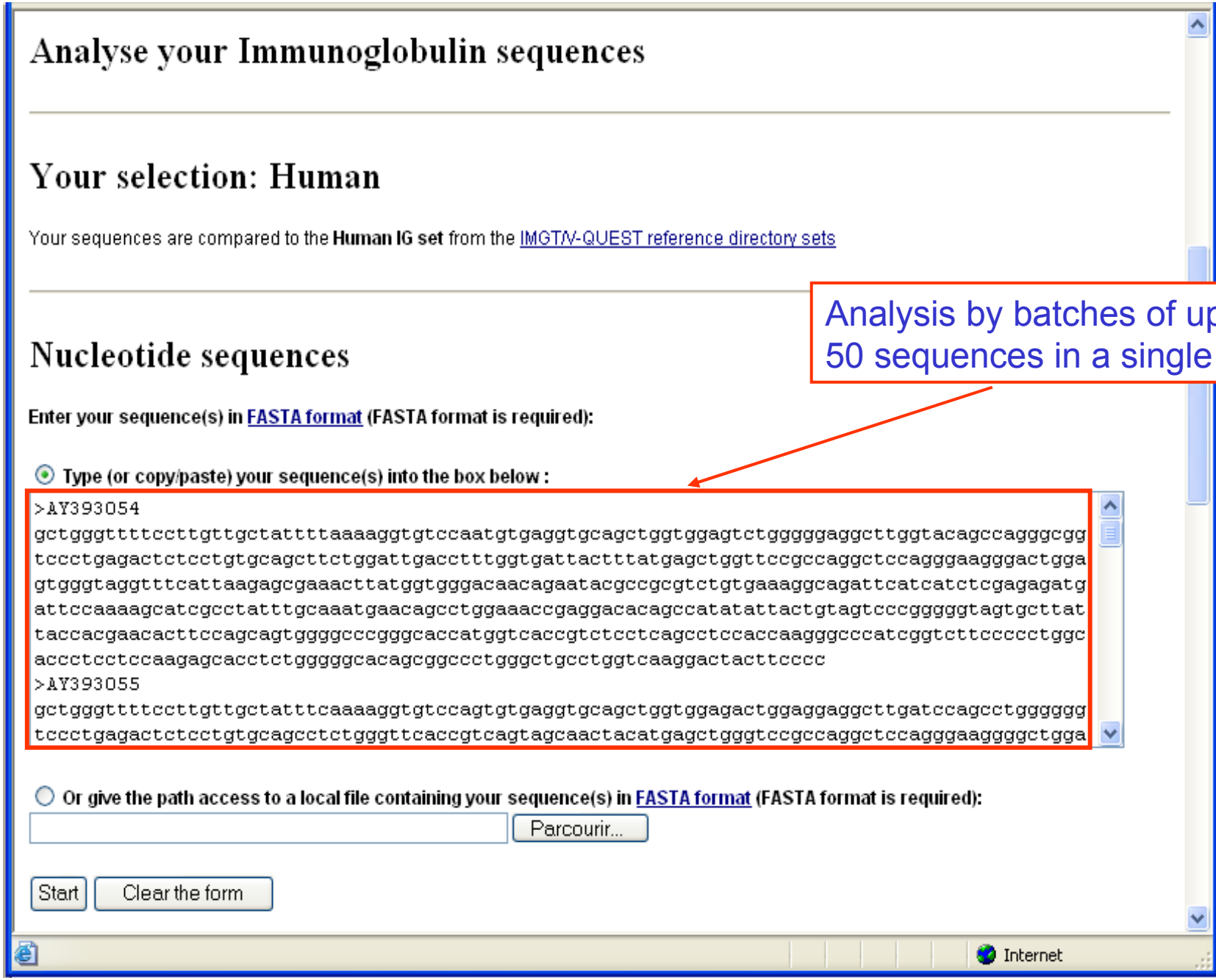
Current version: 3.1.2 (18 July 2008)

Analyse your Immunoglobulin nucleotide sequences

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

Analyse your T cell Receptor nucleotide sequences

- Human
- Nonhuman primates



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

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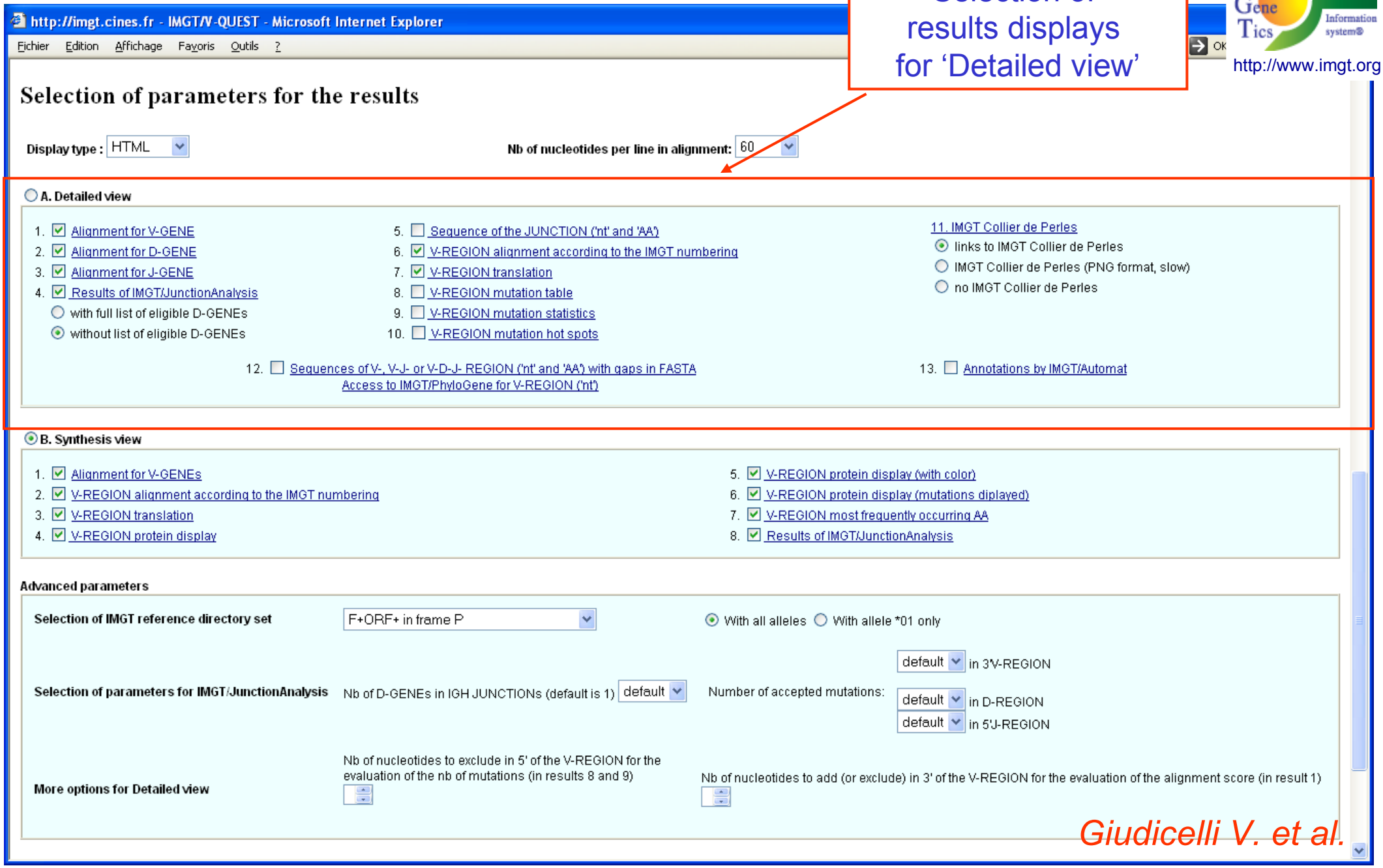
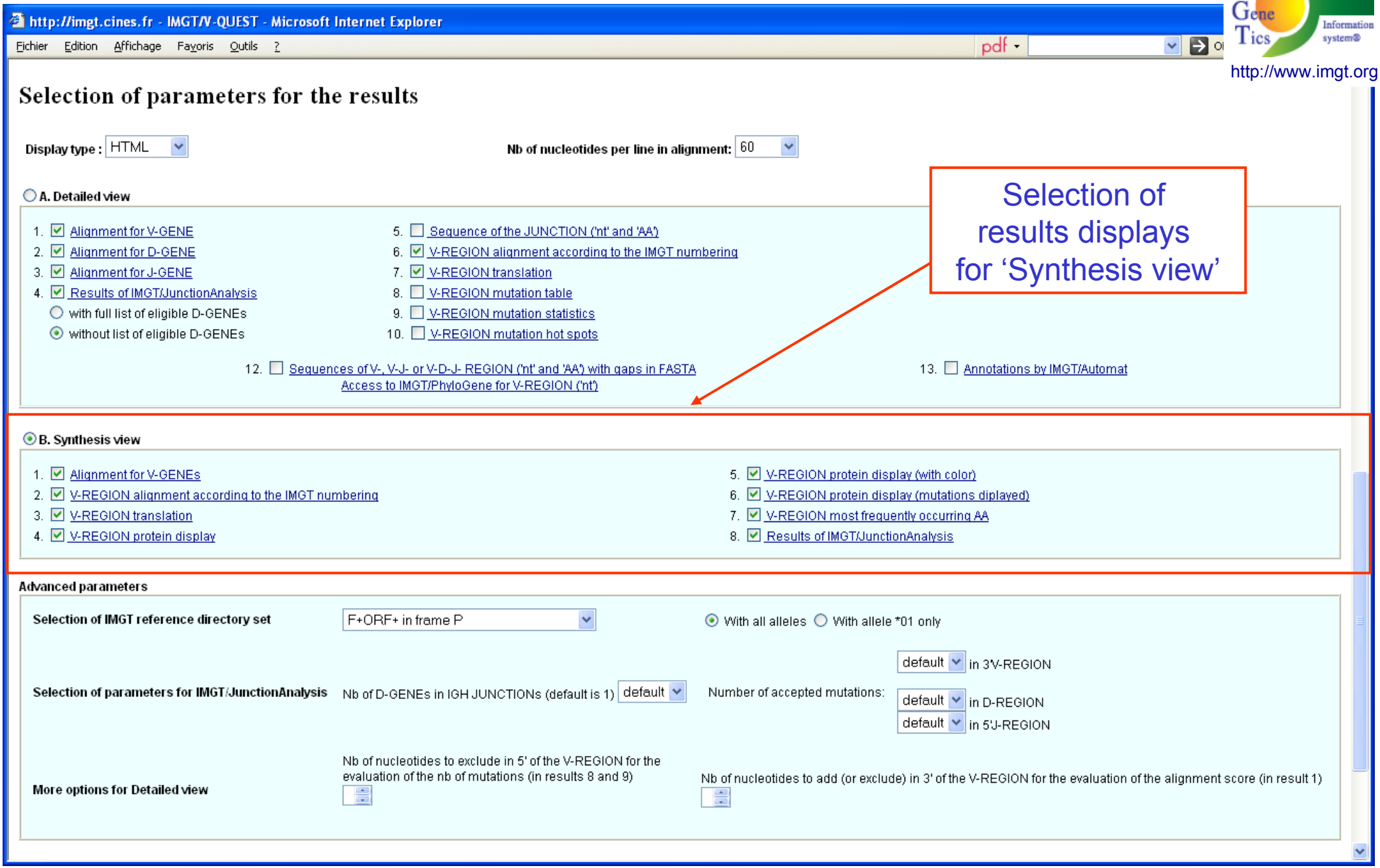
http://www.imgt.org


Selection of results displays for 'Detailed view'
http://imgt.cines.fr - IMGT/V-QUEST - Microsoft Internet Explorer
Fichier Edition Affichage Favoris Outils ?
http://www.imgt.org
Selection of parameters for the results
Display type : HTML
Nb of nucleotides per line in alignment: 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 according to the IMGT numbering
7. V-REGION translation
8. V-REGION mutation table
9. V-REGION mutation statistics
10. V-REGION mutation hot spots
11. IMGT Collier de Perles
links to IMGT Collier de Perles
IMGT Collier de Perles (PNG format, slow)
no IMGT Collier de Perles
12. Sequences of V-, V-J- or V-D-J- REGION ('nt' and 'AA') with gaps in FASTA
Access to IMGT/PhyloGene for V-REGION ('nt')
13. Annotations by IMGT/Automat
B. Synthesis view
1. Alignment for V-GENEs
2. V-REGION alignment according to the IMGT numbering
3. V-REGION translation
4. V-REGION protein display
5. V-REGION protein display (with color)
6. V-REGION protein display (mutations diplayed)
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
Selection of parameters for IMGT/JunctionAnalysis
Nb of D-GENEs in IGH JUNCTIONs (default is 1)
default
Number of accepted mutations:
default in 3'V-REGION
default in D-REGION
default in 5'J-REGION
More options for Detailed view
Nb of nucleotides to exclude in 5' of the V-REGION for the evaluation of the nb of mutations (in results 8 and 9)
Nb of nucleotides to add (or exclude) in 3' of the V-REGION for the evaluation of the alignment score (in result 1)
Giudicelli V. et al.



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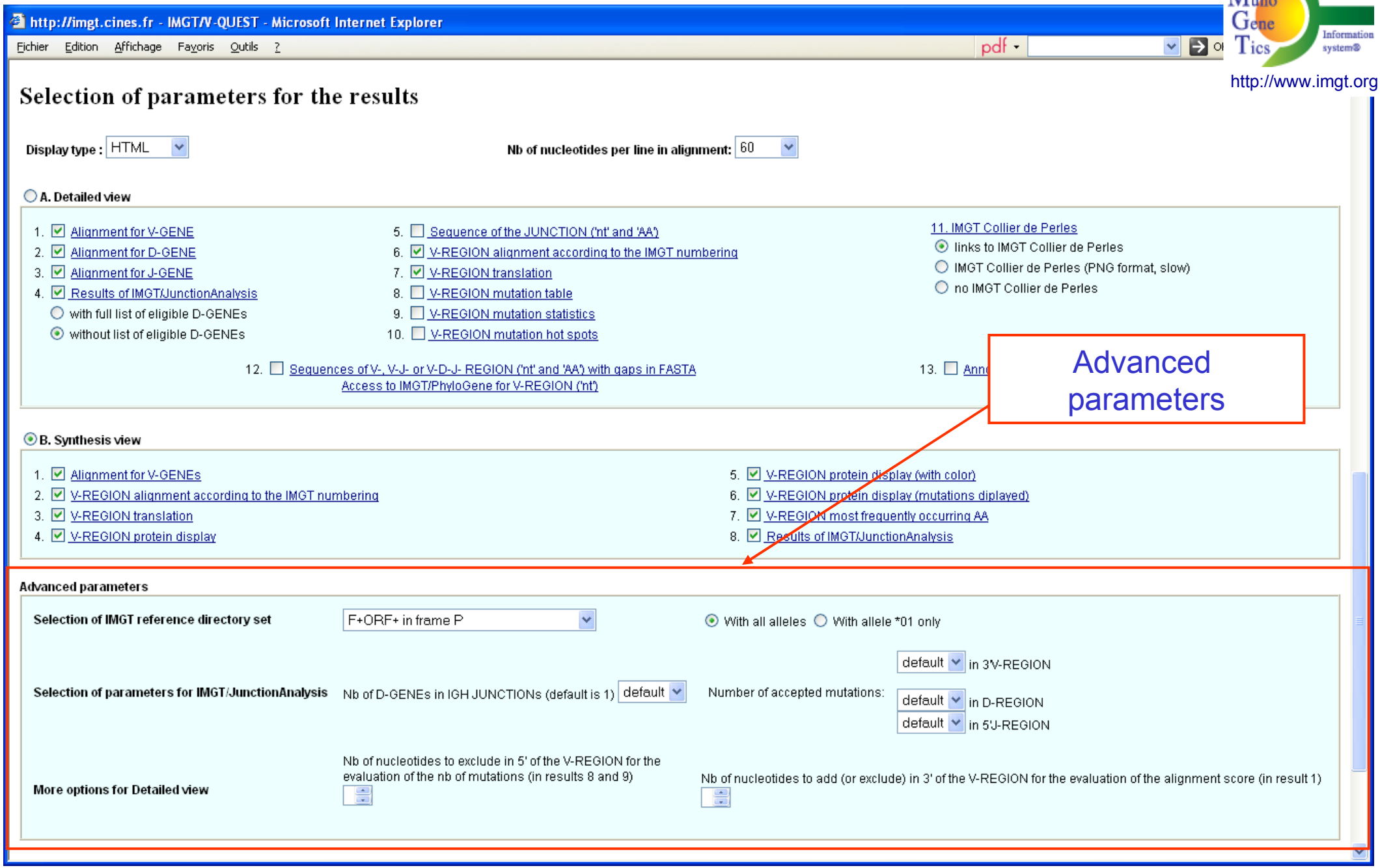
http://www.imgt.org



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

A. '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)

1-3. 'Detailed view': Alignments for V-, D- and J-GENE

http://www.imgt.org

V-GENE

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
Z27508 IGHV3-73*01	1240	91,50% (269/294 nt)
AB019437 IGHV3-73*02	1231	91,16% (268/294 nt)
X92206 IGHV3-72*01	1024	83,33% (245/294 nt)
X92216 IGHV3-15*01	979	81,63% (240/294 nt)
M99406 IGHV3-15*07	979	81,63% (240/294 nt)

Alignment with FR-IMGT and CDR-IMGT delimitations

```
                    <------------------------------- FR1-IMGT --------------
AF184762            gaggtgcagctggtggagtctgggggga...ggcttagtccagcctgggggatccctgaaa
Z27508 IGHV3-73*01  ------------------------...-----g-------------g---------
AB019437 IGHV3-73*02------------------c-----...-----g-------------g---------
X92206 IGHV3-72*01  ------------------------...-----g----------a--g-------g-
X92216 IGHV3-15*01  ------------------------...-----g--aa-------g-----t-g-
M99406 IGHV3-15*07  ------------------------...-----g--aa-------g-----t-g-

                                                                  <-----
AF184762                                                    .....gtgcac
Z27508 IGH                                                  .....a-----
AB019437 IGHV3-73*02------------------------t----------tgc-....a-----
X92206 IGHV3-72*01  ------------------a-----t------a-cact-c....a--g--
X92216 IGHV3-15*01  ------------------a-----tt-----aa-g-ctgg....a--ag-
M99406 IGHV3-15*07  ------------------t-----tt-----aa-g-ctgg....a--a--
```

Score and nucleotide identity

D-GENE

2. Alignment for D-GENE and allele identifica

Closest D-REGIONs

	Score	Identity
X13972 IGHD3-10*01	28	72,73% (8/11 nt)
X93615 IGHD3-10*02	19	63,64% (7/11 nt)
J00256 IGHD7-27*01	14	60,00% (6/10 nt)
X97051 IGHD3-16*02	13	62,50% (5/8 nt)
X93614 IGHD3-16*01	10	54,55% (6/11 nt)

Alignment

```
AF184762            gtgatccgggg
X13972 IGHD3-10*01  a--g-t-----agttattataac
X93615 IGHD3-10*02  a--t--g---agttattataac
J00256 IGHD7-27*01  .ct-a-t----a
X97051 IGHD3-16*02  --t--a-c
X93614 IGHD3-16*01  ac-t-tg----agttatgctt
```

J-GENE

3. Alignment for J-GENE and allele identification

Closest J-REGIONs

	Score	Identity
J00256 IGHJ1*01	179	82,69% (43/52 nt)
X86355 IGHJ4*02	150	79,17% (38/48 nt)
J00256 IGHJ4*01	141	77,08% (37/48 nt)
X86355 IGHJ5*02	138	74,51% (38/51 nt)
M25625 IGHJ4*03	132	75,00% (36/48 nt)

Note that the highest number of consecutive identical nucleotides has been found in the alignment with IGI

Alignment

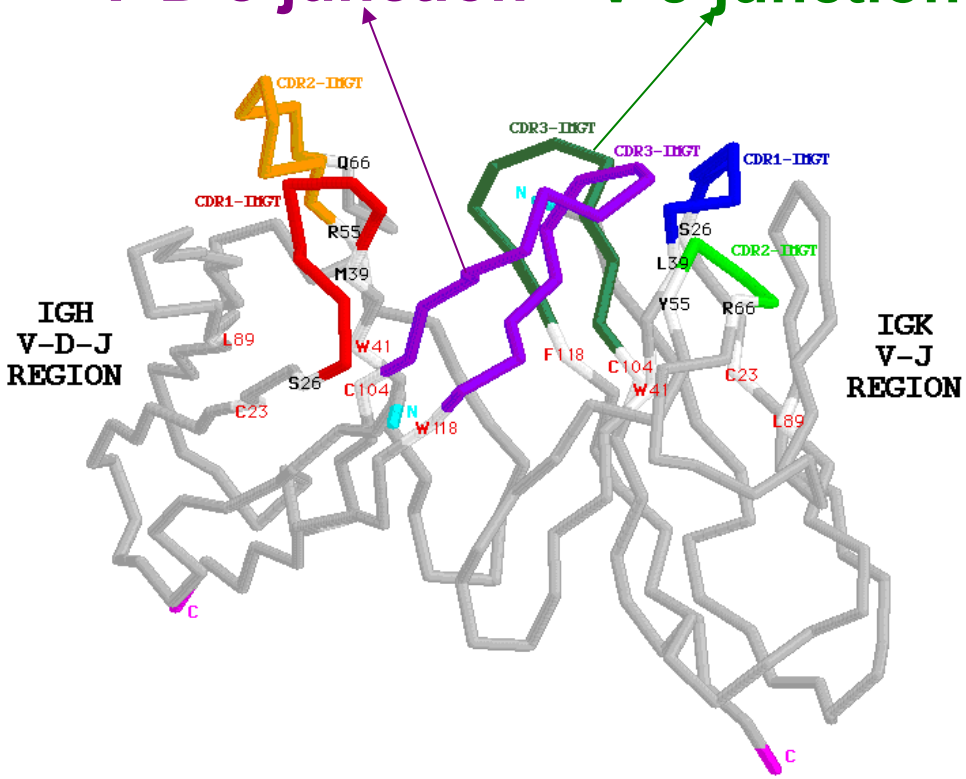
```
AF184762            gtgatccggggagatgtttacaaccgacagtggggccagggaaccctggtcaccgtctcc
J00256 IGHJ1*01     ............-c--aa---tt--ag--c----------c------------------
X86355 IGHJ4*02     ..............ac---tttgact-c-----------------------------
J00256 IGHJ4*01     ..............ac---tttgact-c--------a---------------------
X86355 IGHJ5*02     ............-caac-ggtt-gac-cc-----------------------------
M25625 IGHJ4*03     ..............gc---tttgact-c--------a--g------------------
```

Junctions of the V-DOMAINs

http://www.imgt.org

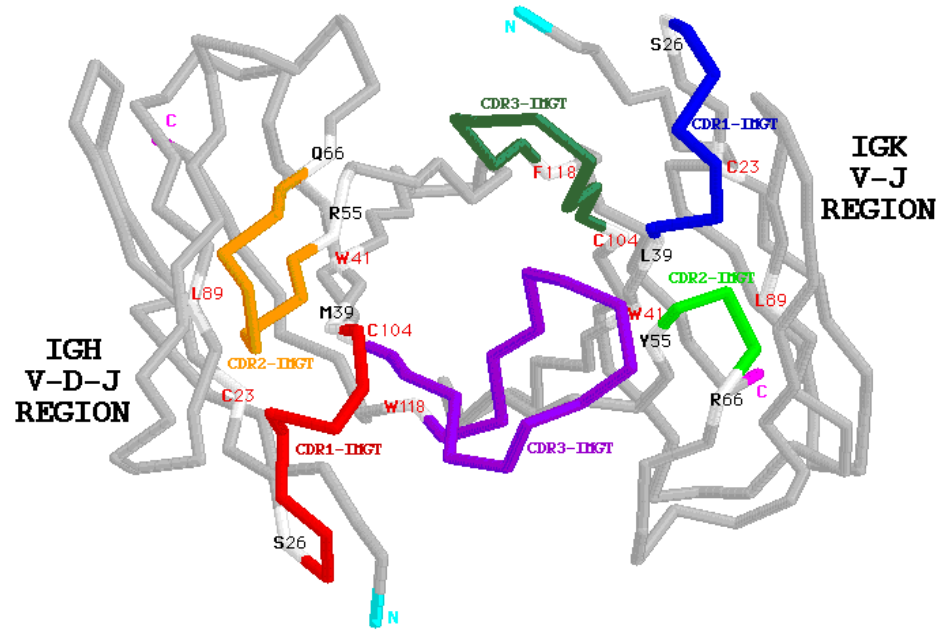
VH V-KAPPA

V-D-J junction V-J junction



Side view

VH V-KAPPA



View from above

Mouse(Mus musculus) E5.2Fv

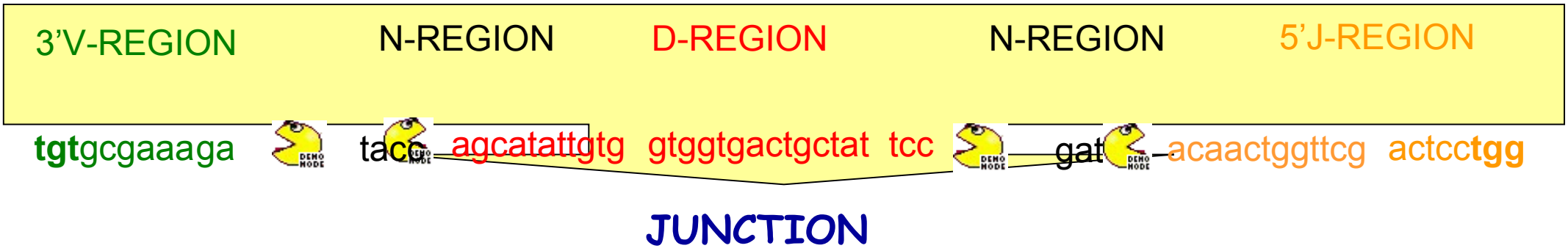
CDR3-IMGT= Complementarity determining region (105-117)

V-J junction (104-118)

V-D-J junction (104-118)

Generation of the JUNCTION 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

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.	ggggggctaagg	....tcgaatttttggagtggtt........	tcatgggt

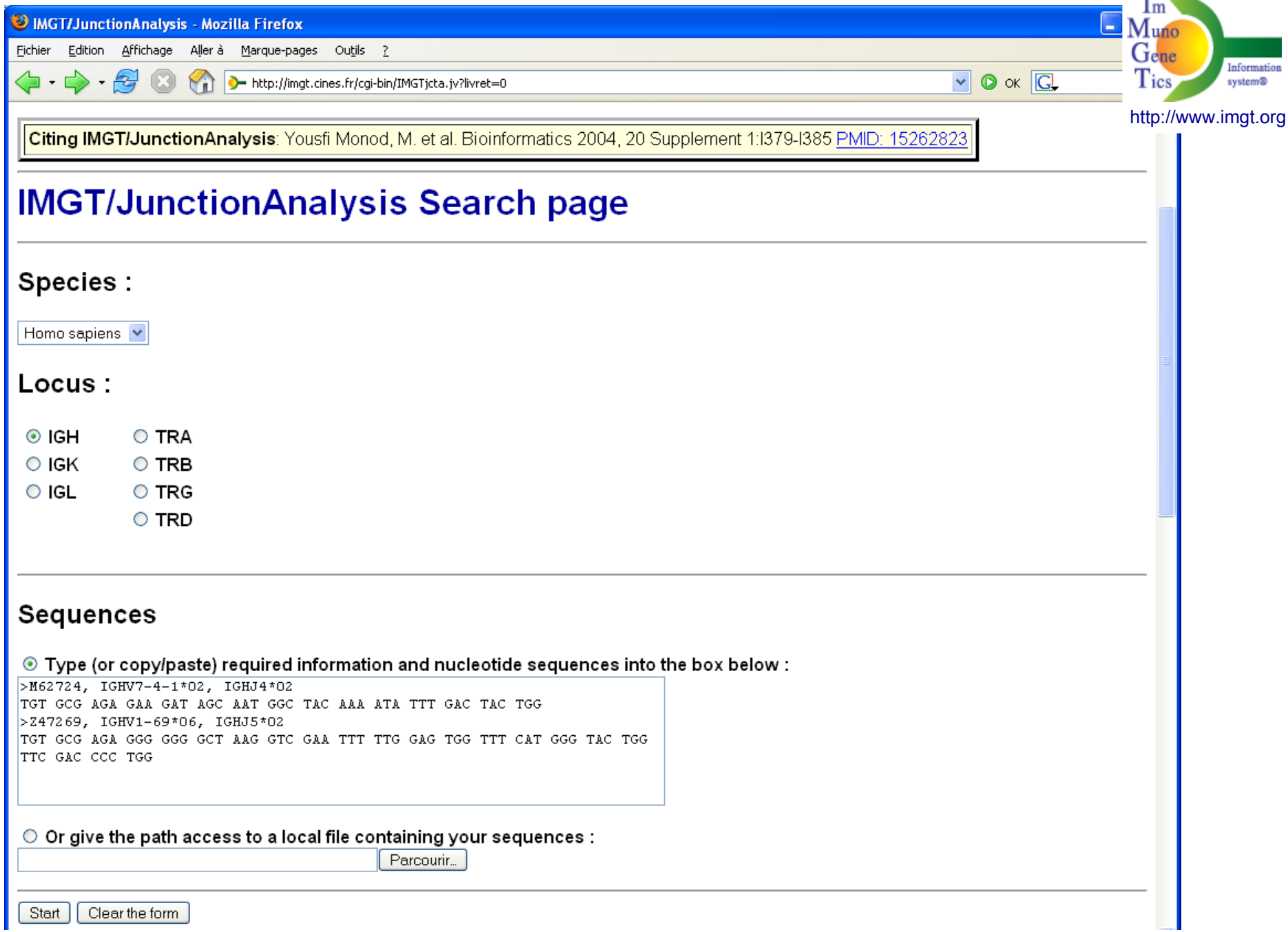
	Input	J-REGION	J name	D name	Vmut	Dmut	Jmut	Ngc
#1	M62724	.....tttgactactgg	IGHJ4*02	IGHD5-24*01	0	2	0	1/7
#2	Z47269	...actggttcgacccctgg	IGHJ5*02	IGHD3-3*02	0	2	0	13/20

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	F	F	L	F	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 Search page
-> IMGT/JunctionAnalysis Documentation

Yousfi Monod et al. Bioinformatics, 20, I379-I385 (2004)



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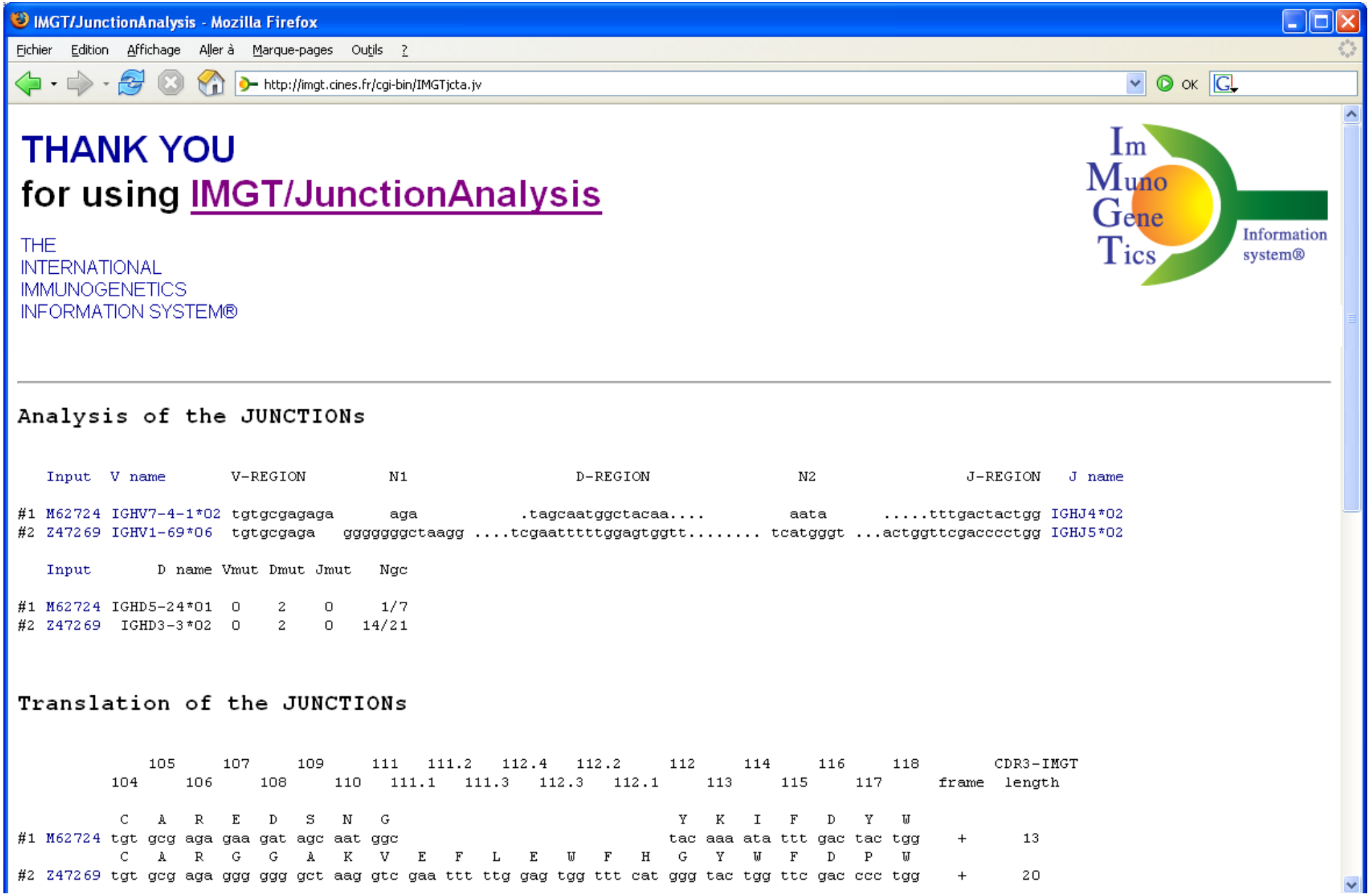
http://www.imgt.org

Yousfi Monod et al. Bioinformatics, 20, I379-I385 (2004)



Yousfi Monod et al. Bioinformatics, 20, I379-I385 (2004)

IMGT/JunctionAnalysis Results

http://www.imgt.org

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	.....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

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The eleven IMGT amino acid classes according to the physico-chemical properties

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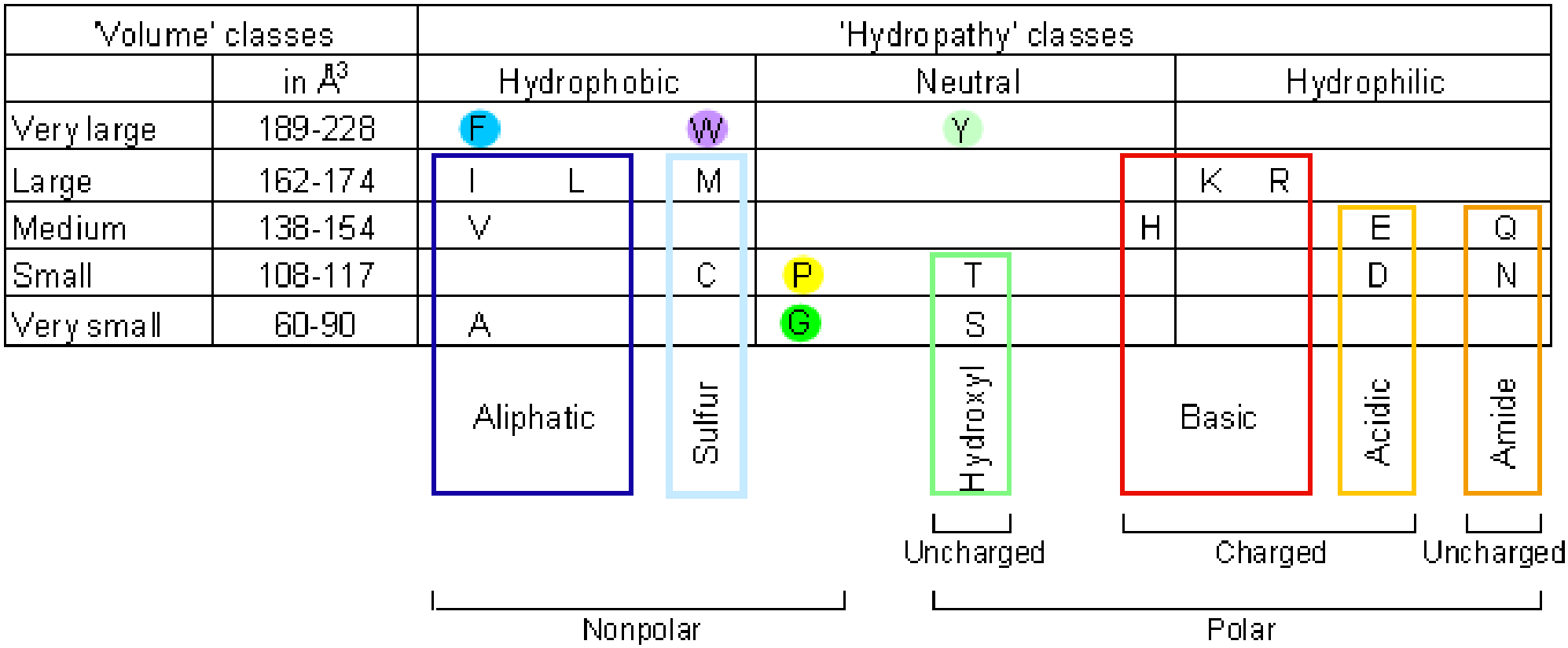

Pommié et al. J. Mol Recognit. ***17****, 17-32, 2004*

4. 'Detailed view': Results of IMGT/JunctionAnalysis

http://www.imgt.org

4. Results of IMGT/JunctionAnalysis

Maximum number of accepted mutations in: 3'V-REGION = 2, D-REGION = 4, 5'J-REGION = 2

Analysis of the JUNCTION

D-REGION is in reading frame 3.

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

Input	V name	3'V-REGION	N1	D-REGION	N2	5'J-REGION	J name	D name	Vmut	Dmut	Jmut	Ngc
AF184762	IGHV3-73*01	tgt.....	g	.....tgatccggggagatgtt.....	tacaaccga	.....cagtgg	IGHJ1*01	IGHD3-10*01	0	4	1	5/10

Translation of the JUNCTION

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

	104	105	106	107	108	109	113	114	115	116	117	118	Frame	CDR3-IMGT length	Molecular mass	pI
	C	V	I	R	G	D	V	Y	N	R	Q	W				
AF184762	tgt	gtg	atc	cgg	gga	gat	gtt	tac	aac	cga	cag	tgg	+	10	1,508.72	9.24

5. 'Detailed view': Sequence of the JUNCTION ('nt' and 'AA')

5. Sequence of the JUNCTION ('nt' and 'AA')

```
104 105 106 107 108 109 113 114 115 116 117 118
 C   V   I   R   G   D   V   Y   N   R   Q   W
tgt gtg atc cgg gga gat gtt tac aac cga cag tgg
```

IMGT/JunctionAnalysis - Mozilla Firefox
Fichier Edition Affichage Aller à Marque-pages Outils ?

JUNCTION alignments

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

		104	105	106	107	108	109	110	111	111.1	111.2	111.3	111.4	112.5	112.4	112.3	112.2	112.1	112	113	114	115	116	117	118	Frame	CDR3-IMGT length	Molecular mass
		C	V	R	V	V	Q	R	L	V								P	K	Y	H	F	D	H	W			
#1	Z70256	tgt	gta	cgt	gtt	gtg	cag	cgc	ctg	gta	...	...	...	...	...	...	...	ccc	aaa	tat	cac	ttt	gac	cac	tgg	+	15	2,438.76
		C	A	R	D	G	S	S	Y	A							R	P	Y	W	Y	F	D	L	W			
#2	Z70257	tgt	gcg	agg	gat	ggc	agc	tct	tat	gcc	...	...	...	...	...	...	cgc	ccc	tac	tgg	tac	ttc	gat	ctc	tgg	+	16	2,256.49
		C	A	R	A	T	T	H												Y	A	F	D	V	W			
#3	Z70606	tgt	gcg	aga	gcg	act	acg	cac	...	...	...	...	...	...	...	...	...	...	...	tat	gct	ttt	gat	gtc	tgg	+	11	1,604.77
		C	A	R	V	T	I	F	G	V	V					I	P	R	G	N	A	F	D	I	W			
#4	Z70608	tgt	gcc	aga	gta	acg	att	ttt	gga	gtg	gtt	...	...	...	...	att	ccc	cgg	ggg	aat	gct	ttt	gat	atc	tgg	+	18	2,426.78
		C	A	R	V	G	S	D	F	W	S	G				Y	S	R	H	D	A	F	D	I	W			
#5	Z70610	tgt	gcg	aga	gtc	ggg	agc	gat	ttt	tgg	agt	ggt	...	...	...	tat	tcc	cga	cat	gat	gct	ttt	gat	atc	tgg	+	19	2,539.73
		C	A	R	H	G	N	Y	N	A								G	V	D	W	F	D	P	W			
#6	Z70611	tgt	gcg	aga	cat	ggt	aac	tat	aat	gcc	...	...	...	...	...	...	...	ggc	gtt	gac	tgg	ttc	gac	ccc	tgg	+	15	2,072.21
		C	A	R	A	A	A	G											T	S	L	F	D	Y	W			
#7	Z70613	tgt	gcg	aga	gca	gca	gct	ggt	...	...	...	...	...	...	...	...	...	...	acc	tcc	ctc	ttt	gac	tac	tgg	+	12	1,531.71
		C	A	R	H	Y	N	S	G										T	Y	P	L	D	Y	W			
#8	Z70614	tgt	gcg	aga	cac	tat	aat	tcg	ggg	...	...	...	...	...	...	...	...	...	act	tat	ccc	ctc	gac	tac	tgg	+	13	1,846.01
		C	A	R	G	L	V	K	R	V							S	E	Y	W	Y	F	D	L	W			
#9	Z70615	tgt	gcg	aga	ggg	ctg	gta	aag	agg	gtt	...	...	...	...	...	...	tcg	gaa	tac	tgg	tac	ttc	gat	ctc	tgg	+	16	2,419.75
		C	A	R	A	G	L	G											S	H	W	F	D	P	W			
#10	Z70616	tgt	gcg	aga	gcg	ggt	ttg	ggt	...	...	...	...	...	...	...	...	...	...	tcc	cac	tgg	ttc	gac	ccc	tgg	+	12	1,602.8
		C	A	R	D	R	G	G	M									V	R	D	A	F	D	I	W			
#11	Z70620	tgt	gcg	aga	gac	cgg	ggc	ggg	atg	...	...	...	...	...	...	...	...	gtt	cgg	gat	gct	ttt	gat	atc	tgg	+	14	1,932.17
		C	A	R	H	H	D	L	W	F							G	E	F	D	P	L	D	Y	W			
#12	Z70621	tgt	gcg	aga	cac	cac	gat	tta	tgg	ttc	...	...	...	...	...	...	ggg	gag	ttt	gac	ccc	ctt	gac	tac	tgg	+	16	2,307.53
		C	A	R	D	C	P	A	P	A	K	M	Y	Y	Y	G	S	G	I	C	T	F	D	Y	W			

Terminé

6. 'Detailed view': V-REGION alignment

http://www.imgt.org

6. V-REGION alignment according to the IMGT unique numbering

```
                                <------------------------------------------  FR1 - IMGT
                                1               5                   10                  15
AF184762                        gag gtg cag ctg gtg gag tct ggg gga ... ggc tta gtc cag cct
Z27508 IGHV3-73*01              --- --- --- --- --- --- --- --- --- ... --- --g --- --- ---
AB019437 IGHV3-73*02            --- --- --- --- --- --- --c --- --- ... --- --g --- --- ---
X92206 IGHV3-72*01              --- --- --- --- --- --- --- --- --- ... --- --g --- --- ---
X92216 IGHV3-15*01              --- --- --- --- --- --- --- --- --- ... --- --g --a a-- ---
M99406 IGHV3-15*07              --- --- --- --- --- --- --- --- --- ... --- --g --a a-- ---

                                ------------------------------------------> _____________
                                                20                  25                  30
AF184762                        ggg gga tcc ctg aaa ctc tcc tgt gca gcc tct ggg ttc acc ctc
Z27508 IGHV3-73*01              --- --g --- --- --- --- --- --- --- --- --- --- --- --- t--
AB019437 IGHV3-73*02            --- --g --- --- --- --- --- --- --- --- --- --- --- --- t--
X92206 IGHV3-72*01              --a --g --- --- -g- --- --- --- --- --- --- --a --- --- t--
X92216 IGHV3-15*01              --- --g --- --t -g- --- --- --- --- --- --- --a --- --t t--
M99406 IGHV3-15*07              --- --g --- --t -g- --- --- --- --- --- --- --t --- --t t--
```

7. 'Detailed view': V-REGION translation

7. V-REGION translation

```
                                <------------------------------------------  FR1 - IMGT
                                1               5                   10                  15
                                 E   V   Q   L   V   E   S   G   G       G   L   V   Q   P
AF184762                        gag gtg cag ctg gtg gag tct ggg gga ... ggc tta gtc cag cct

Z27508 IGHV3-73*01              --- --- --- --- --- --- --- --- --- ... --- --g --- --- ---

                                ------------------------------------------> _____________
                                                20                  25                  30
                                 G   G   S   L   K   L   S   C   A   A   S   G   F   T   L
AF184762                        ggg gga tcc ctg aaa ctc tcc tgt gca gcc tct ggg ttc acc ctc
                                                                                        F
Z27508 IGHV3-73*01              --- --g --- --- --- --- --- --- --- --- --- --- --- --- t--
```

8-10. ‘Detailed view’: mutation analysis

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8. V-REGION mutation table

FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT
g36>a	t88>c, F30>L (+ - -)	a115>g, M39>V (+ - -)	t168>c	g211>a, V71>M (+ - -)	a313>g, T105>V (- - -)
g51>a	t99>a	t135>c	g170>a, R57>K (+ + +)	a215>g, K72>R (+ + +)	c314>t, T105>V (- - -)
	g100>a, A34>N (- - -)		c174>g, S58>R (- - -)	t226>c, F76>L (+ - -)	t315>g, T105>V (- - -)
	c101>a, A34>N (- - -)		a177>t, K59>N (+ - -)	a263>t, Y88>F (- + -)	g317>t, R106>I (- + -)
			a181>g, N61>E (+ - -)	c287>g, T96>S (+ - +)	a318>c, R106>I (- + -)
			c183>g, N61>E (+ - -)	g291>t, E97>D (+ - +)	
			a184>t	g301>a, V101>M (+ - -)	
			g185>c	c309>t	
			t187>g, Y63>D (- - -)		

8-10. ‘Detailed view’: mutation analysis

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9. V-REGION mutation statistics

Nucleotides

IMGT Label		V-REGION	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT
Total nucleotides with gaps		312 (318)	78	36	51	30	117	0 (6)
Mutations	Total	25 (30)	2	4	2	9	8	0 (5)
	Silent	8	2	1	1	3	1	0
	Non silent	17 (22)	0	3	1	6	7	0 (5)
Transitions	a>g	3 (4)	0	0	1	1	1	0 (1)
	g>a	6	2	1				
	c>t	1 (2)	0	0				
	t>c	4	0	1				
Transversions	a>c	0 (1)	0	0				
	c>a	1	0	1				
	a>t	3	0	0				
	t>a	1	0	1				
	g>c	1	0	0				
	c>g	3	0	0				
	g>t	1 (2)	0	0				
	t>g	1 (2)	0	0				

Amino acids

IMGT labels			V-REGION	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT
Total amino acids (AA) with gaps			104 (106)	26	12	17	10	39	0 (2)
Identical AA			89	26	10	16	5	32	0
AA changes	Total		15 (17)	0	2	1	5	7	0 (2)
	Conserved IMGT AA classes (hydropathy, volume, chemical)	(- - -)	3 (4)	0	1	0	2	0	0 (1)
		(+ + +)	2	0	0	0	1	1	0
		(+ - -)	7	0	1	1	2	3	0
		(- + -)	1 (2)	0	0	0	0	1	0 (1)
		(- - +)	0	0	0	0	0	0	0
		(+ + -)	0	0	0	0	0	0	0
		(+ - +)	2	0	0	0	0	2	0

8-10. ‘Detailed view’: mutation analysis

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10. Mutation hot spots (in germline V-REGION)

(a/t)a
wa

Motif	Positions
aa	58-59 (FR1)
aa	142-143 (FR2)
ta	165-166 (FR2-CDR2)
ta	168-169 (CDR2)
aa	171-172 (CDR2)
aa	175-176 (CDR2)
ta	180-181 (CDR2)
ta	187-188 (CDR2)
ta	199-200 (FR3)
aa	214-215 (FR3)
aa	249-250 (FR3)
aa	253-254 (FR3)
ta	262-263 (FR3)
aa	269-270 (FR3)
aa	274-275 (FR3)
aa	283-284 (FR3)
aa	285-286 (FR3)
ta	304-305 (FR3)
ta	307-308 (FR3)
ta	312-313 (FR3)
ta	315-316 (CDR3)

(a/g)g(c/t)(a/t)
rgyw

Motif	Positions
agct	8-11 (FR1)
ggct	31-34 (FR1)
ggtt	80-83 (CDR1)
ggct	94-97 (CDR1)
ggct	132-135 (FR2)
ggct	146-149 (FR2)
ggtt	156-159 (FR2)
agca	172-175 (CDR2)
agct	177-180 (CDR2)
agtt	184-187 (CDR2)
agca	195-198 (CDR2)
ggca	220-223 (FR3)
ggtt	224-227 (FR3)

(a/t)(a/g)c(c/t)
wrcy

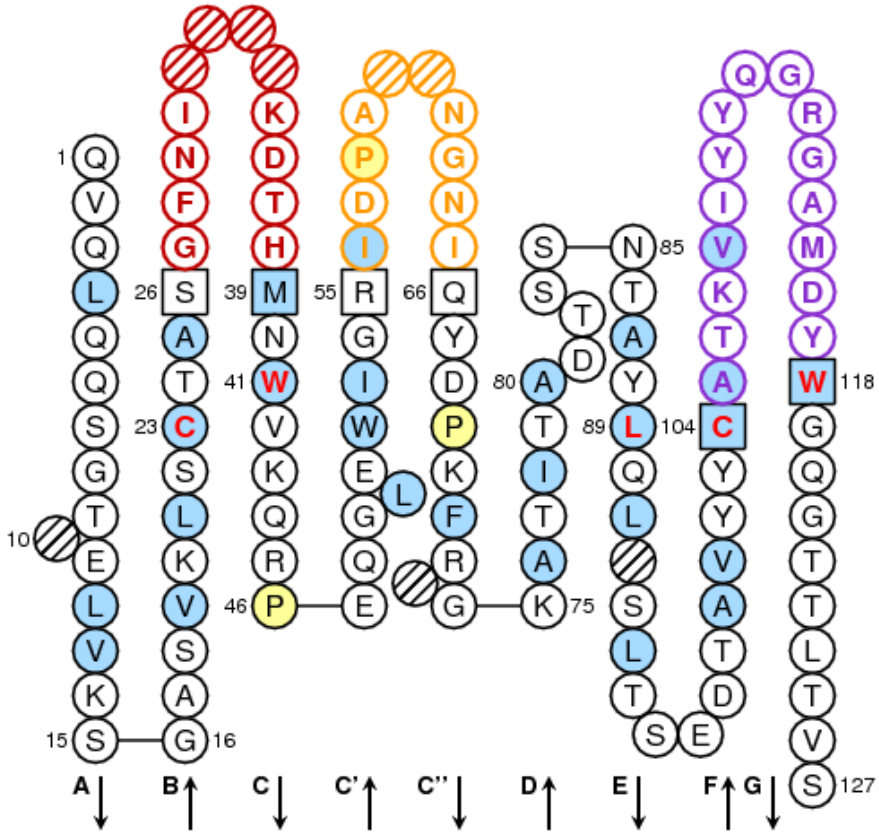
Motif	Positions
agct	8-11 (FR1)
agcc	41-44 (FR1)
aact	59-62 (FR1)
agcc	72-75 (FR1)
tgct	99-102 (CDR1)
agct	177-180 (CDR2)
tgct	201-204 (FR3)
agcc	277-280 (FR3)
aacc	285-288 (FR3)
tact	307-310 (FR3)
tact	312-315 (FR3)

t(a/t)
tw

Motif	Positions
tt	34-35 (FR1)
tt	82-83 (CDR1)
tt	88-89 (CDR1)
tt	135-136 (FR2)
tt	158-159 (FR2)
ta	165-166 (FR2-CDR2)
tt	167-168 (CDR2)
ta	180-181 (CDR2)
tt	186-187 (CDR2)
ta	199-200 (FR3)
tt	226-227 (FR3)
tt	246-247 (FR3)
ta	262-263 (FR3)
ta	304-305 (FR3)
tt	306-307 (FR3)
ta	312-313 (FR3)
ta	315-316 (CDR3)

11. IMGT Collier de Perles

http://www.imgt.org



IMGT unique numbering rules

- maintain conserved AA, and therefore codons, at the same positions
- standardize the delimitations of FR-IMGT and CDR-IMGT

CDR-IMGT lengths are in themselves a crucial information.

[8.8.15]

Standardized description of the V-DOMAIN, whatever the antigen receptor, the chain type and the species.

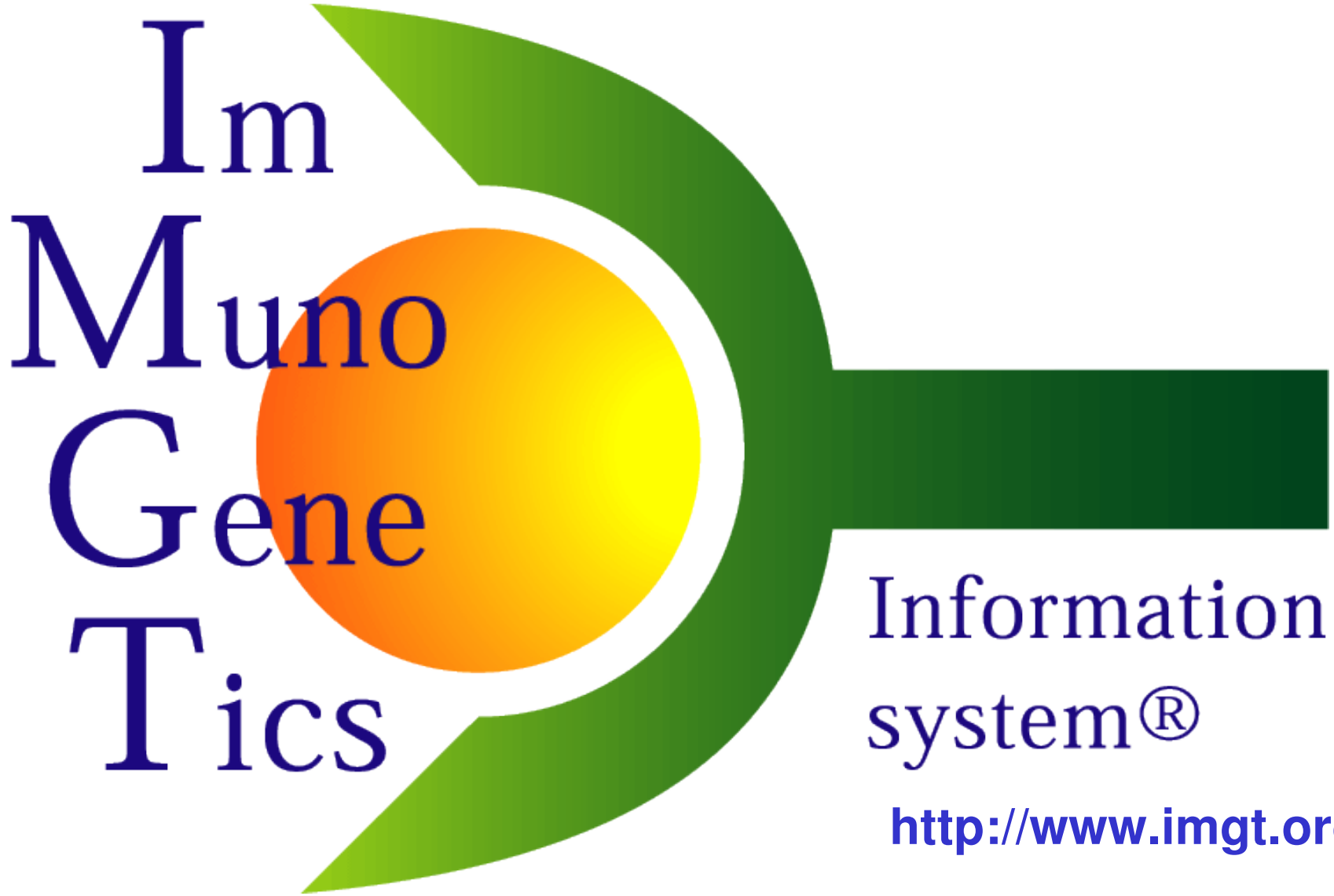
13. ‘Detailed view’: Annotation by IMGT/Automat

http://www.imgt.org

13. Annotations by IMGT/Automat

Label	Location/Qualifiers
V-D-J-REGION	58..415 /Nucleotide sequence gaggtgcagctggtggagtctgggggaggcttagtccagcctgggggatccctgaaactc tcctgtgcagcctctgggttcaccctcagtggctcaaatgtgcactgggtccgccaggcc tccgggaaagggctggagtgggttggccgtatcaaaaggaatgctgagtctgacgcgaca gcatatgctgcgtcgatgagaggcaggctcaccatctccagagatgattcaaagaacacg gcgtttctgcaaatgaacagcctgaaaagcgatgacacggccatgtattattgtgtgatc cggggagatgtttacaaccgacagtggggccagggaaccctggtcaccgtctcctcag /Translation EVQLVESGGGLVQPGGSLKLSCAASGFTLSGSNVHWVRQASGKGLEWVGRIKRNAESDAT AYAASMRGRLTISRDDSKNTAFLQMNSLKSDDTAMYYCVIRGDVYNRQWGQGTLVTVSS
V-REGION	58..351 /allele="IGHV3-73*01" /CDR_length="[8.10.10]" /gene="IGHV3-73" /Nucleotide sequence gaggtgcagctggtggagtctgggggaggcttagtccagcctgggggatccctgaaactc tcctgtgcagcctctgggttcaccctcagtggctcaaatgtgcactgggtccgccaggcc tccgggaaagggctggagtgggttggccgtatcaaaaggaatgctgagtctgacgcgaca gcatatgctgcgtcgatgagaggcaggctcaccatctccagagatgattcaaagaacacg gcgtttctgcaaatgaacagcctgaaaagcgatgacacggccatgtattattgt /Translation EVQLVESGGGLVQPGGSLKLSCAASGFTLSGSNVHWVRQASGKGLEWVGRIKRNAESDAT AYAASMRGRLTISRDDSKNTAFLQMNSLKSDDTAMYYC
FR1-IMGT	58..132 /AA_IMGT="AA 1 to 26, AA 10 is missing" /Nucleotide sequence gaggtgcagctggtggagtctgggggaggcttagtccagcctgggggatccctgaaactc tcctgtgcagcctct /Translation EVQLVESGGGLVQPGGSLKLSCAAS
1st-CYS	121..123 /Nucleotide sequence tgt /Translation C
CDR1-IMGT	133..156 /AA_IMGT="AA 27 to 34" /Nucleotide sequence gggttcaccctcagtggctcaaat /Translation GFTLSGSN
FR2-IMGT	157..207 /AA_IMGT="AA 39 to 55" /Nucleotide sequence gtgcactgggtccgccaggcctccgggaaagggctggagtgggttggccgt /Translation VHWVRQASGKGLEWVGR
CONSERVED-TRP	163..165 /Nucleotide sequence tgg /Translation W

IMGT/V-QUEST provides a full automatic annotation of the V-J-REGION or V-D-J-REGION.


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