Immunoinformatique

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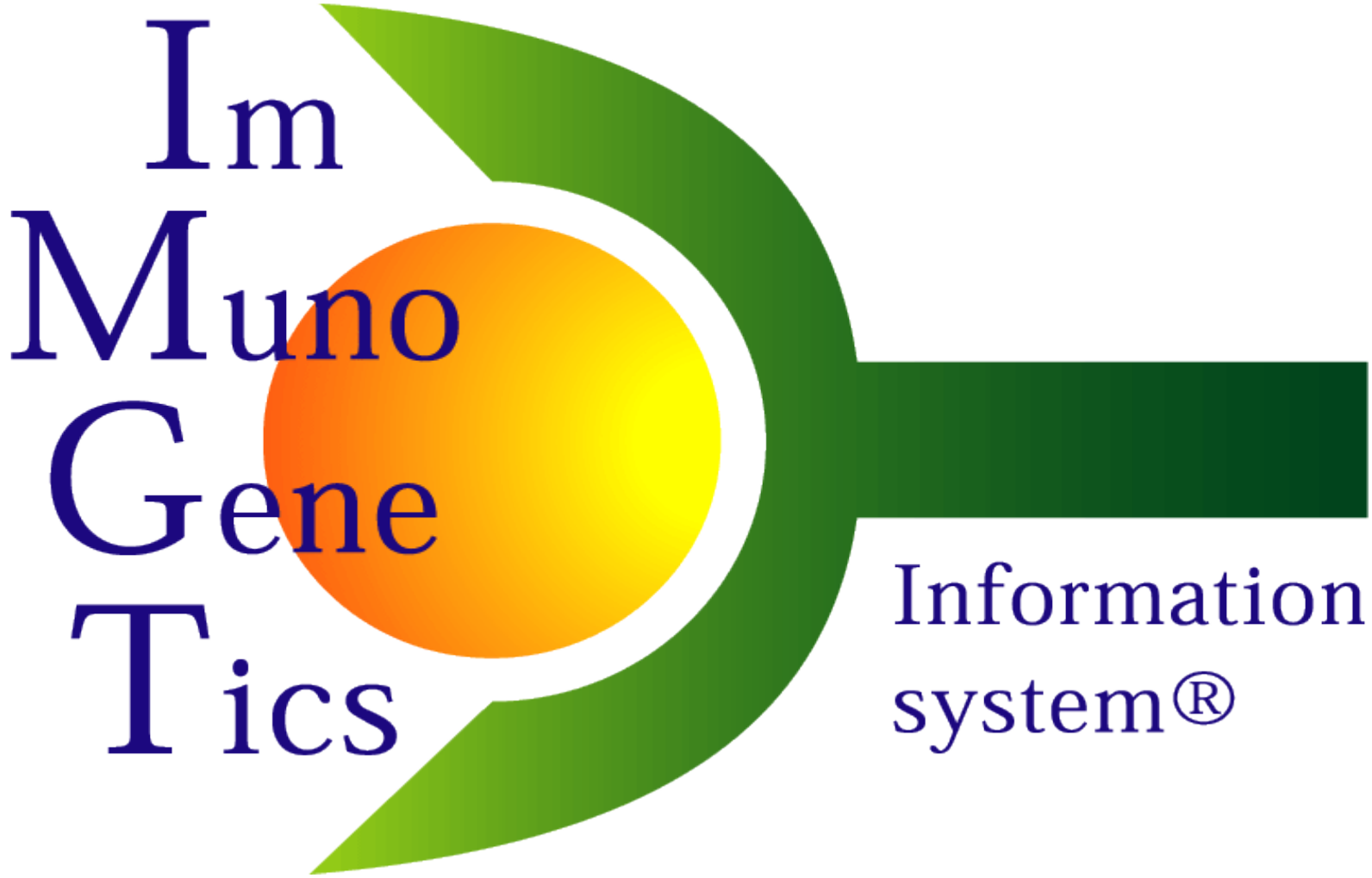
26 septembre 2011

IMGT®, the international ImMunoGeneTics information system®

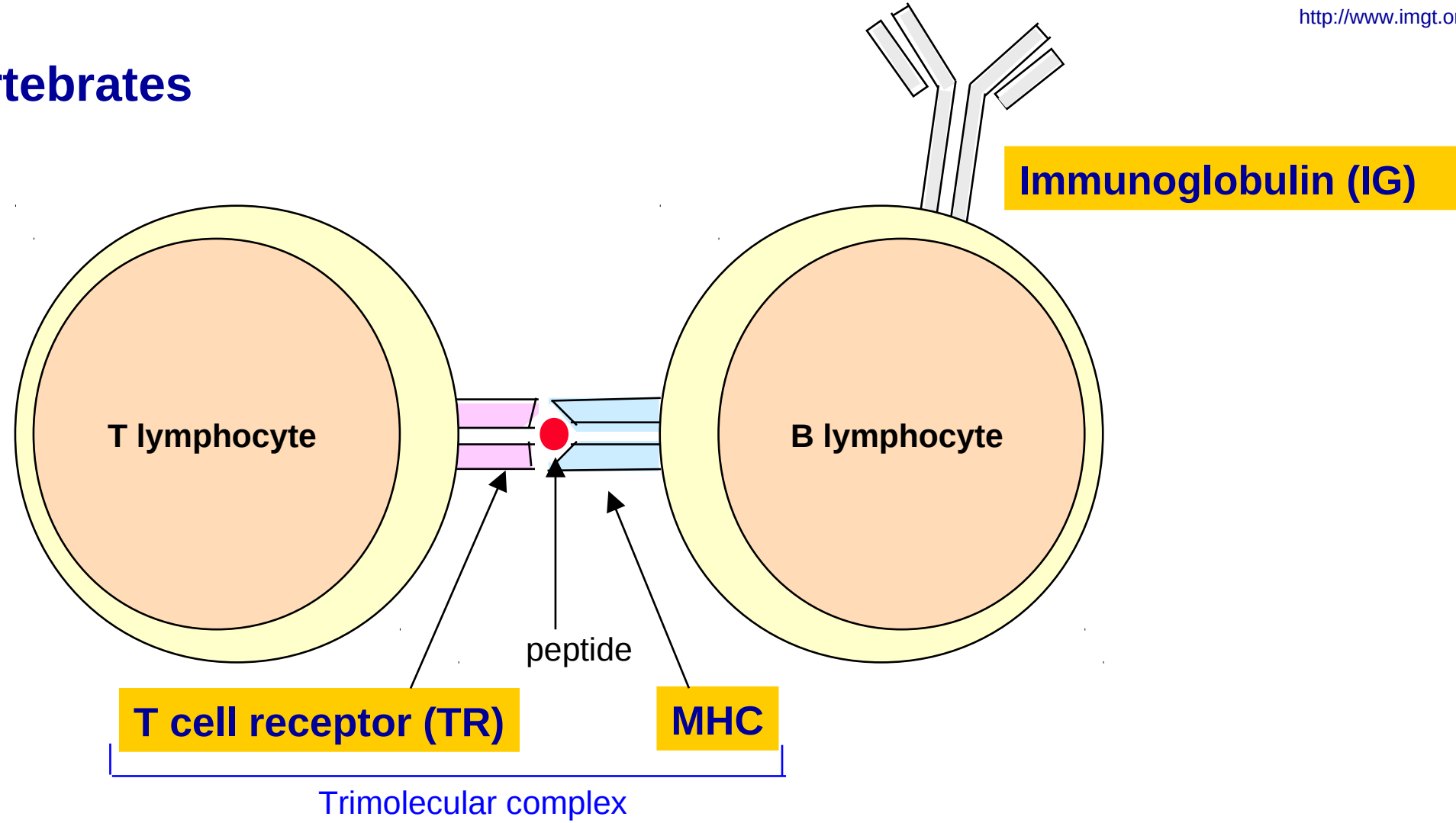
http://www.imgt.org



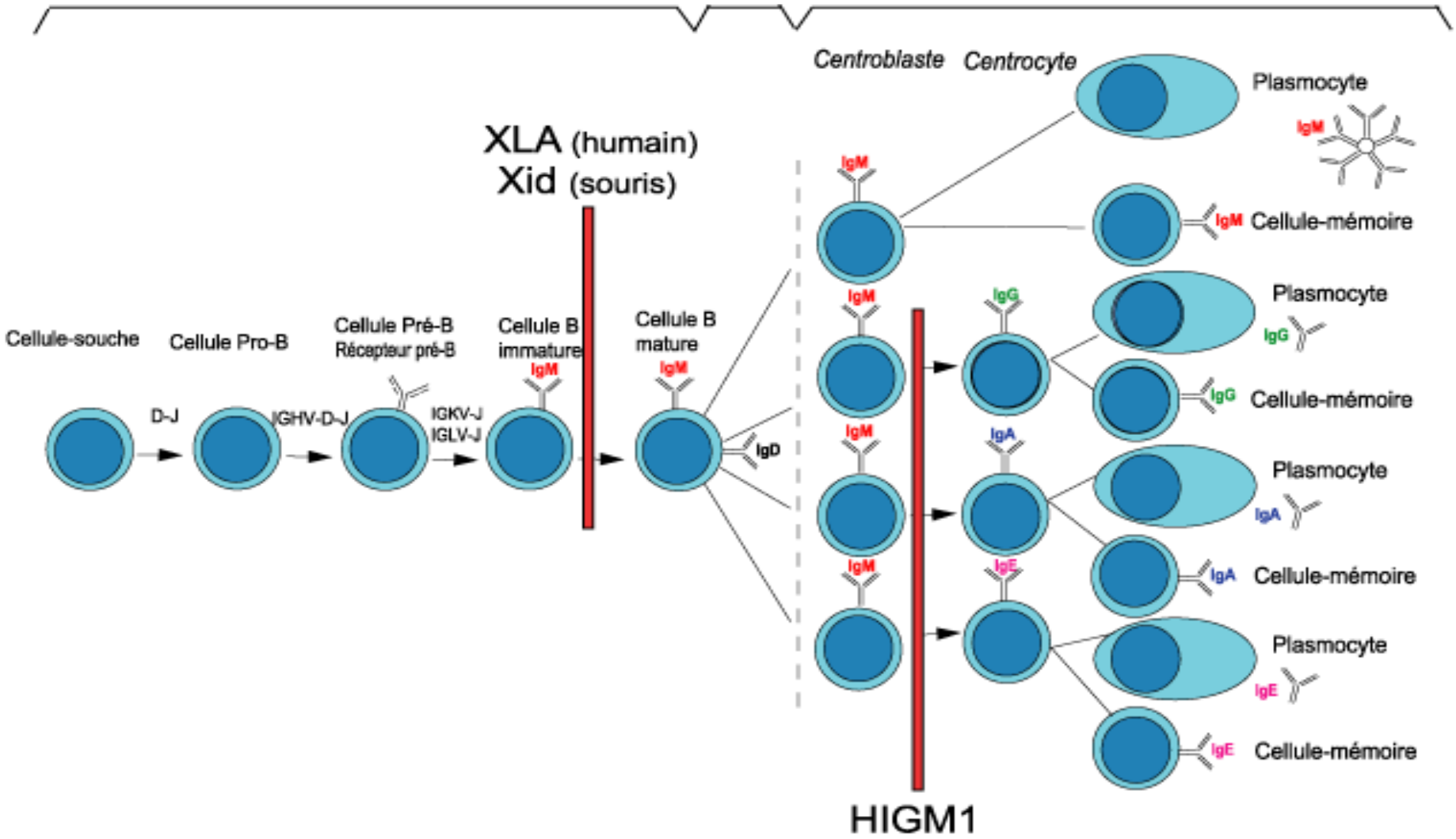
IMGT® domain: the adaptive immune response

http://www.imgt.org

Vertebrates



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



V-D-J and V-J rearrangements

Hypermutations, selection

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

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

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
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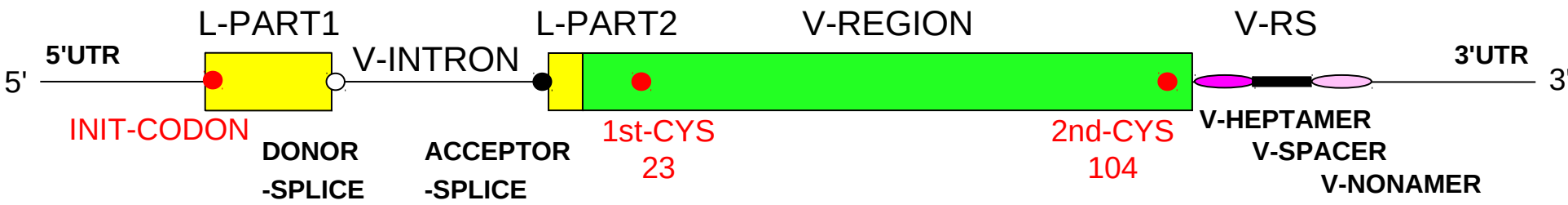

Genomic DNA in germline configuration

http://www.imgt.org

D-GENE

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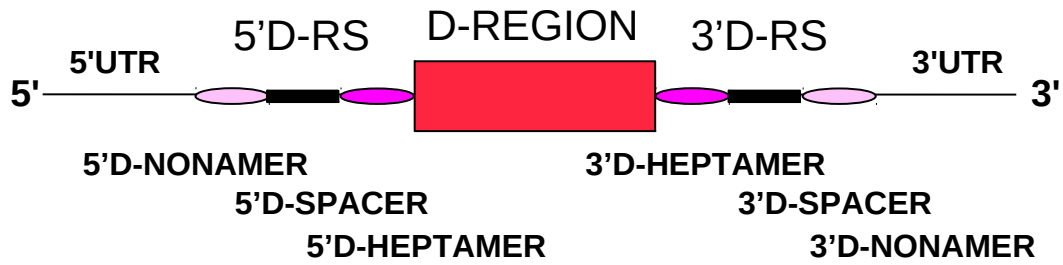
ggcagctcta caaaaacc



J-GENE

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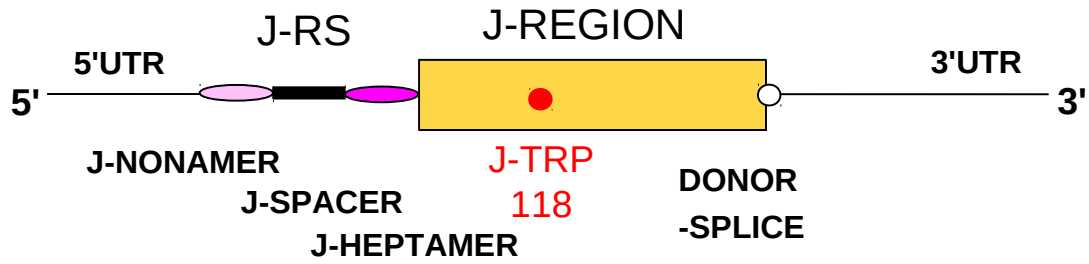
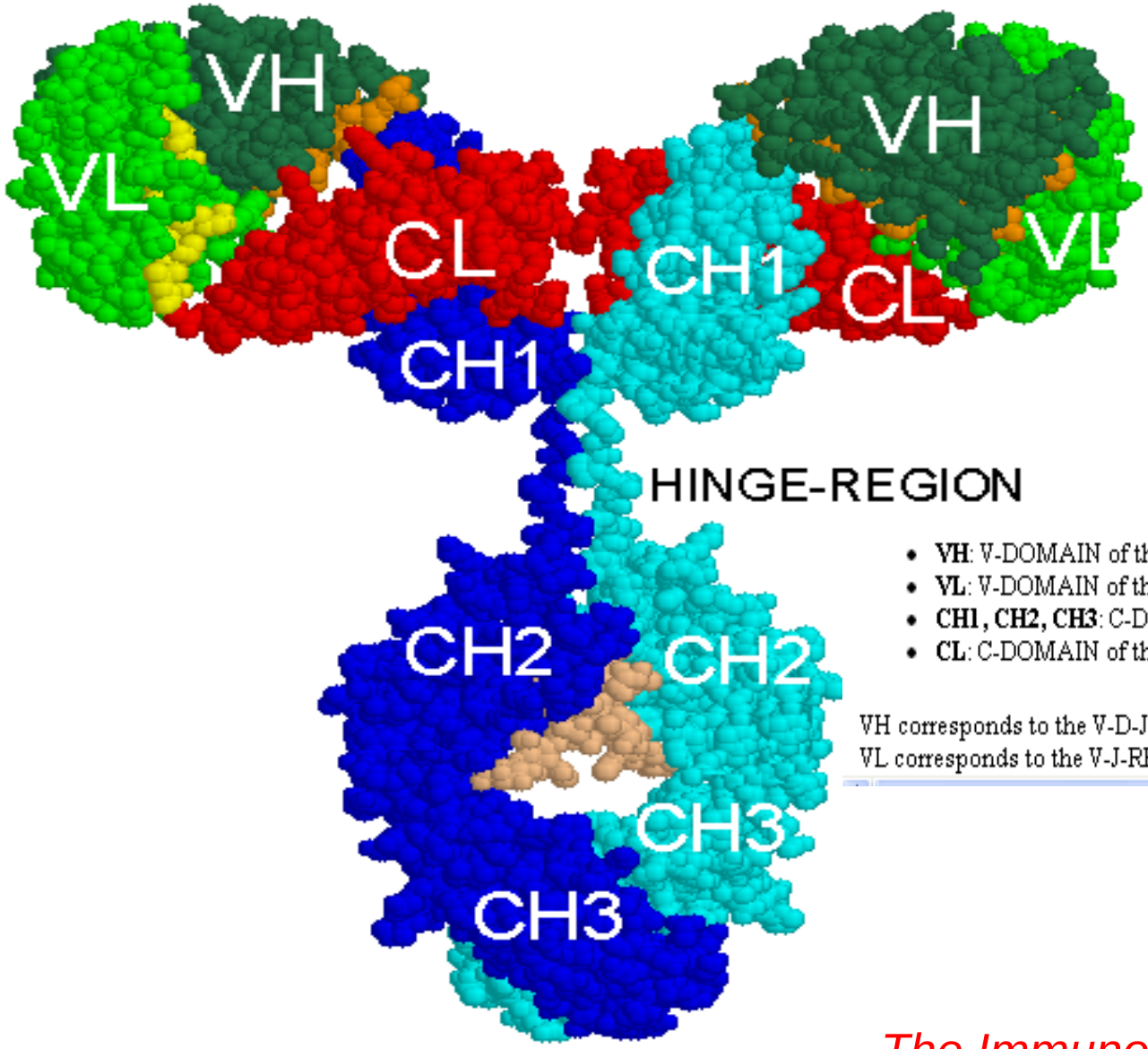


Why was IMGT necessary?

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

Spacefill 3D representation of an IgG

http://www.imgt.org



- **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

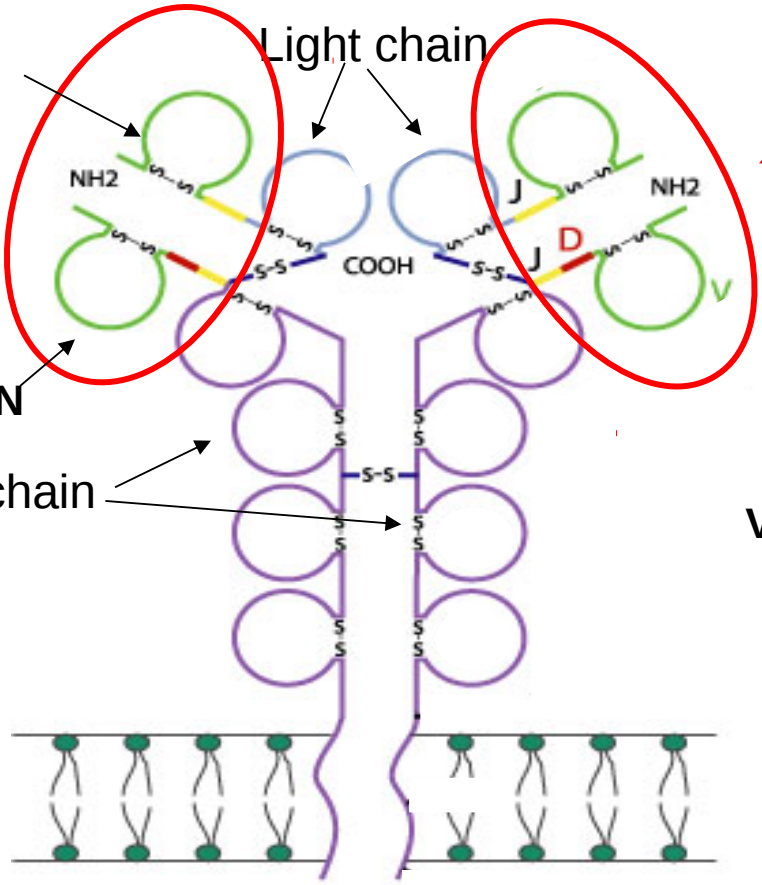
V-J-REGION

V-DOMAIN

V-D-J-REGION

Light chain

Heavy chain



Membrane IgM

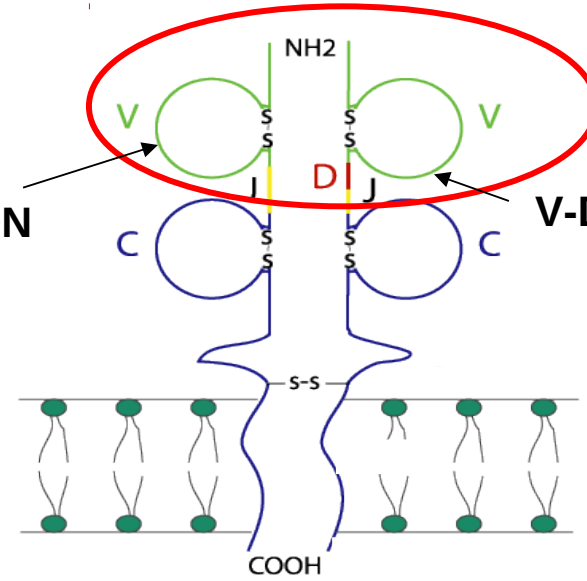
Contribution of the
2 V-DOMAINs
to the antigen binding site

Alpha - Beta

Gamma - Delta

V-J-REGION

V-DJ-REGION

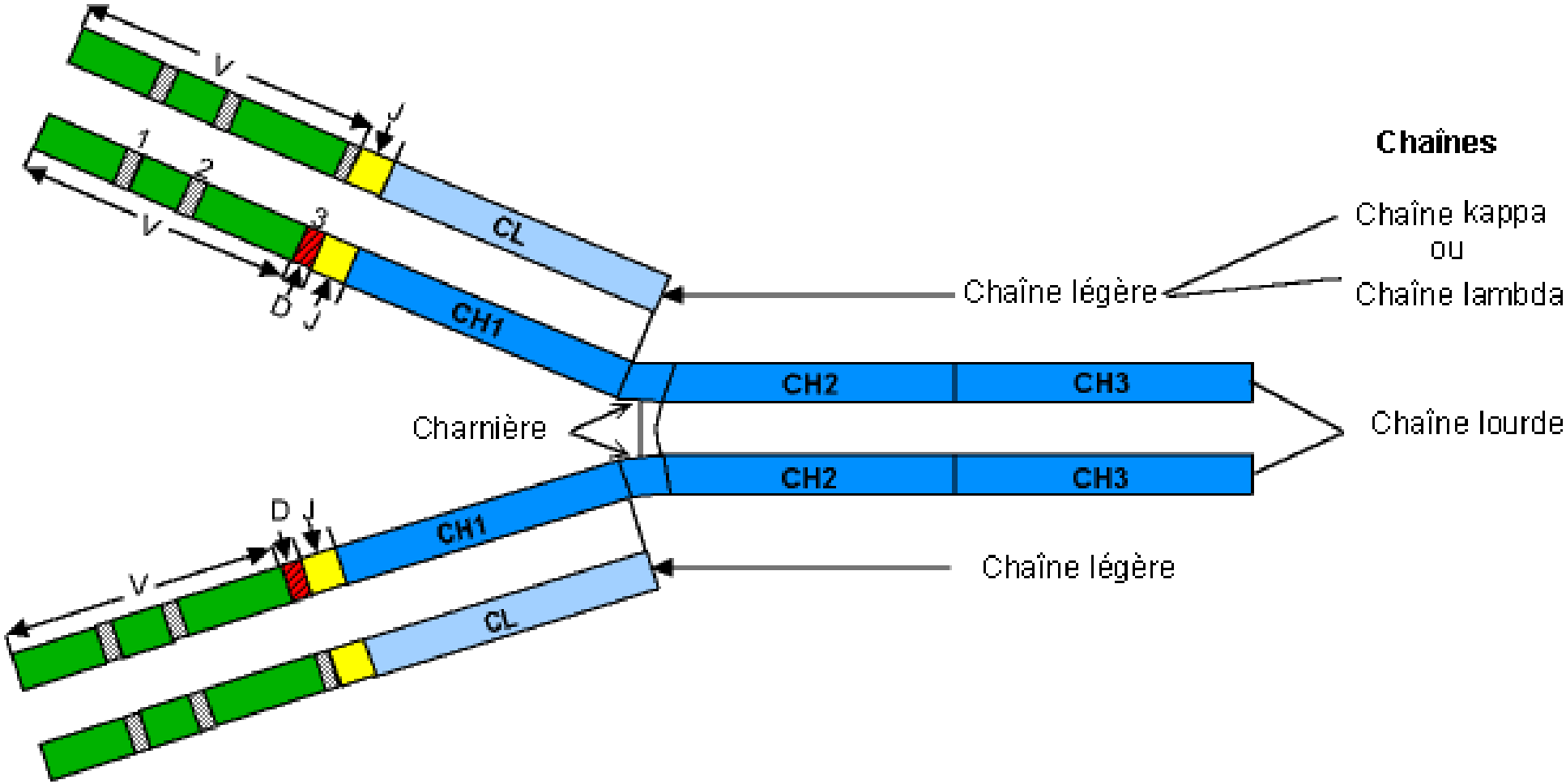


T cell receptor

The Immunoglobulin FactsBook, 2001

Immunoglobulin IgG

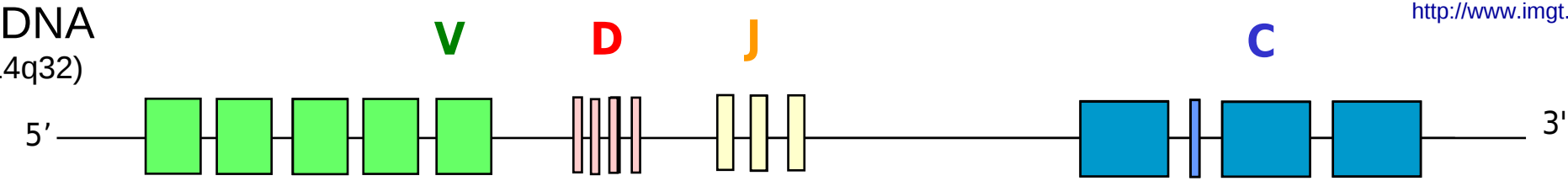
http://www.imgt.org



Immunoglobulin (IG) synthesis

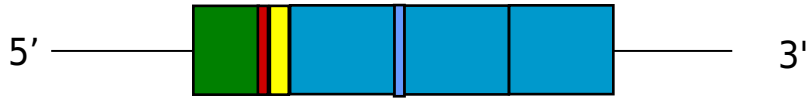
http://www.imgt.org

genomic DNA
(IGH Locus 14q32)

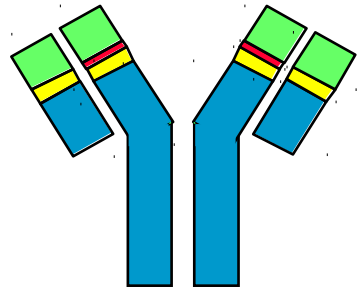


rearranged DNA

mRNA



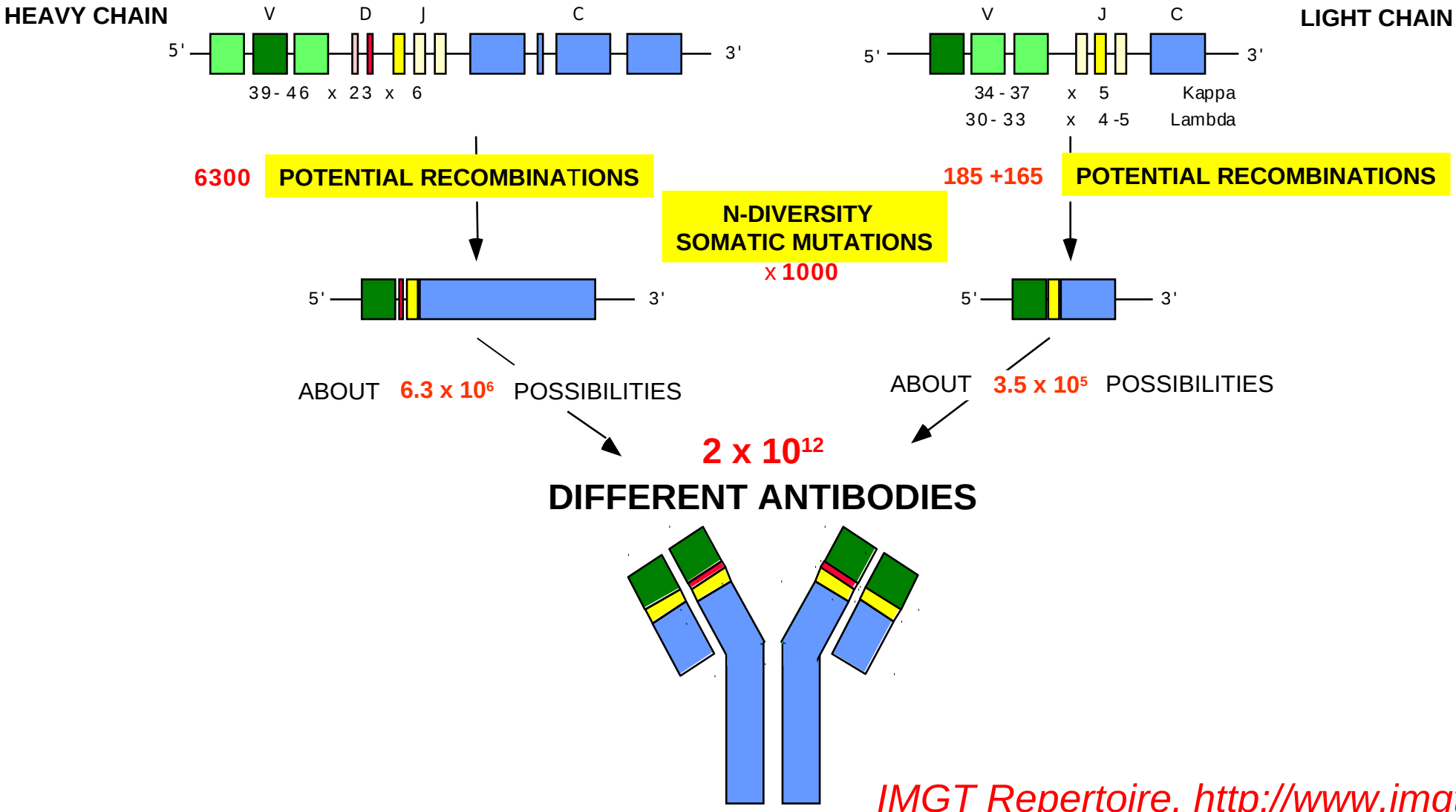
2 x 10^{12} different IG per individual



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

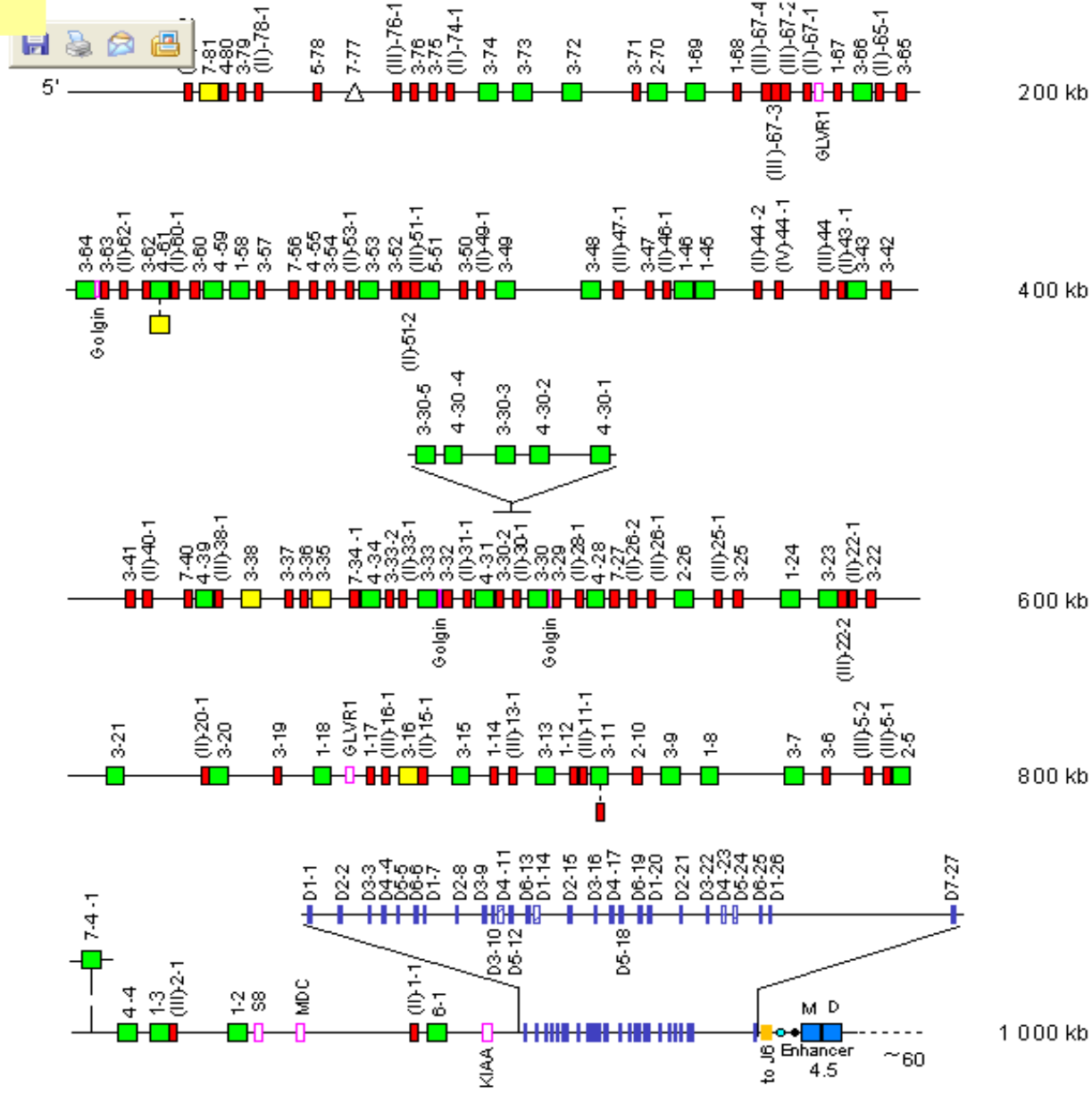
- Interesting links, PubMed,
- Meeting announcements
- IMGT Immunoinformatics page,...

IMGT Education

- Tutorials, IMGT Lexique, ...

Human IGH locus

Chromosome 14q32.33



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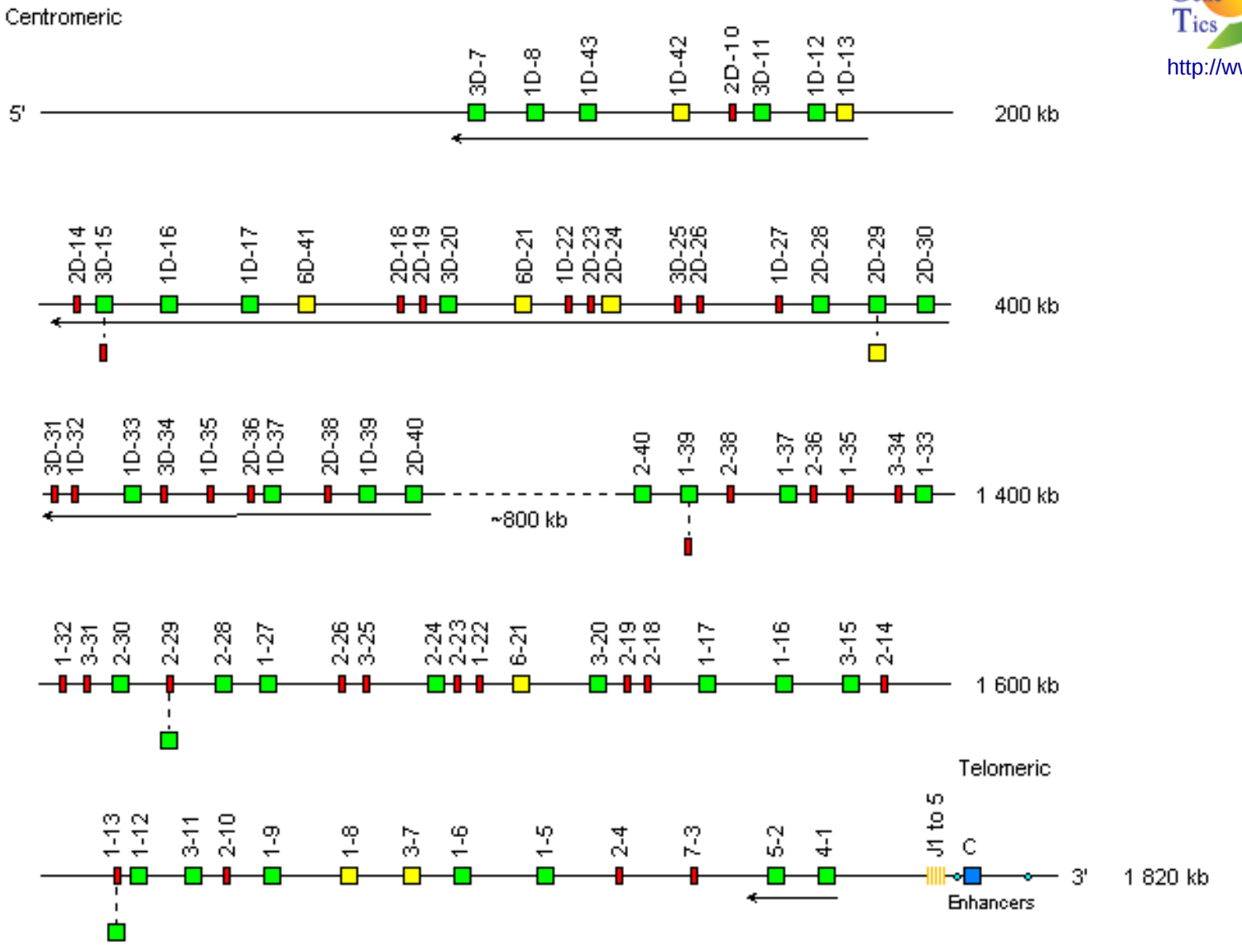
Human IGK locus

Chromosome 2p11.2

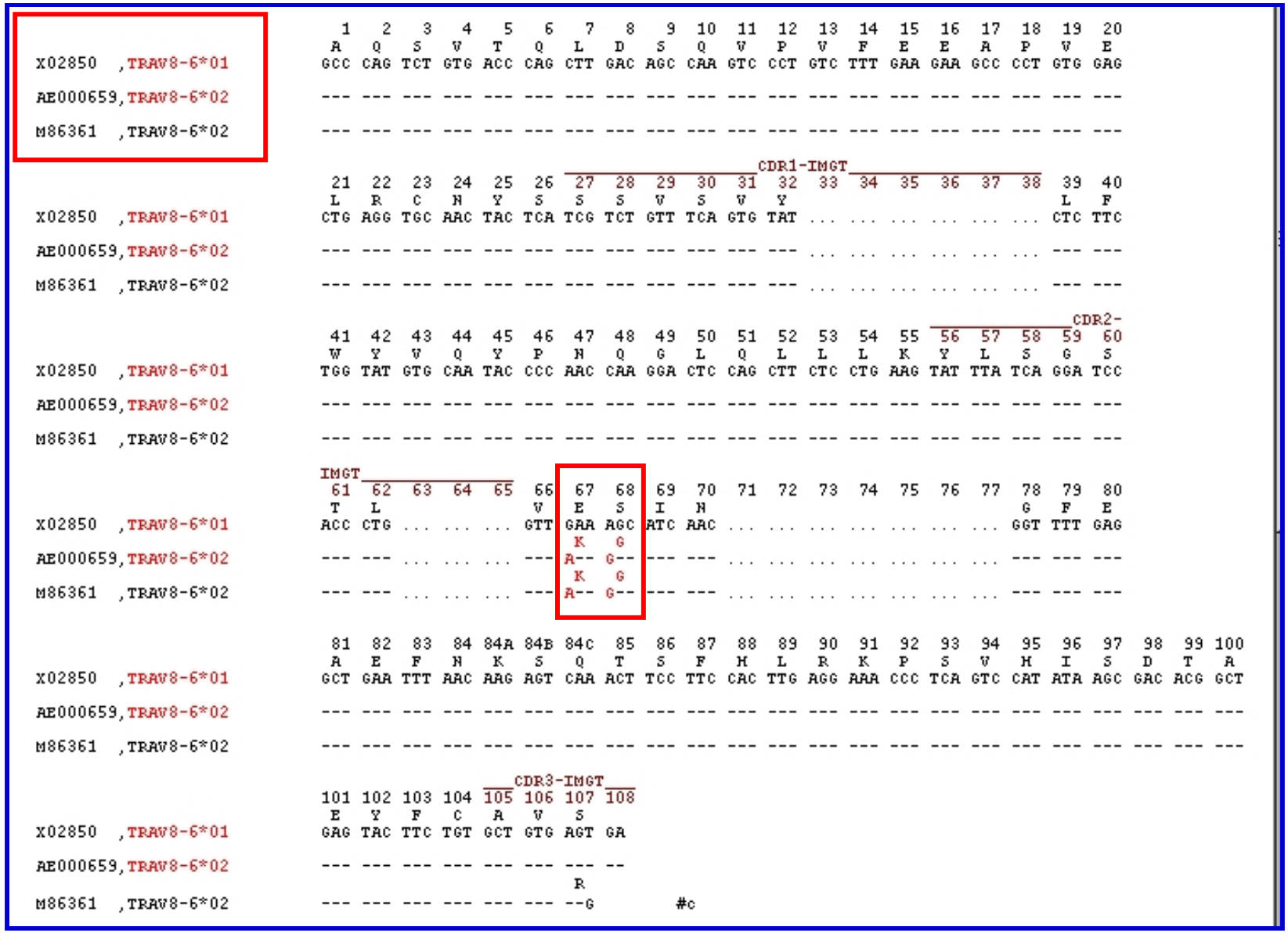


Human IGHV genes on chromosome 14 at 14q32.33

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**

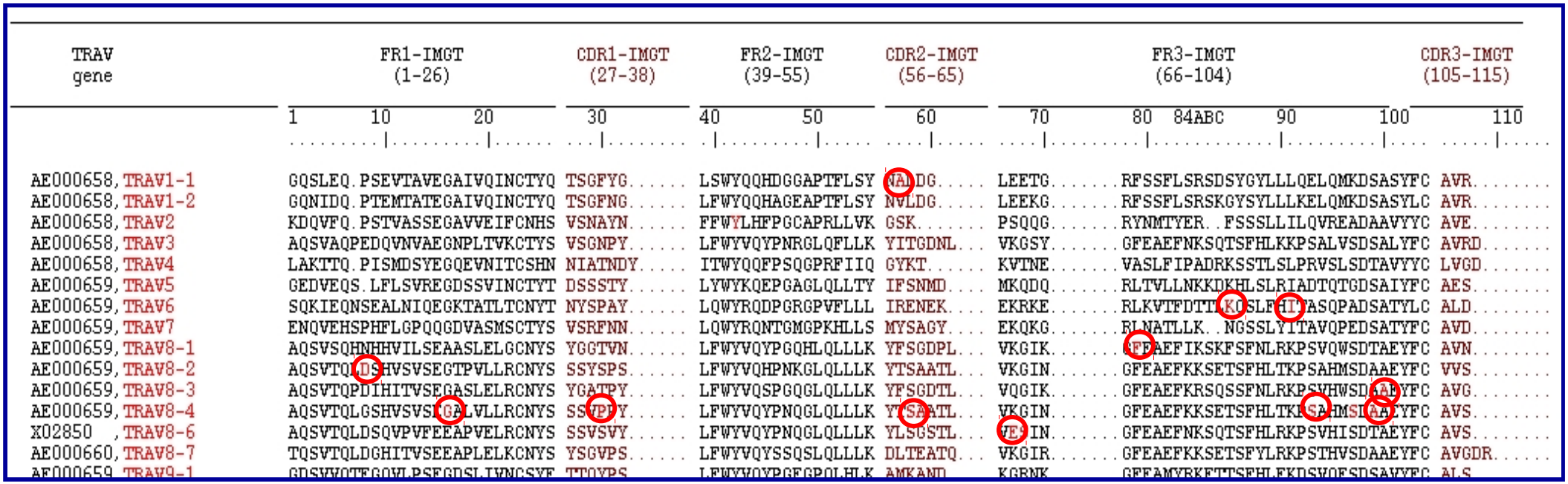
IMGT Alignment of alleles



IMGT Information system®
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.....
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AE000659,TRAV5	GEDVEQS.LFLSVREGDSSVINCTYT	DSSSTY.....	LYWYKQEPGAGLQLLTY	IFSNMD....	MKQDQ.....RLTVLLNKKDKHLSLRIADTQTGDSAIYFC	AES.....
AE000659,TRAV6	SQKIEQNSEALNIQEGKTATLTCNYT	NYSPAY.....	LQWYRQDPGRGPVFLLL	IRENEK....	EKRKE.....RLKVTFDTTLKQSLFHITASQPADSATYLC	ALD.....
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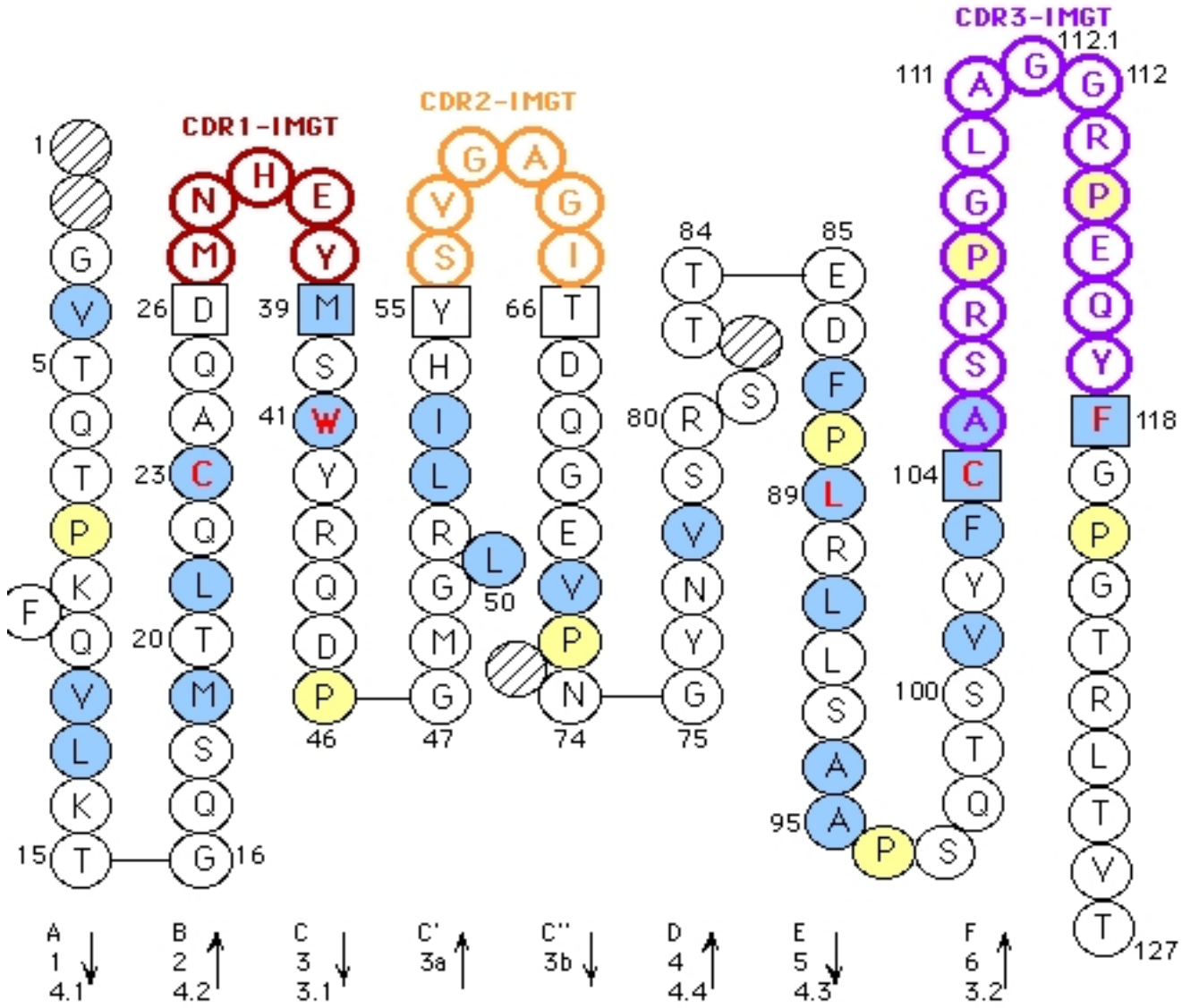
AE000659,TRAV9-1	GDSVVQTEGQVLPSEGDSLIVNCSYE	TTQYPS.....	LFWYVQYPGEGPQLHLK	AMKAND....	KGRNK.....GFEAMYRKETTSFHLEKDSVQESDSAVYFC	ALS.....

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

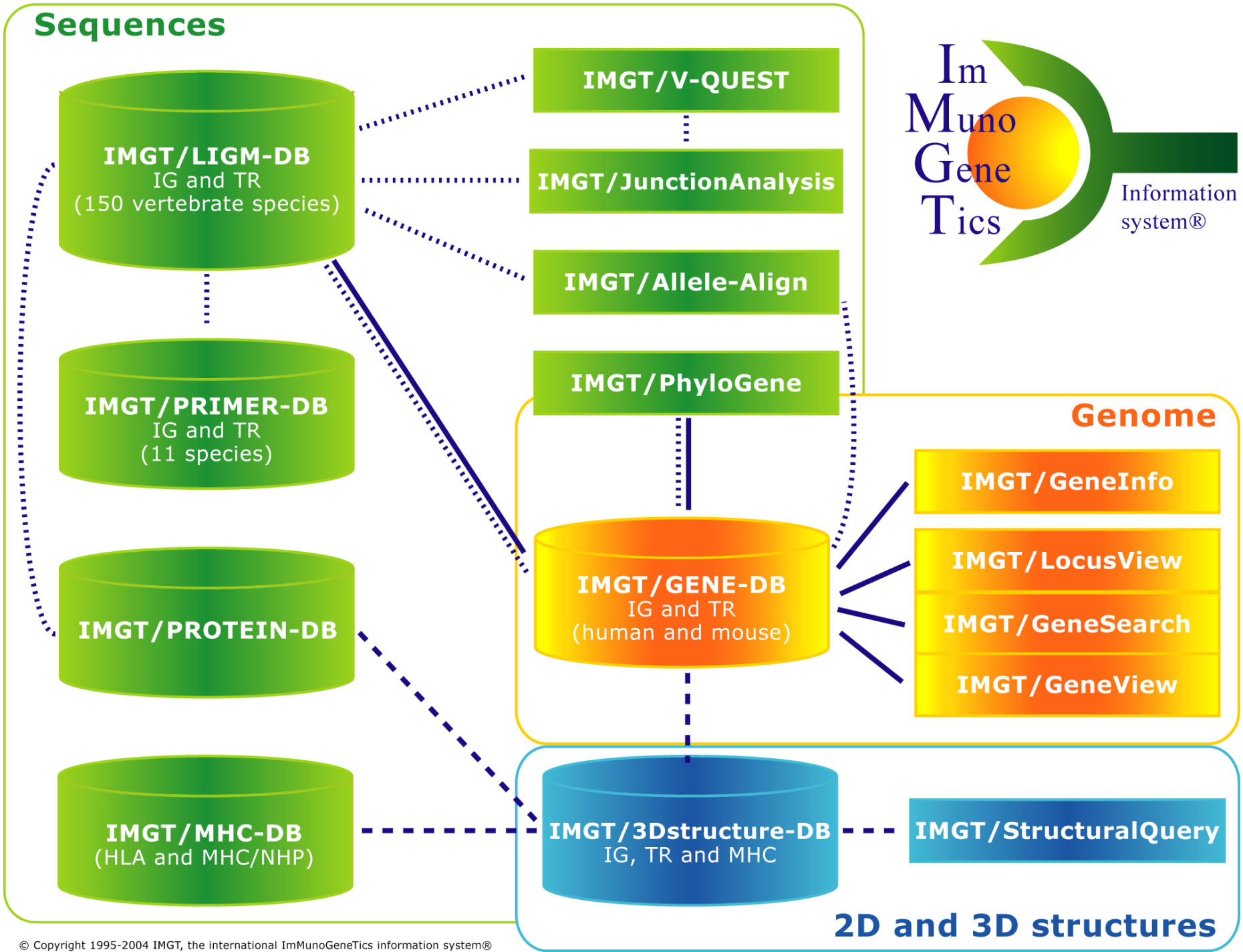
IMGT Collier de Perles

http://www.imgt.org



IMGT Repertoire, 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

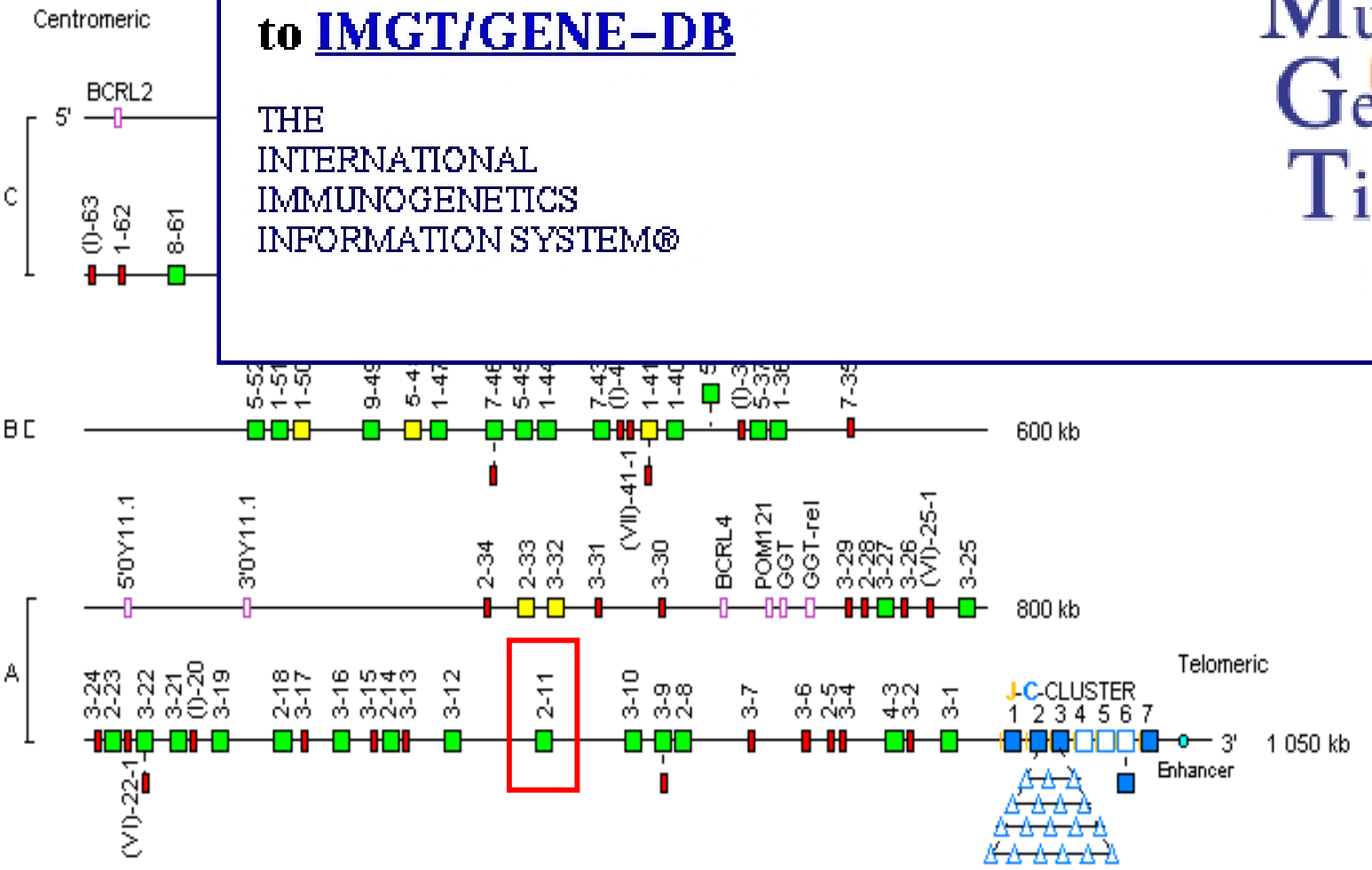
Locus representation: Human IGL

Human IGL 22q11.2

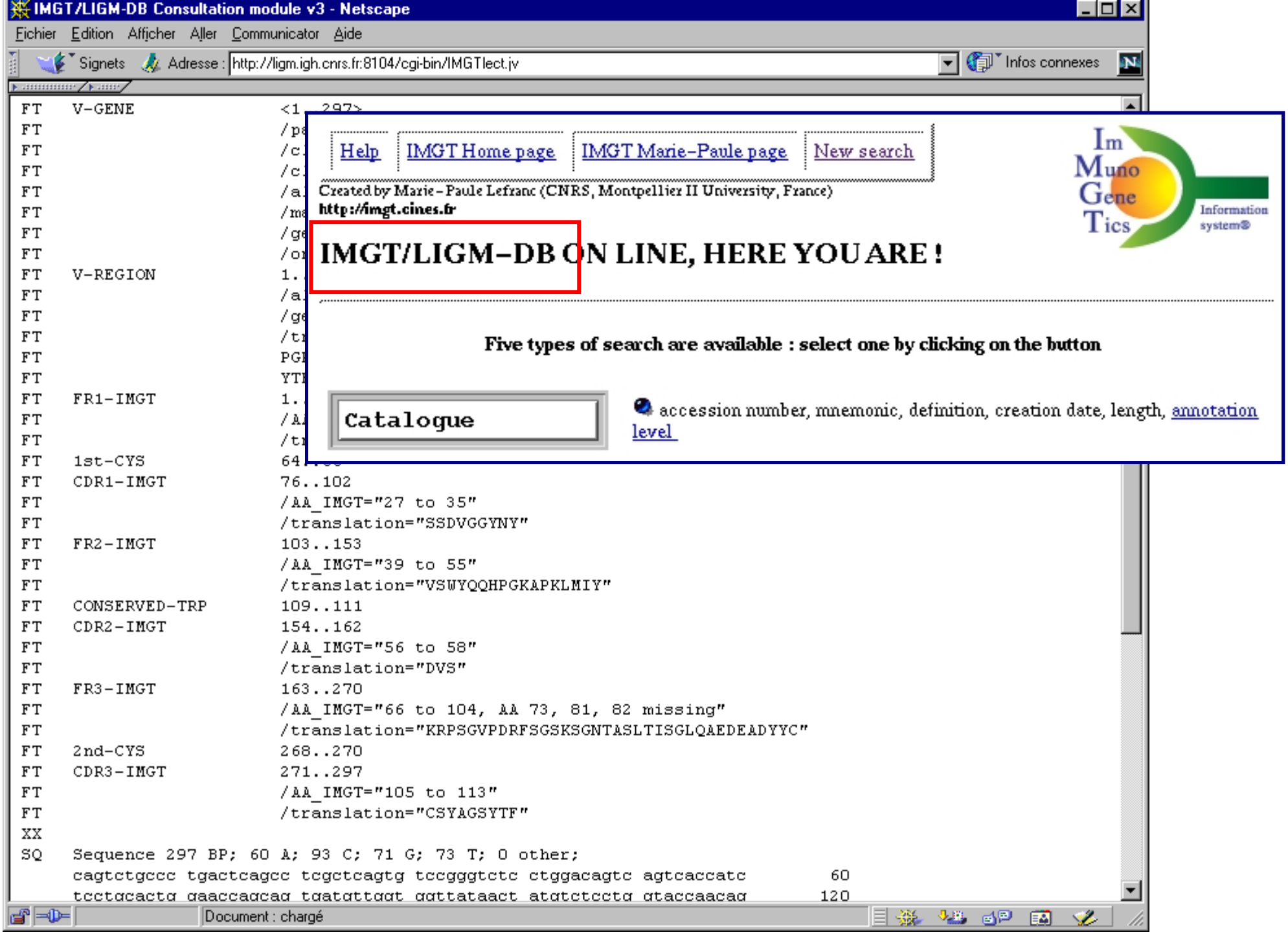
WELCOME !
to IMGT/GENE-DB

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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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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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

156.529 sequences from 280 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

```
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cacacagtgc ctagccggca agtccgtgac atgccacgtg aagcactaca cgaatcccag 780
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cgaggacctg ctcttaggtt cagaagcgaa cctcacgtgc acactgaccg gcctgagaga 960
tgcctcgggt gtcaccttca cctggacgcc ctcaagtggg aagagcgctg ttcaaggacc 1020
acctgagcgt gacctctgtg gctgctacag cgtgtccagt gtcctgccgg gctgtgccga 1080
gccatggaac catgggaaga ccttcacttg cactgctgcc taccccgagt ccaagacccc 1140
gctaaccgcc accctctcaa aatccggaaa cacattccgg cccgaggtcc acctgctgcc 1200
gccgccgtcg gaggagctgg ccctgaacga gctggtgacg ctgacgtgcc tggcacgtgg 1260
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gaagtacctg acttgggcat cccggcagga gcccagccag ggcaccacca ccttcgctgt 1380
gaccagcata ctgcgcgtgg cagccgagga ctggaagaag ggggacacct tctcctgcat 1440
ggtgggccac gaggccctgc cgctggcctt cacacagaag accatcgacc gcttggcggg 1500
taaacccacc catgtcaatg tgtctgttgt catggcggag gtggacggca cctgctactga 1560 …..
```

cDNA

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```
……..gagga ttcaccatgg aactggggct ccgctgggtt ttccttgttg ctttttttaga 120
aggtgtccag tgtgaggtgc aactggtgga gtctgggggа ggcctggtca agccgggggg 180
gtccctgaga ctctcctgtg cagcctctgg attaagcttc agtacctatg ccatgaactg 240
ggtccgccag gctccaggga aggggctgga atgggtctca agtattagta gtagaagtga 300
ttacatatac tatagagact cagtgaaggg ccgattcacc atctccagag acaacgccaa 360
gaattcactg tatctgcaaa tgaatagcct gagagtcgac gacacggctg tctattactg 420
tgcgagagat tcttgtaatg gtgctatatg ttatggtttc agtccctggg gccagggaac 480
cctggtcacc gtctcctcag catccccgac cagccccaag gtcttcccgc tgagcctctg 540
cagcacccag ccagatggga acgtggtcat cgcctgcctg gtccagggct tcttccccca 600
ggagccactc agtgtgacct ggagcgaaag cggacagggc gtgaccgcca gaaacttccc 660
acccagccag gatgcctccg gggacctgta caccacgagc agccagctga ccctgccggc 720
cacacagtgc ctagccggca agtccgtgac atgccacgtg aagcactaca cgaatcccag 780
ccaggatgtg actgtgccct gcccagttcc ctcaactcca cctaccccat ctccctcaac 840
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acctgagcgt gacctctgtg gctgctacag cgtgtccagt gtcctgccgg gctgtgccga 1080
gccatggaac catgggaaga ccttcacttg cactgctgcc taccccgagt ccaagacccc 1140
gctaaccgcc accctctcaa aatccggaaa cacattccgg cccgaggtcc acctgctgcc 1200
gccgccgtcg gaggagctgg ccctgaacga gctggtgacg ctgacgtgcc tggcacgtgg 1260
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gaagtacctg acttgggcat cccggcagga gcccagccag ggcaccacca ccttcgctgt 1380
gaccagcata ctgcgcgtgg cagccgagga ctggaagaag ggggacacct tctcctgcat 1440
ggtgggccac gaggccctgc cgctggcctt cacacagaag accatcgacc gcttggcggg 1500
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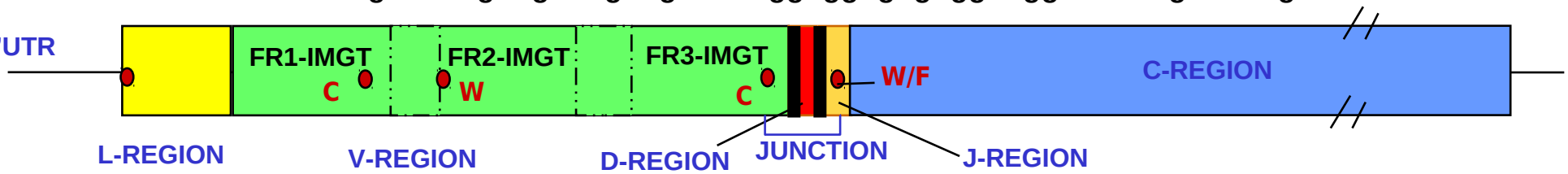

The IMGT-ONTOLOGY concepts

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"
FT                       /gene="IGHV3-33"
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

```
AF402940                    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
```

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

WELCOME !
to IMGT/V-QUEST

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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**

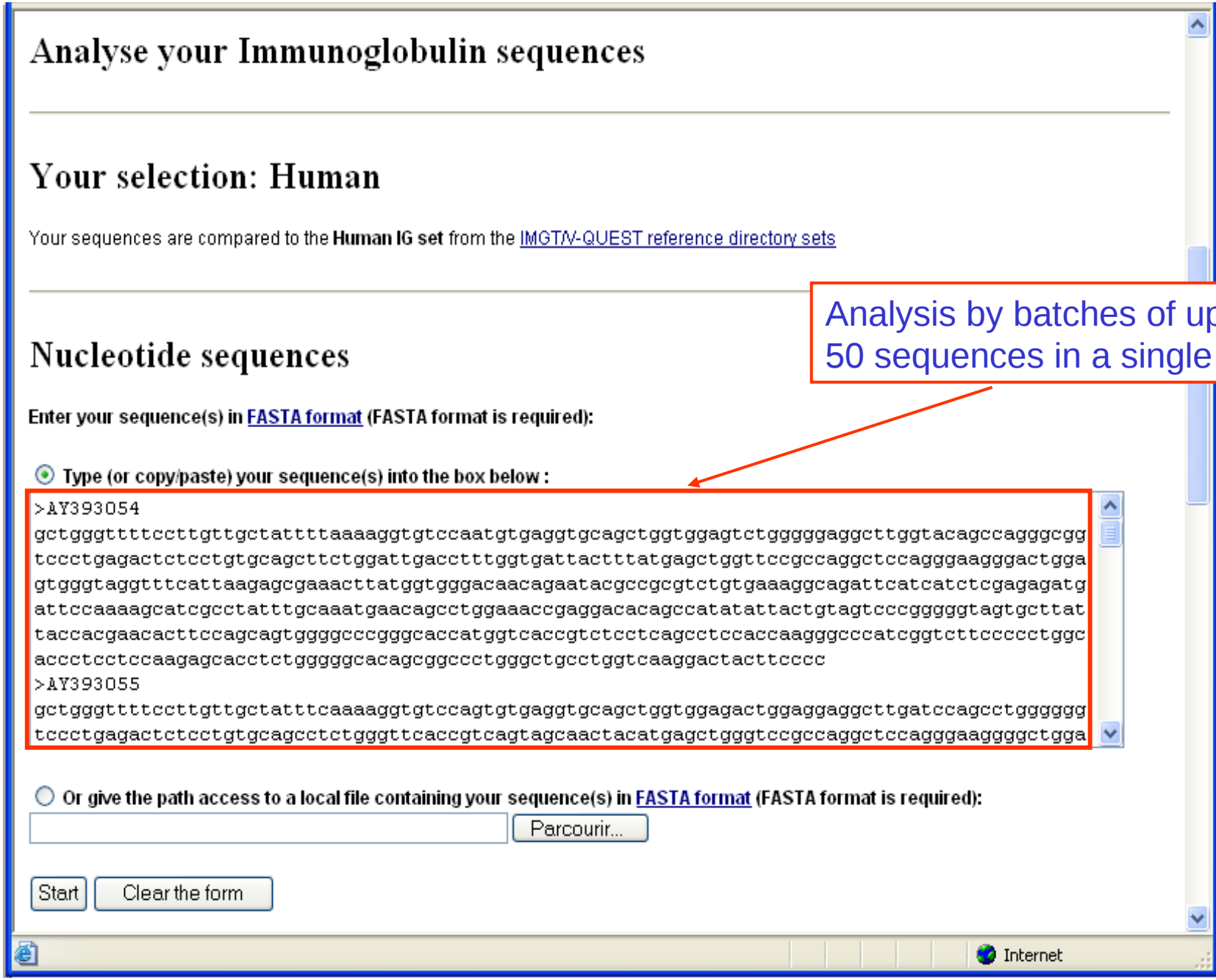
Current version: 3.1.2 (18 July 2008)

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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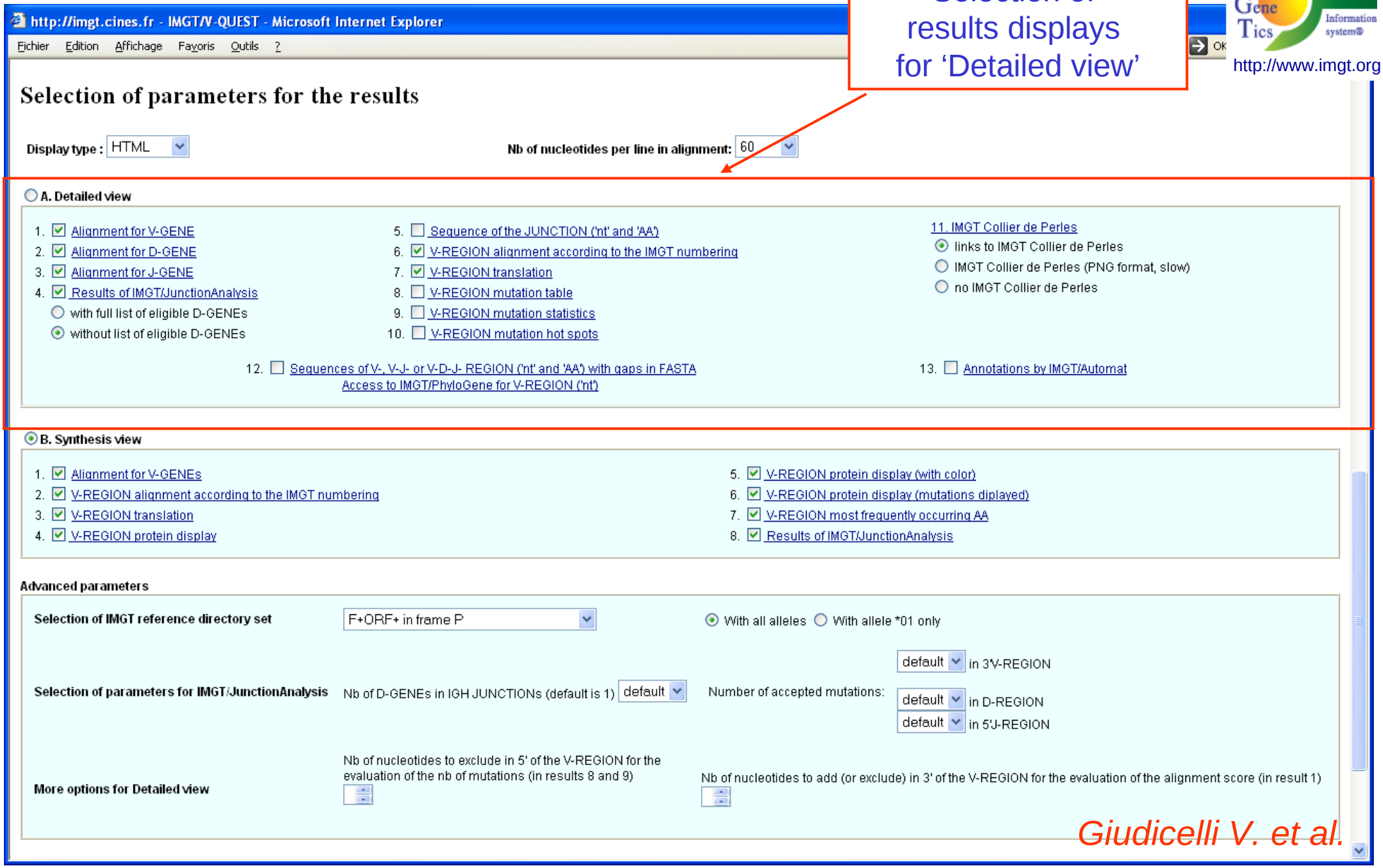
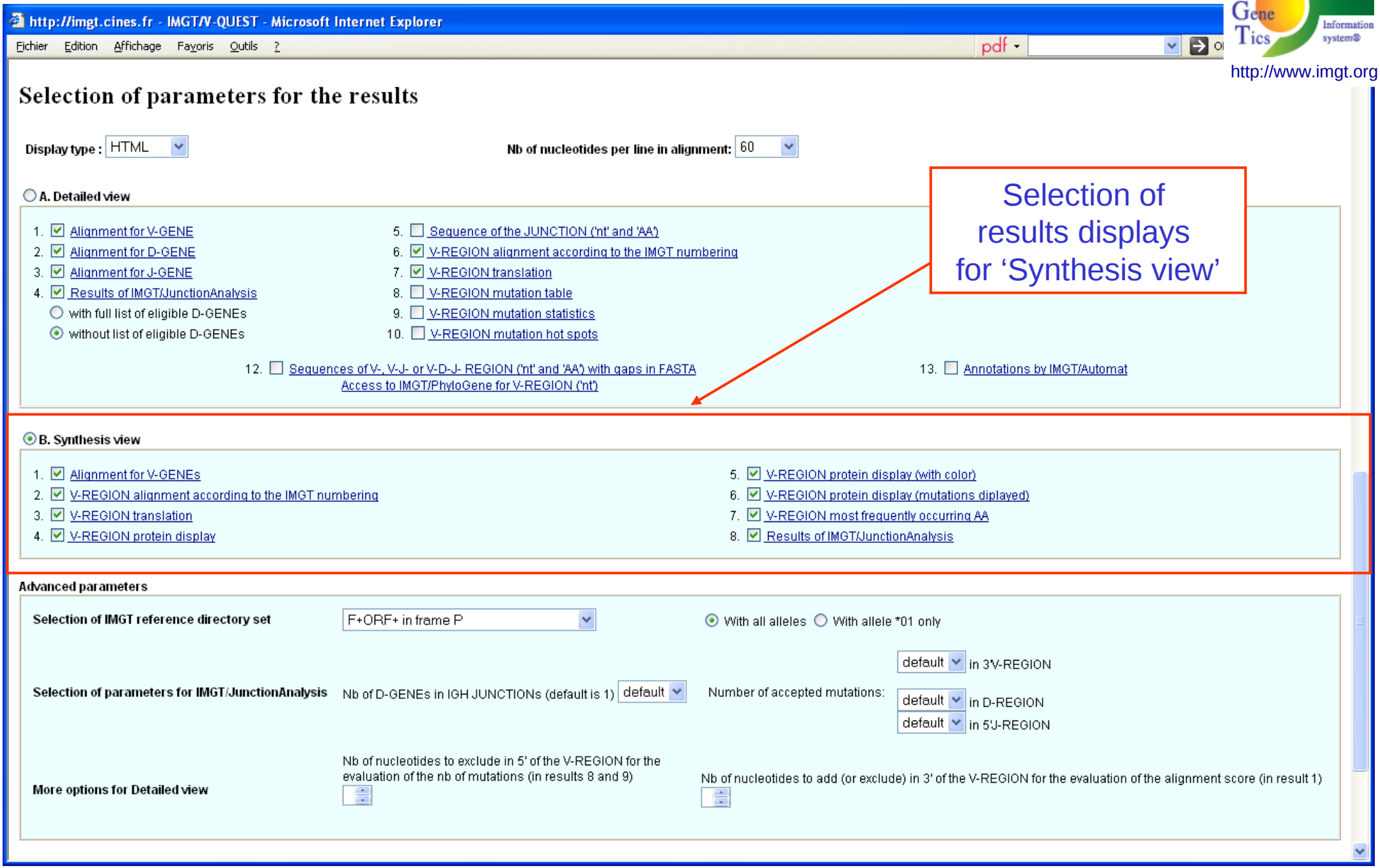

Selection of results displays for 'Detailed view'
http://imgt.cines.fr - IMGT/V-QUEST - Microsoft Internet Explorer
Fichier Edition Affichage Favoris Outils ?
http://www.imgt.org
Selection of parameters for the results
Display type : HTML
Nb of nucleotides per line in alignment: 60
A. Detailed view
1. 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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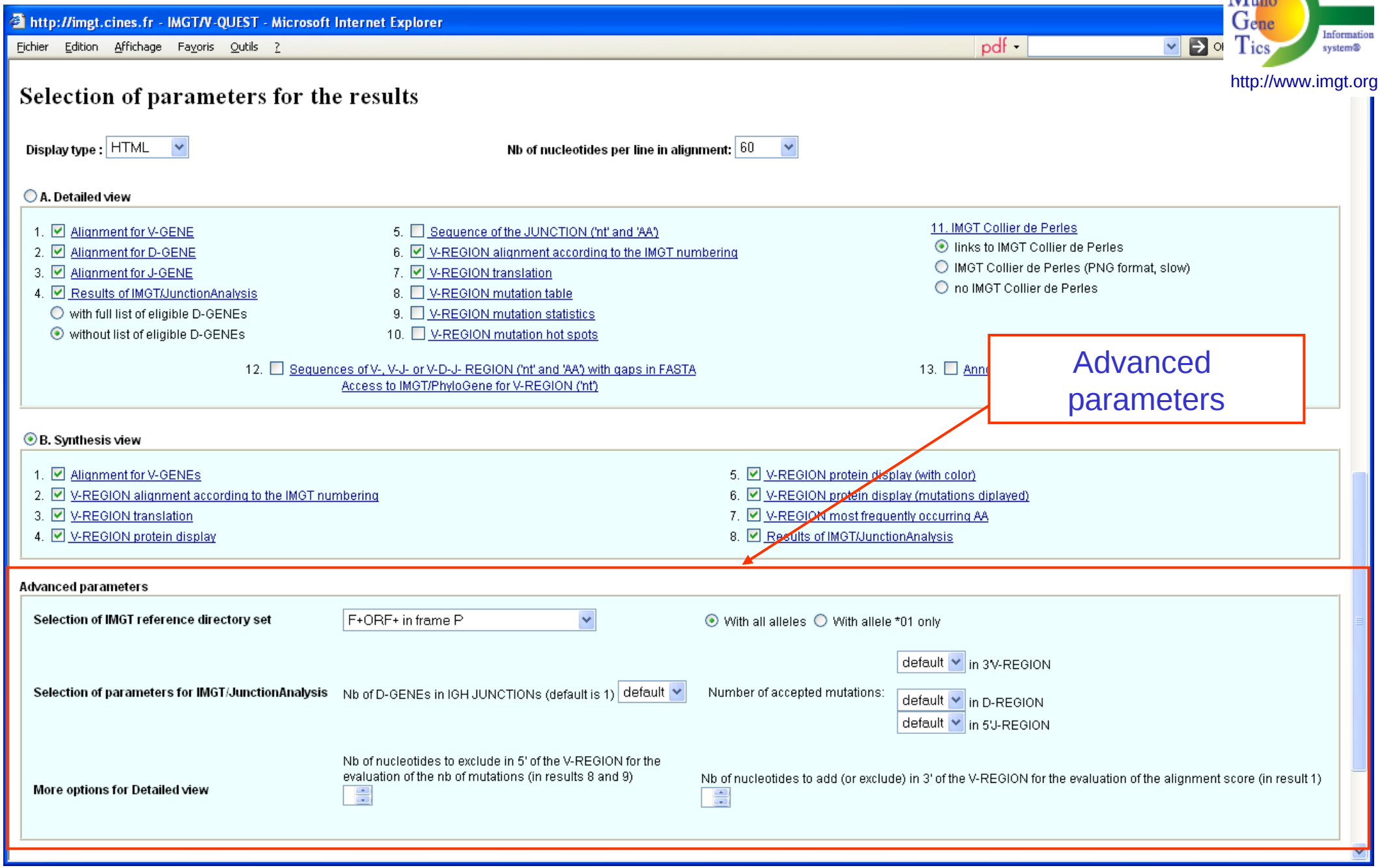
http://www.imgt.org



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

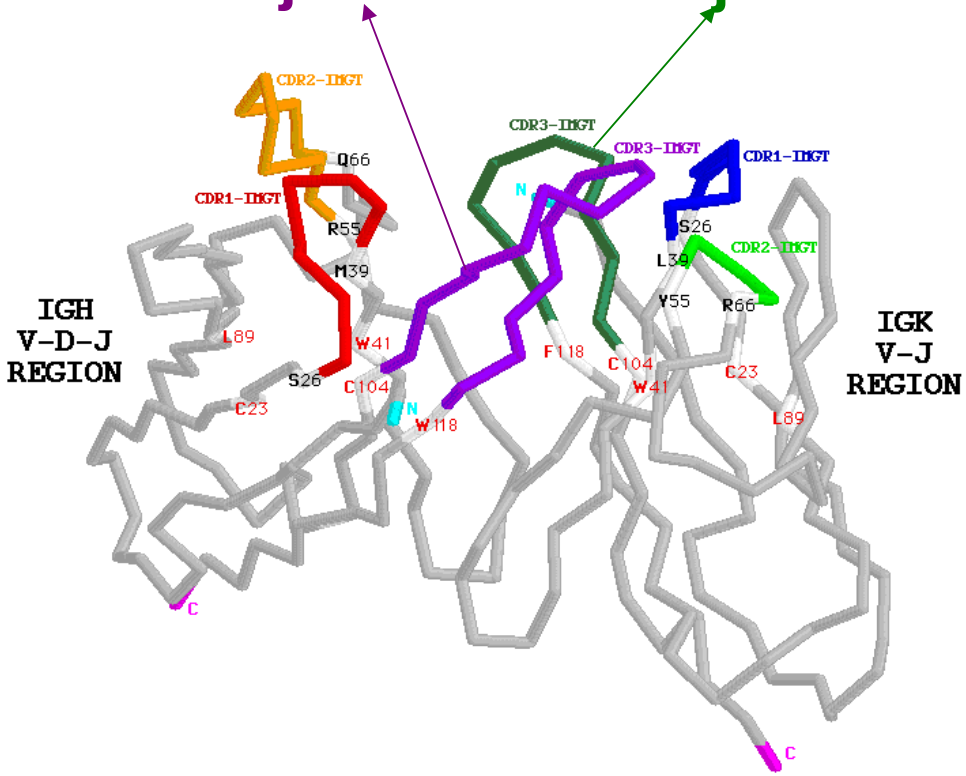
```
AF184762            gtgatccggggagatgtttacaaccgacagtggggccagggaaccctggtcaccgtctcc
J00256 IGHJ1*01     ............-c--aa---tt--ag--c----------c------------------
X86355 IGHJ4*02     ..............ac---tttgact-c-----------------------------
J00256 IGHJ4*01     ..............ac---tttgact-c--------a---------------------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

Junctions of the V-DOMAINs

http://www.imgt.org

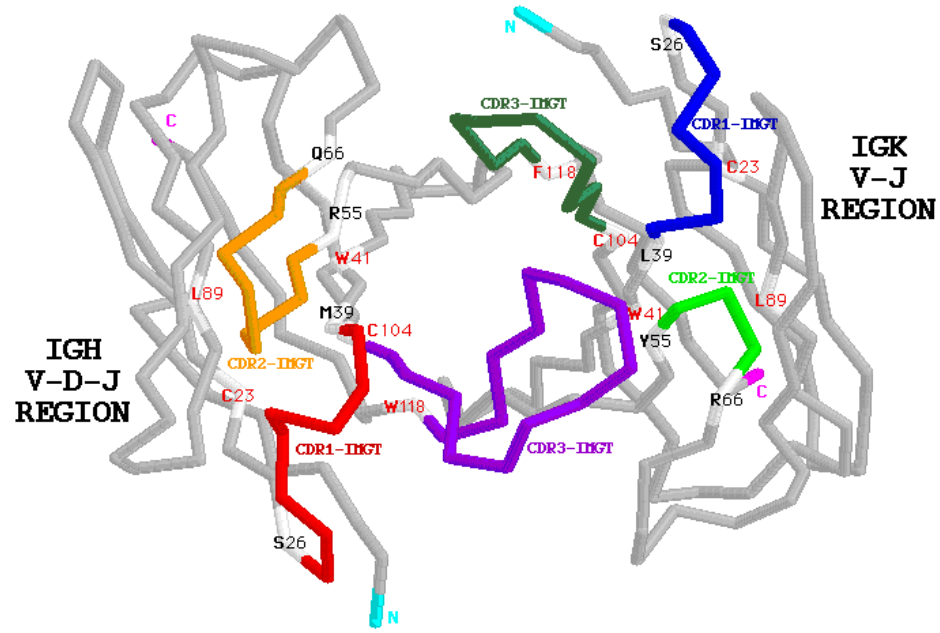
VH **V-KAPPA**

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

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

THANK YOU
for using IMGT/JunctionAnalysis

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INFORMATION SYSTEM®

Analysis of the JUNCTIONs

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

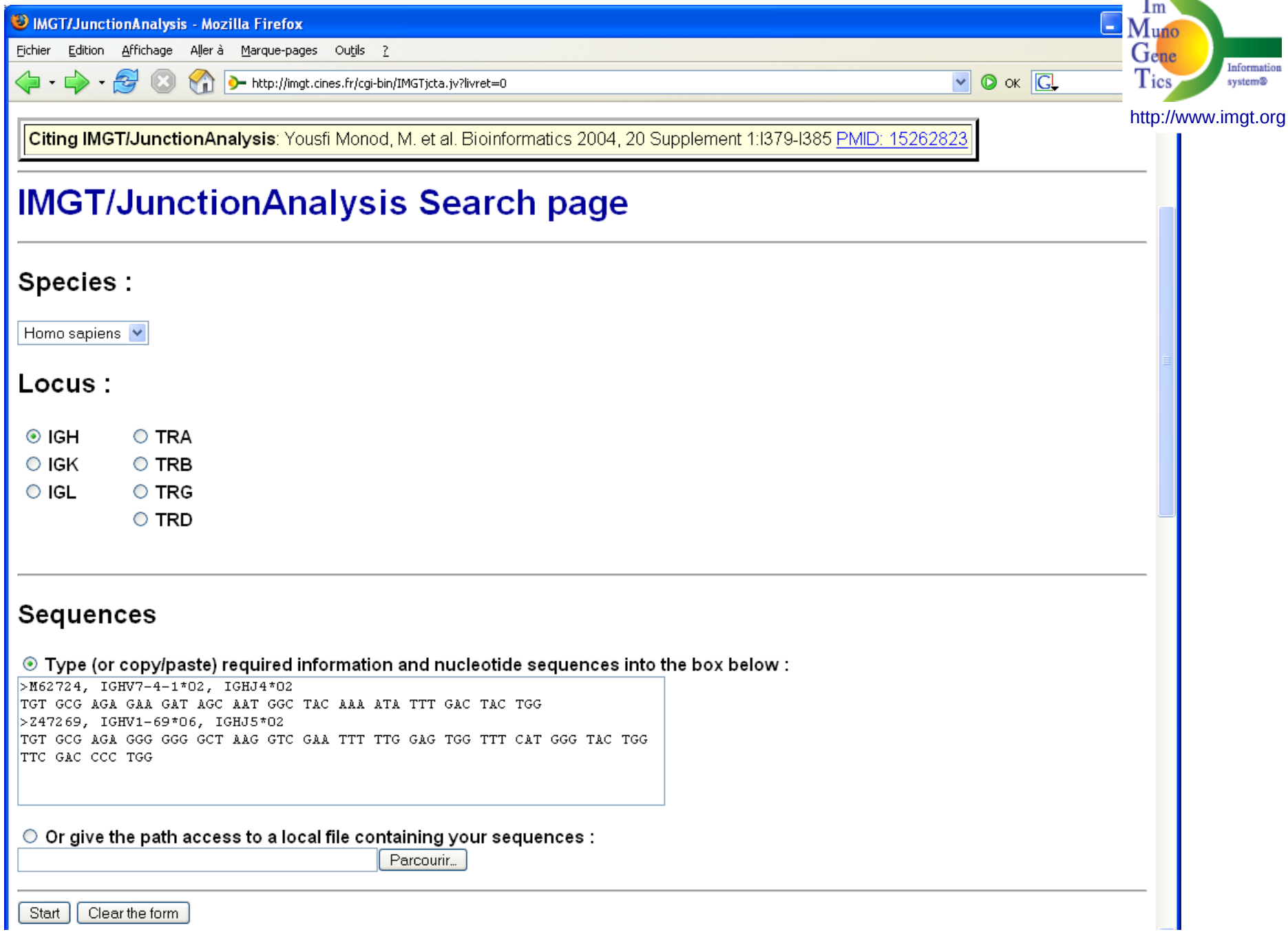
	Input	J-REGION	J name	D name	Vmut	Dmut	Jmut	Ngc
#1	M62724	.....tttgactactgg	IGHJ4*02	IGHD5-24*01	0	2	0	1/7
#2	Z47269	...actggttcgacccctgg	IGHJ5*02	IGHD3-3*02	0	2	0	13/20

Translation of the JUNCTIONs

		104	105	106	107	108	109	110	111	111.1	111.2	111.3	112.4	112.3	112.2	112.1	112	113	114	115	116	117	118	frame	CDR3-IMGT length
			C	A	R	E	D	S	N	G									Y	K	I	F	D	Y	W	
#1	M62724		tgt	gcg	aga	gaa	gat	agc	aat	ggc									tac	aaa	ata	ttt	gac	tac	tgg	+	13
			C	A	R	G	G	A	K	V	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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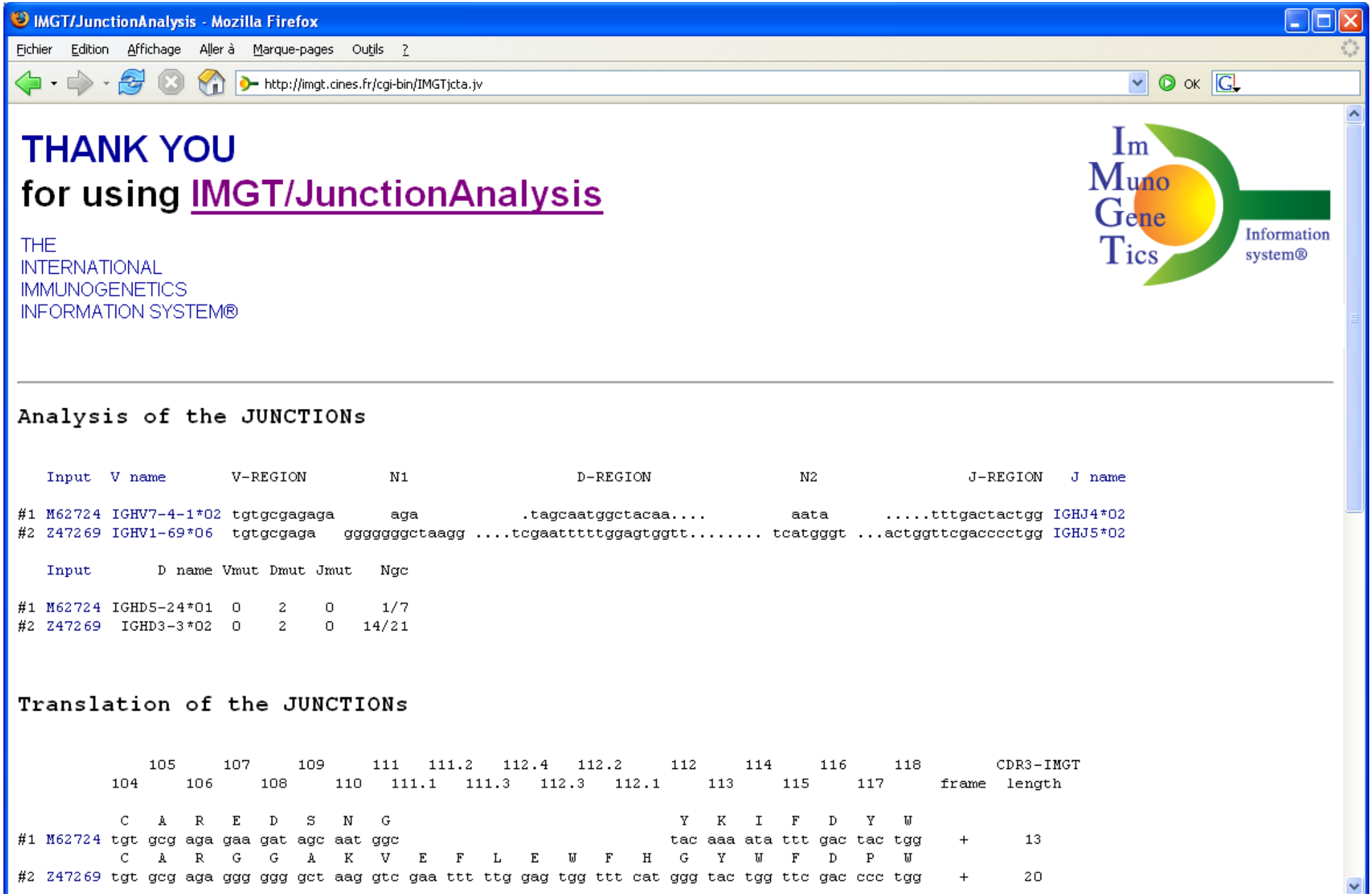
Yousfi Monod et al. Bioinformatics, 20, I379-I385 (2004)



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

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

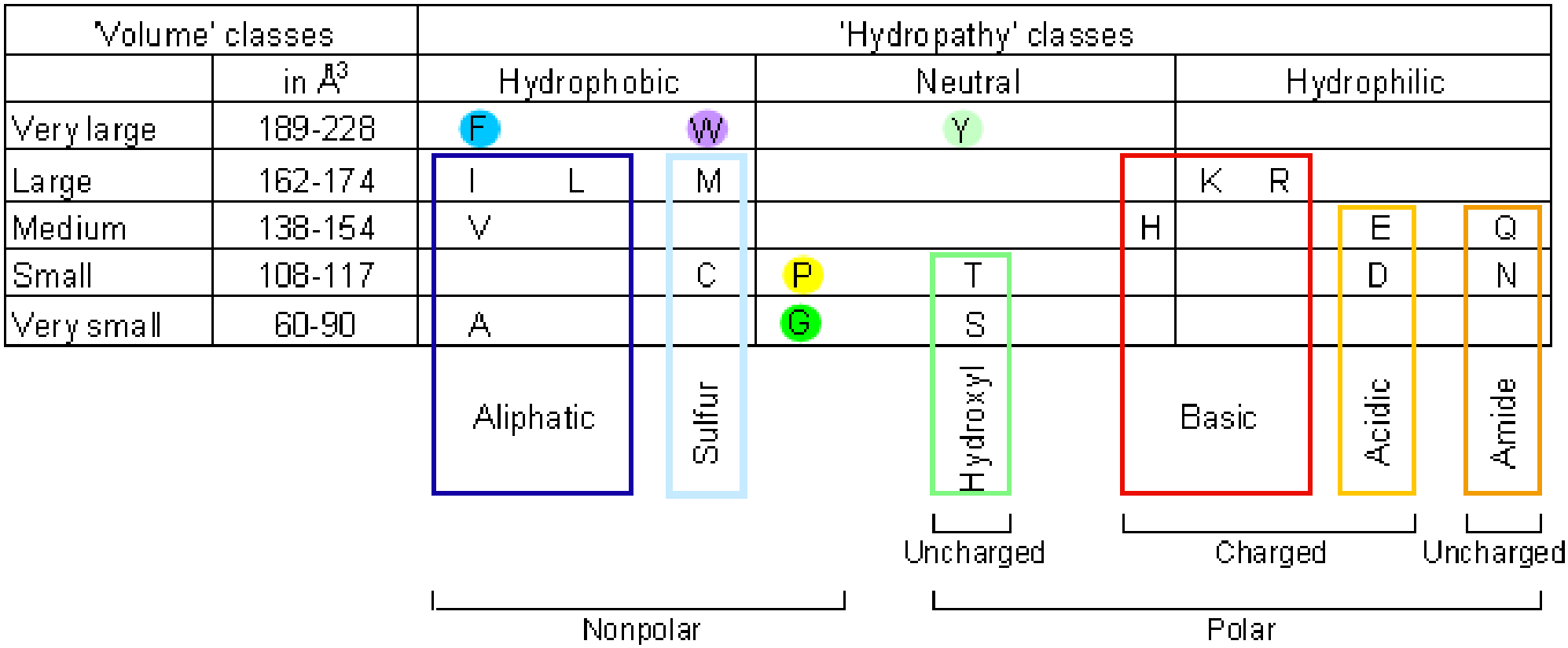
Click on mutated (underscored) nucleotid to see the original one: c

	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	.....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

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

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

http://www.imgt.org



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

http://www.imgt.org

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

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

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

http://www.imgt.org

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

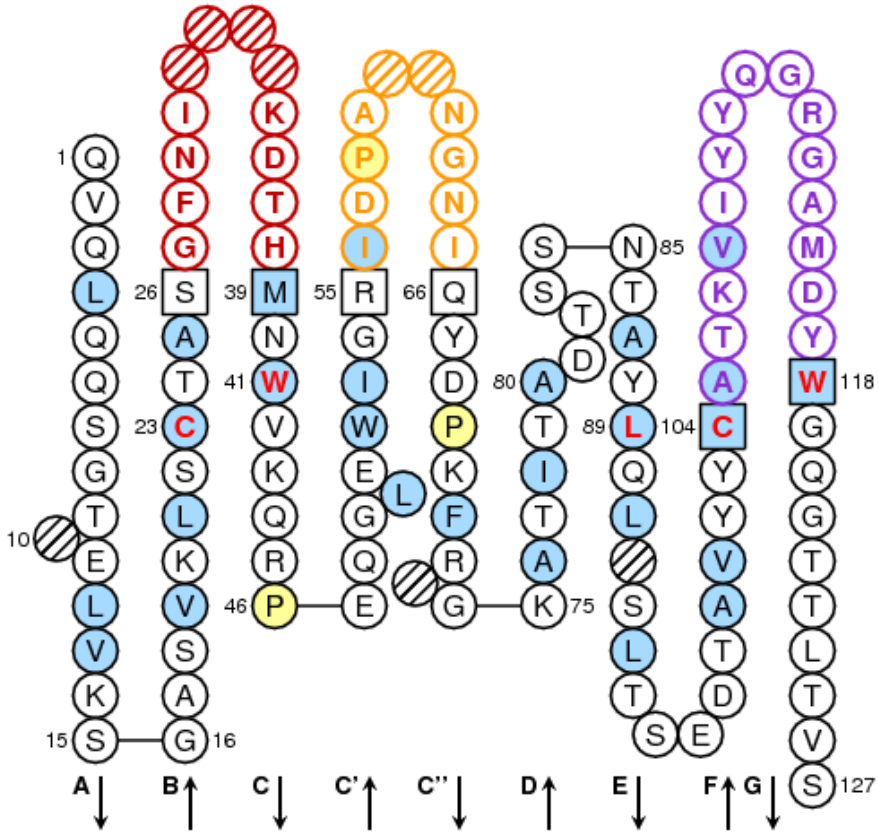
Motif	Positions
agct	8-11 (FR1)
agcc	41-44 (FR1)
aact	59-62 (FR1)
agcc	72-75 (FR1)
tgct	99-102 (CDR1)
agct	177-180 (CDR2)
tgct	201-204 (FR3)
agcc	277-280 (FR3)
aacc	285-288 (FR3)
tact	307-310 (FR3)
tact	312-315 (FR3)

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.

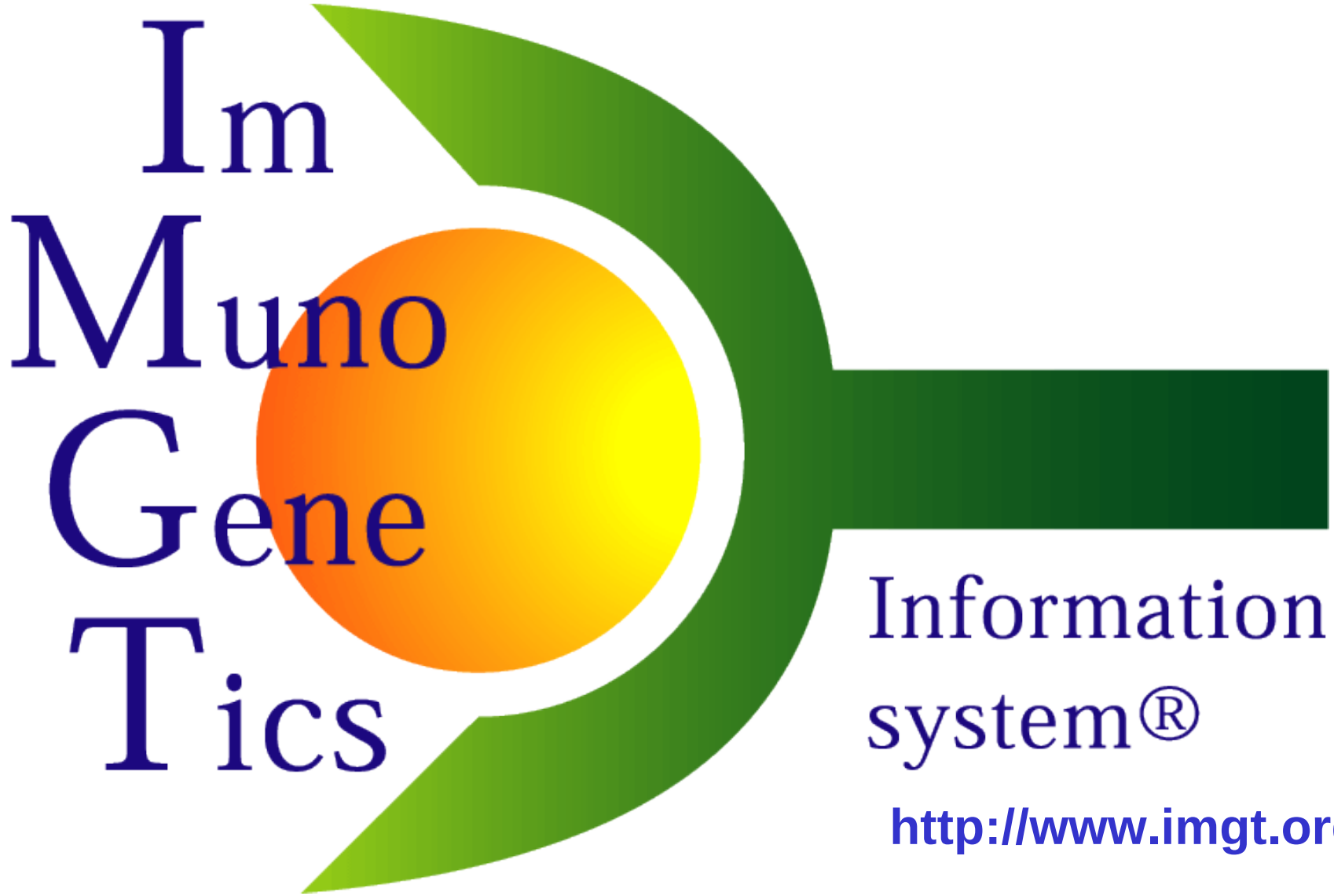
13. ‘Detailed view’: Annotation by IMGT/Automat

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.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Tics
Information
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