

Immunotechnologie

Enseignements d'Immuno-informatique-
IMGT®, the international ImMunoGeneTics information system®

Mardi 25 septembre

Souphatta SASORITH



<http://www.imgt.org>

I. IMGT Bases de données et Outils

II. Les immunoglobulines:

- Structures des IG
- Propriétés structurales et biologiques
- Chromosomes et locus
- Synthèse des IG (génétique moléculaire)

III. Structure des gènes :

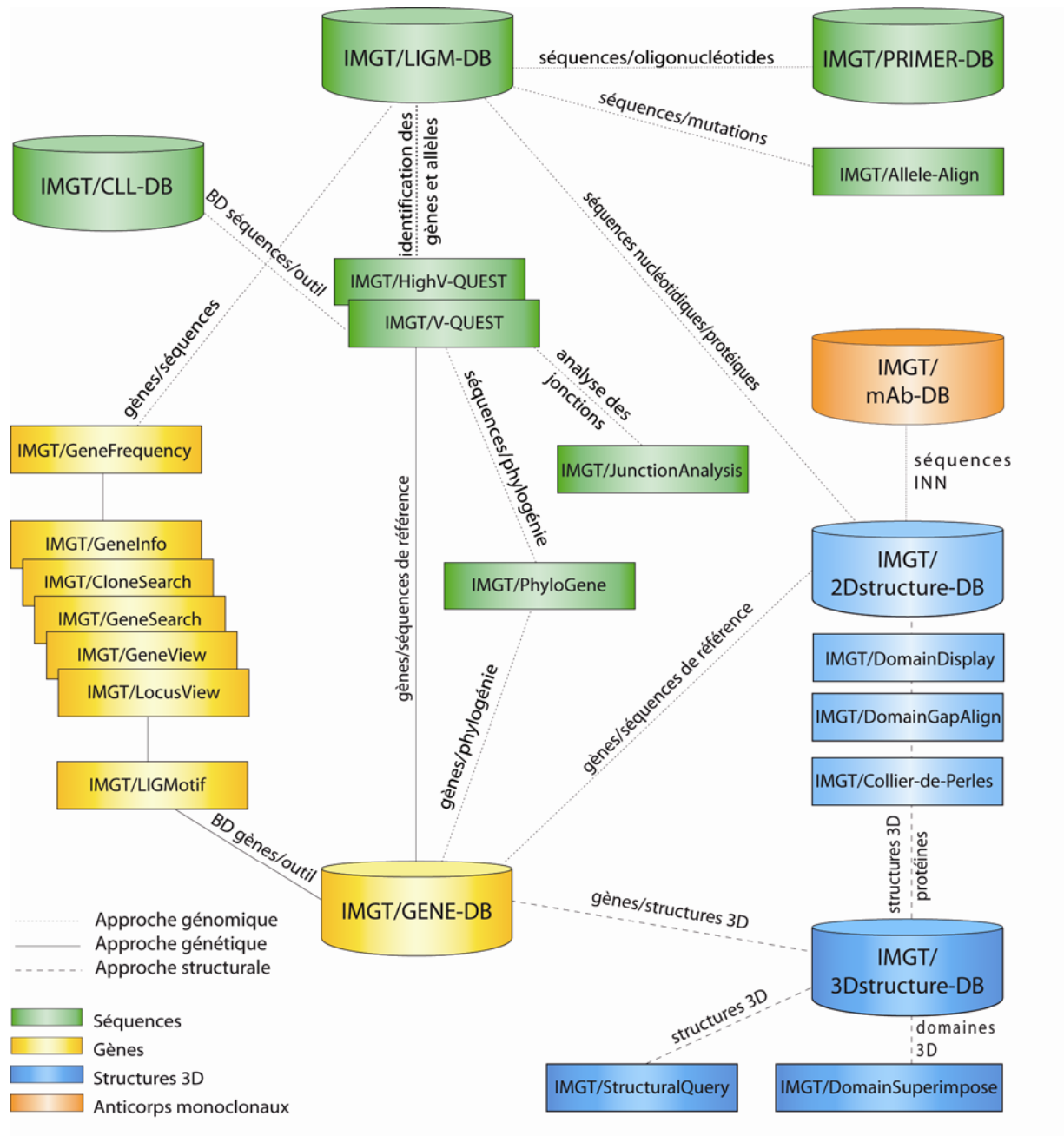
V-GENE, D-GENE, J-GENE et C-GENE

IMGT bases de données et outils



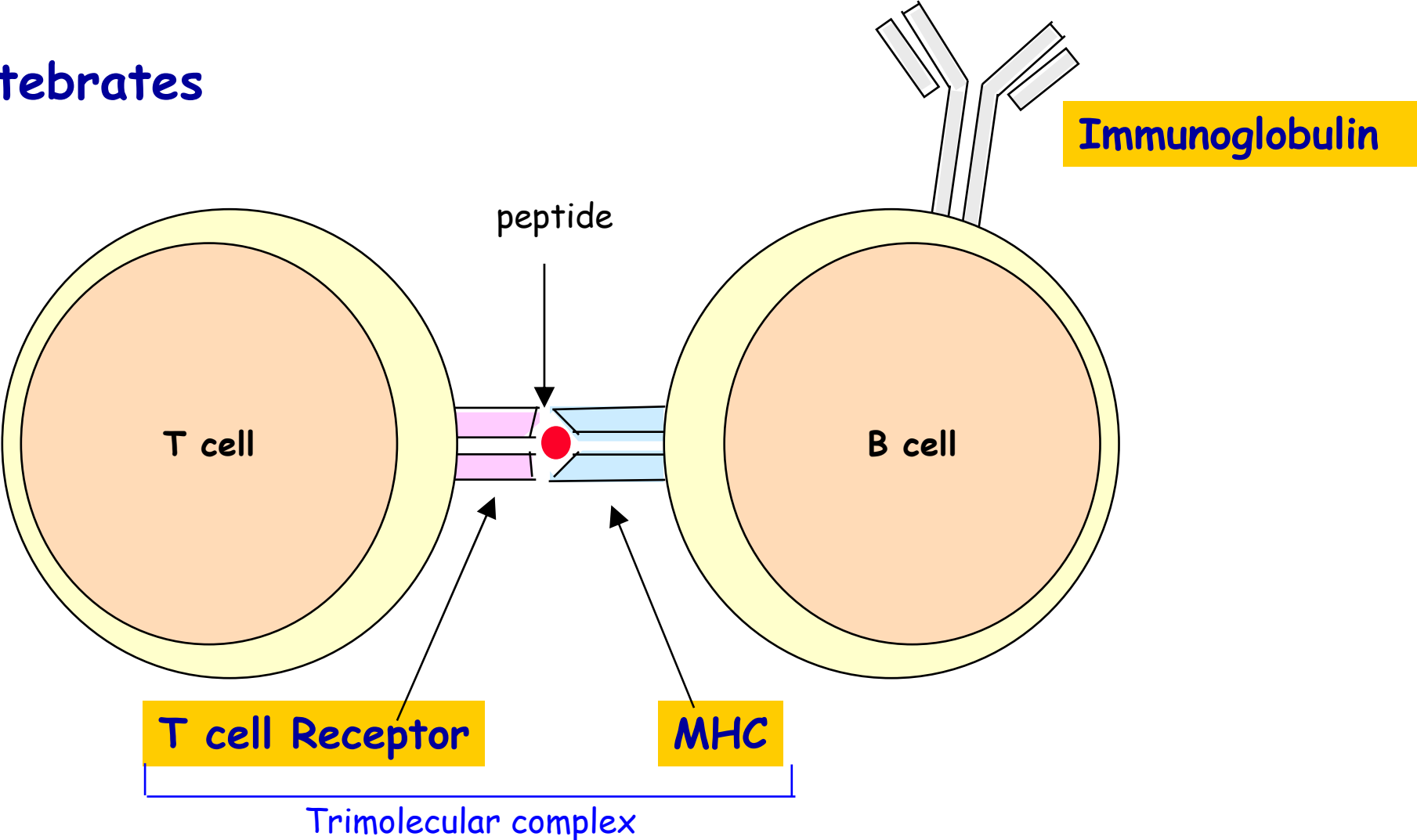
<http://www.imgt.org>

IMGT®, the international ImMunoGeneTics information system®



IMGT domain of research: the adaptive immune system

Vertebrates



Description standardisée des domaines, chaînes et récepteurs

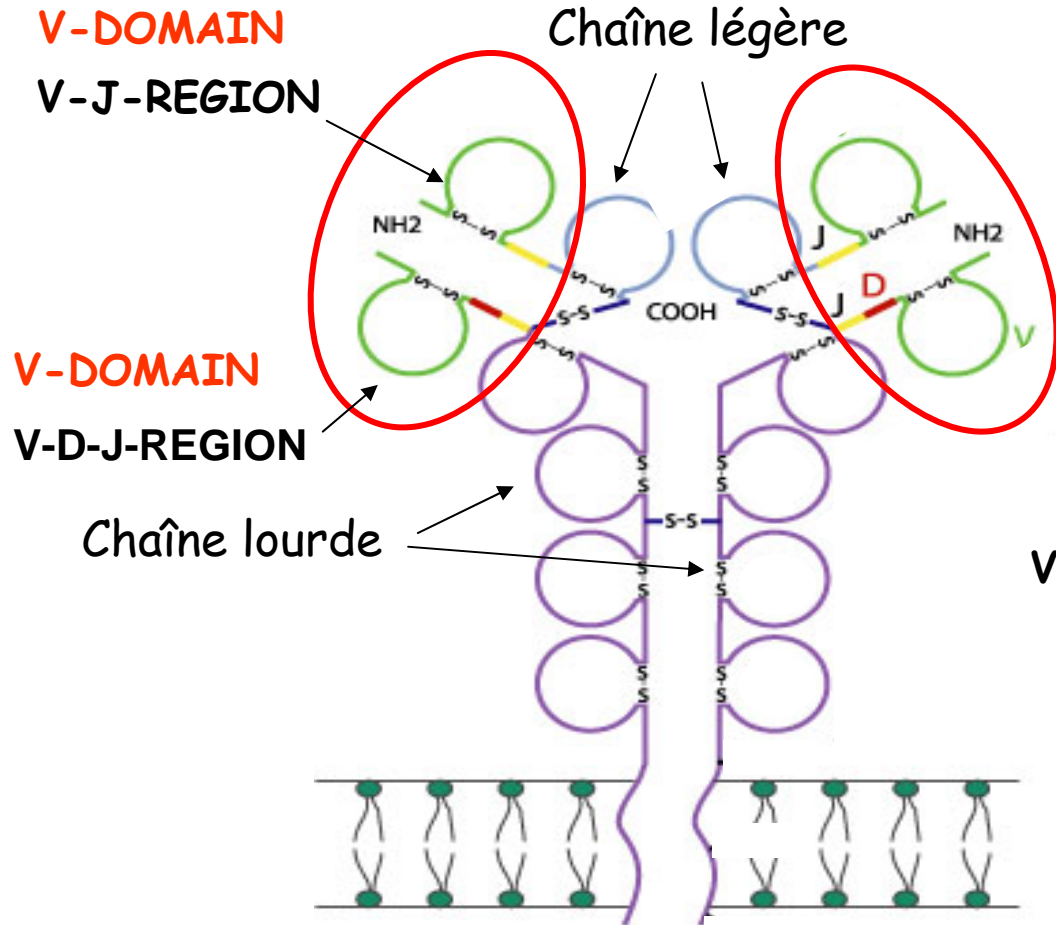
★ IMGT/PROTEIN-DB and IMGT/3Dstructure-DB keywords and labels: IG complete receptors

★ Mammals

IDENTIFICATION		Standardized labels for DESCRIPTION		
Receptor type	Chain type	Receptor [1]	Chain	Domain [2]
IgA_Kappa	IG-Heavy-Alpha	IG-ALPHA_KAPPA	H-ALPHA	VH, CH1, CH2, CH3
	IG-Light-Kappa		L-KAPPA	V-KAPPA, C-KAPPA
IgA1_Kappa	IG-Heavy-Alpha-1	IG-ALPHA-1_KAPPA	H-ALPHA-1	VH, CH1, CH2, CH3
	IG-Light-Kappa		L-KAPPA	V-KAPPA, C-KAPPA
IgA2_Kappa	IG-Heavy-Alpha-2	IG-ALPHA-2_KAPPA	H-ALPHA-2	VH, CH1, CH2, CH3
	IG-Light-Kappa		L-KAPPA	V-KAPPA, C-KAPPA
IgD_Kappa	IG-Heavy-Delta	IG-DELTA_KAPPA	H-DELTA	VH, CH1, CH2, CH3
	IG-Light-Kappa		L-KAPPA	V-KAPPA, C-KAPPA
IgE_Kappa	IG-Heavy-Epsilon	IG-EPSILON_KAPPA	H-EPSILON	VH, CH1, CH2, CH3, CH4
	IG-Light-Kappa		L-KAPPA	V-KAPPA, C-KAPPA
IgG_Kappa	IG-Heavy-Gamma	IG-GAMMA_KAPPA	H-GAMMA	VH, CH1, CH2, CH3
	IG-Light-Kappa		L-KAPPA	V-KAPPA, C-KAPPA
IgG1_Kappa	IG-Heavy-Gamma-1	IG-GAMMA-1_KAPPA	H-GAMMA-1	VH, CH1, CH2, CH3
	IG-Light-Kappa		L-KAPPA	V-KAPPA, C-KAPPA
IgG2_Kappa	IG-Heavy-Gamma-2	IG-GAMMA-2_KAPPA	H-GAMMA-2	VH, CH1, CH2, CH3
	IG-Light-Kappa		L-KAPPA	V-KAPPA, C-KAPPA
IgG2a_Kappa	IG-Heavy-Gamma-2-a	IG-GAMMA-2-A_KAPPA	H-GAMMA-2-A	VH, CH1, CH2, CH3
	IG-Light-Kappa		L-KAPPA	V-KAPPA, C-KAPPA
IgG2b_Kappa	IG-Heavy-Gamma-2-b	IG-GAMMA-2-B_KAPPA	H-GAMMA-2-B	VH, CH1, CH2, CH3
	IG-Light-Kappa		L-KAPPA	V-KAPPA, C-KAPPA
IgG2c_Kappa	IG-Heavy-Gamma-2-c	IG-GAMMA-2-C_KAPPA	H-GAMMA-2-C	VH, CH1, CH2, CH3
	IG-Light-Kappa		L-KAPPA	V-KAPPA, C-KAPPA
IgG3_Kappa	IG-Heavy-Gamma-3	IG-GAMMA-3_KAPPA	H-GAMMA-3	VH, CH1, CH2, CH3
	IG-Light-Kappa		L-KAPPA	V-KAPPA, C-KAPPA

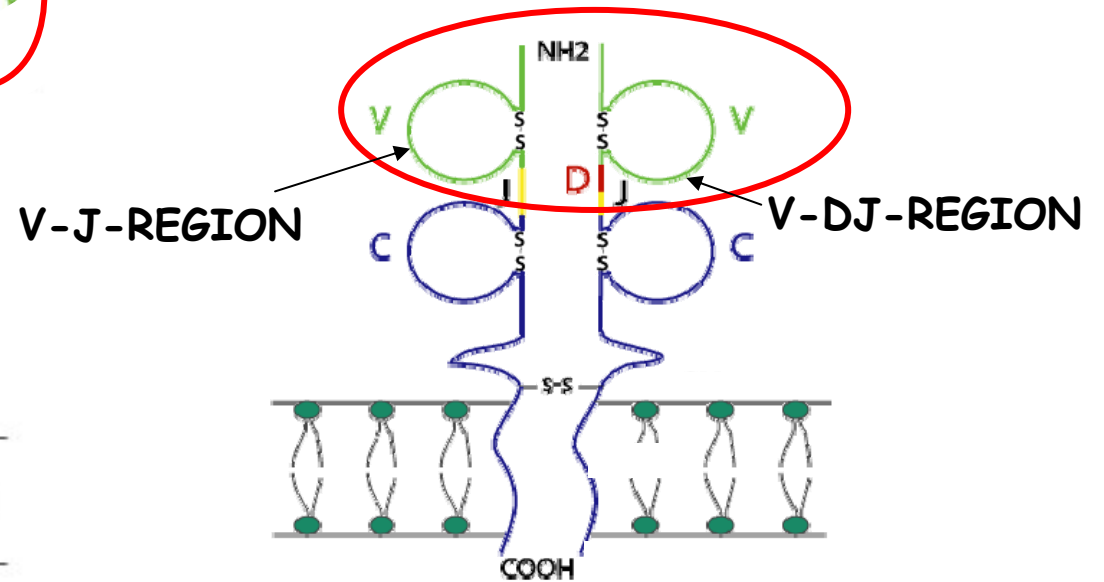
Immunoglobuline membranaire (IGM)

receptor T (TR)



Contribution des 2
2 V-DOMAINS
Au site de fixation de l'antigène

Alpha - Beta
Gamma - Delta

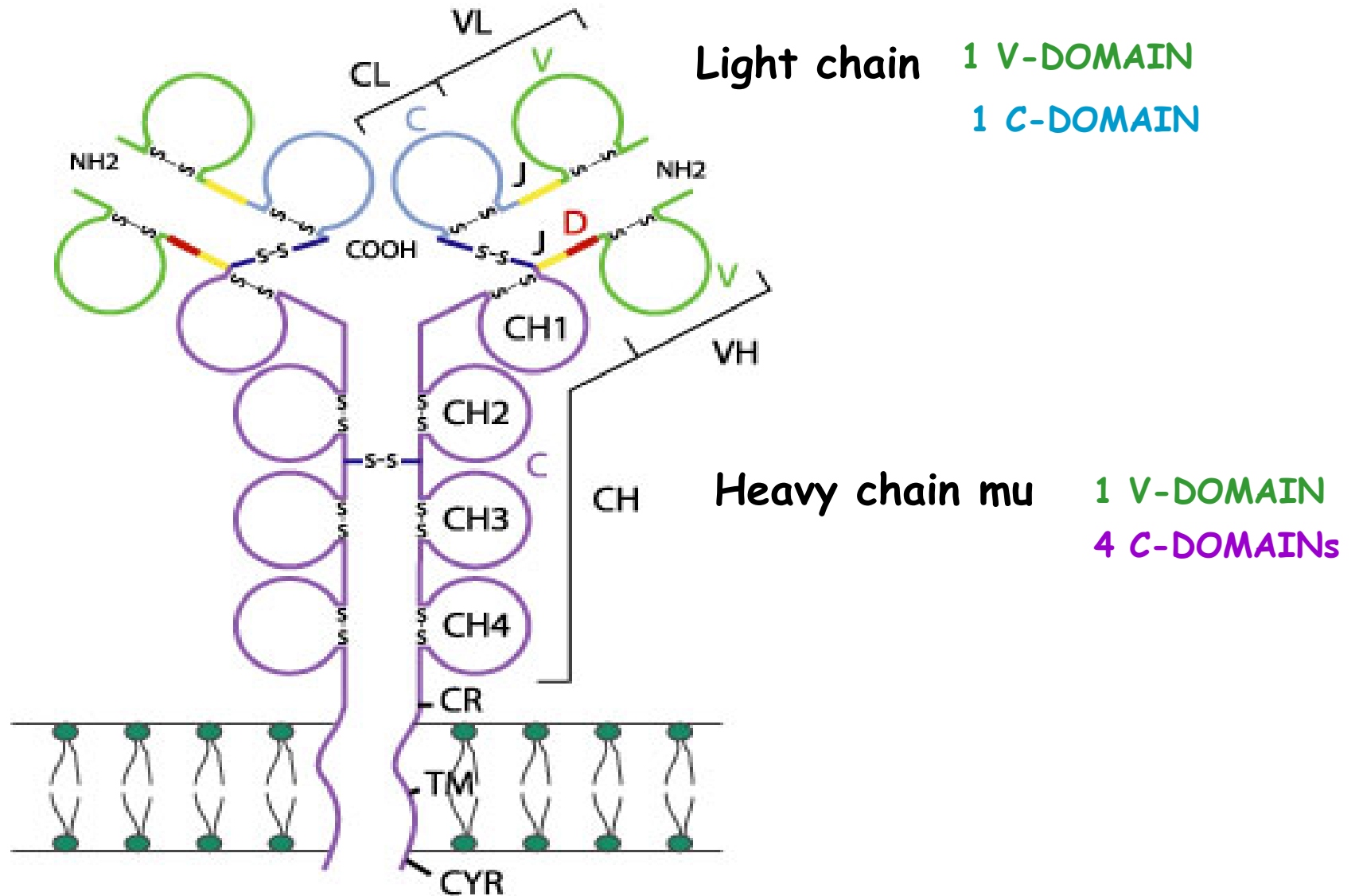


Immunoglobulines

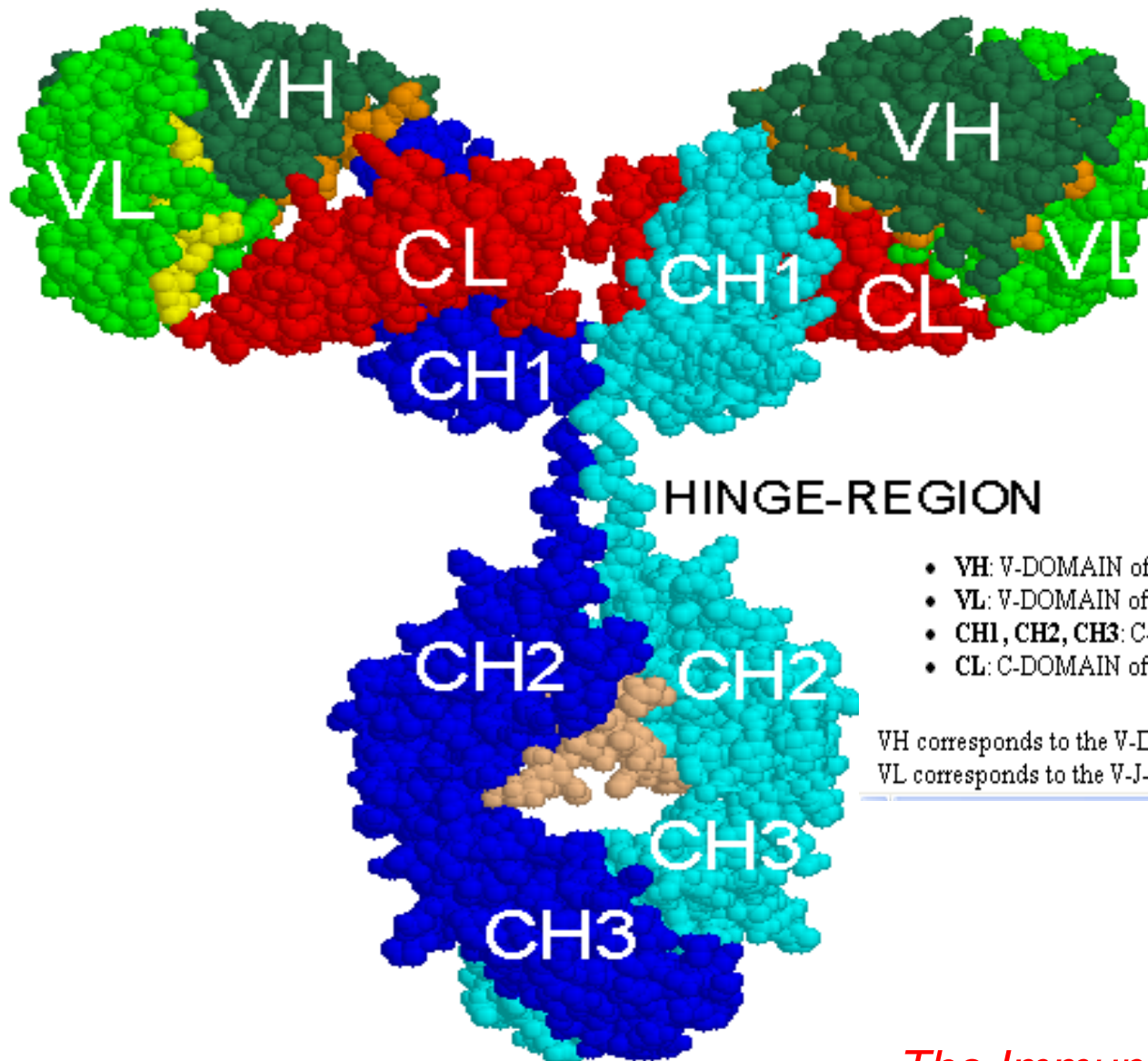


<http://www.imgt.org>

Immunoglobulin IgM



Spacefill 3D representation of an IgG



- 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.

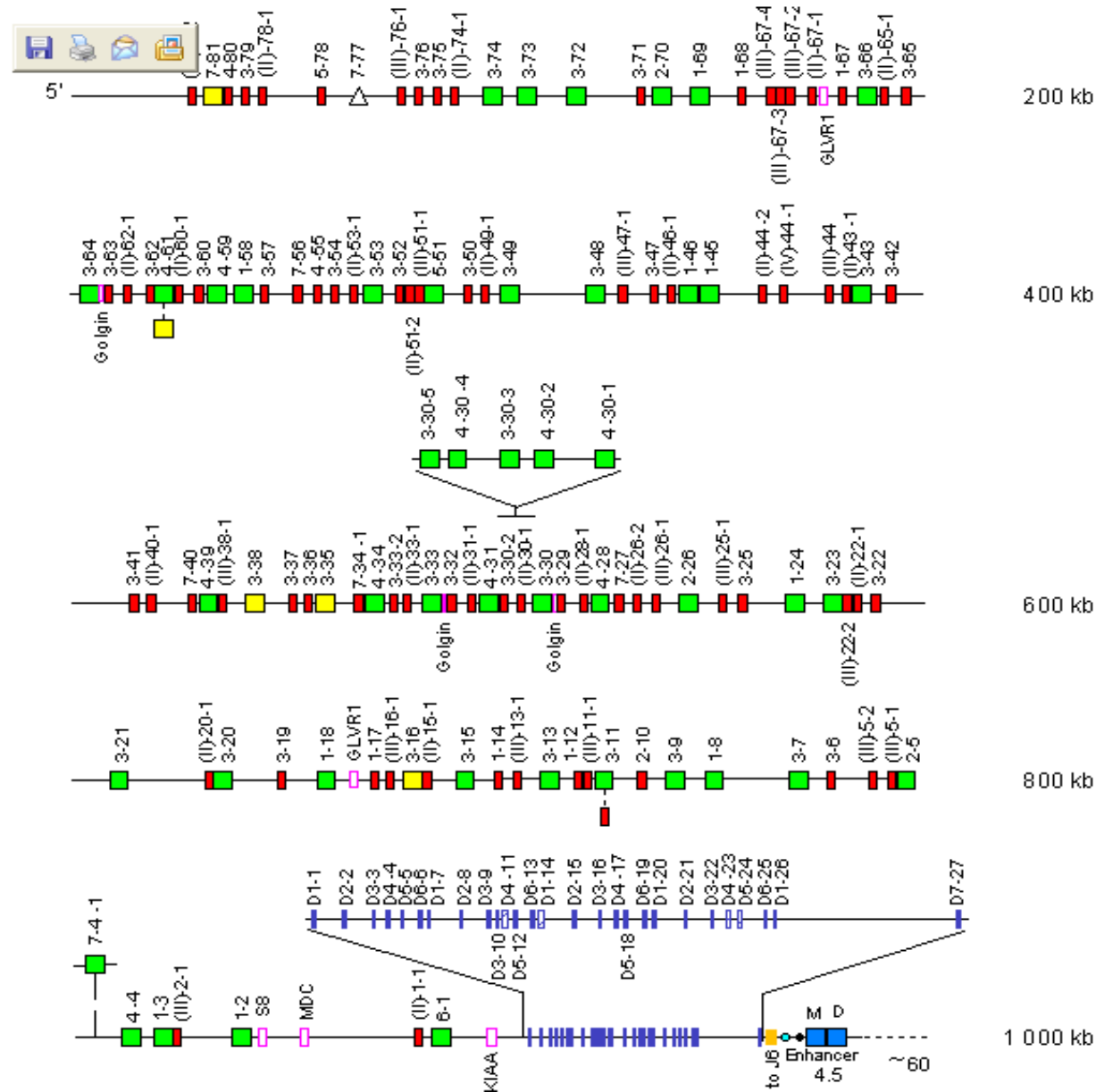
Propriétés structurales et biologiques des IG humains

Print of this table: Lefranc, M.-P. and Lefranc, G., The Immunoglobulin FactsBook, Academic Press, London, UK (458 pages), 2001, ISBN:012441351X

Properties	Classes and subclasses								
	IgM	IgD	IgG				IgA		IgE
			IgG1	IgG2	IgG3	IgG4	IgA1	IgA2	
Molecular weight of secreted form (kDa) (1)	950(p)	170-180	150	150	155-165	150	160 (m) 300 (d)	160 (m) 350 (d)	190
Chain composition	(κ2μ2)5 or (λ2μ2)5	κ2δ2 or λ2δ2	κ2γ12 or λ2γ12	κ2γ22 or λ2γ22	κ2γ32 or λ2γ32	κ2γ42 or λ2γ42	(κ2α12)1-2 or (λ2α12)1-2	(κ2α22)1-2 or (λ2α22)1-2	κ2ε2 or λ2ε2
Functional valency	5 or 10	2	2				2 or 4		2
Structure (2)	monomer (mb) pentamer (s)	monomer	monomer				monomer (mb) dimer (s)		monomer
Interchain disulphide bonds per monomer	1	1	2	4	11	2	2		1
Other chain	J chain (16 kDa)	-	-				J chain (16 kDa) SC secretory component (70 kDa)		-
Sedimentation coefficient in Svedberg unit (S)	18-20	7	6.5-7.0				7, 10, 13, 15, 17		7.9
Carbohydrate average (%)	10-12	9-14	2-3				7-11		12-13
Adult level range (age 16-60) in serum (g/L) (3)	0.25-3.1	0.03-0.4	5-12	2-6	0.5-1	0.2-1	1.4-4.2	0.2-0.5	0.0001-0.0002
			8.0-16.8						
Approximate % total IG in adult serum	10	0.2	45-53	11-15	0.03-0.06	0.015-0.045	11-14	1-4	0.004
Synthetic rate (mg/kg Weight/day)	3.3	0.2	33	33	33	33	19-29	3.3-5.3	0.002
Biological half-life (day)	5-10	0.4	21-24	21-24	7-8	21-24	5-7	4-6	1-5
Transplacental transfer	0	2-8	++	+	++	++	0	0	0
Complement activation classical pathway (C1q)	+++	0	+++	+	+++	0	0	0	0
Complement activation alternative pathway	0	0	0	0	0	0	+	0	0
Binding macrophages and other phagocytic cells (FcγR or FCGR) (4)	0	+	+++	+/-	+++	+/-	0	0	0
Binding to mast cells and basophils (FcεR or FCER)	0	0	0	0	0	0	0	0	+++
Binding to epithelial poly-IG receptor	+	0	0	0	0	0	+++	+++	0
Reactivity with <i>Staphylococcus</i> protein A	0	0	++	++	0	++	0	0	0

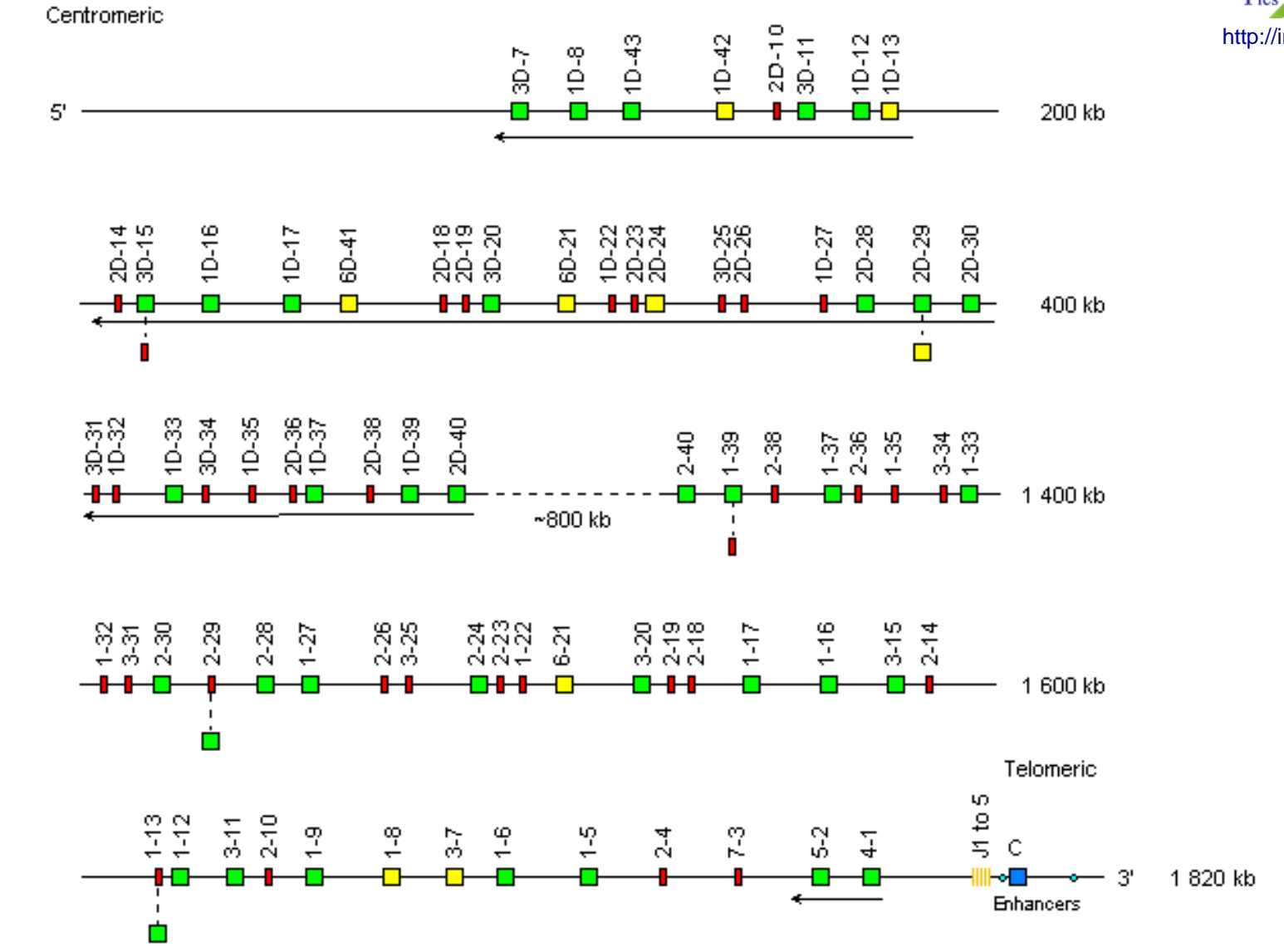
Human IGH locus

Chromosome
14q32.33



Human IGK locus

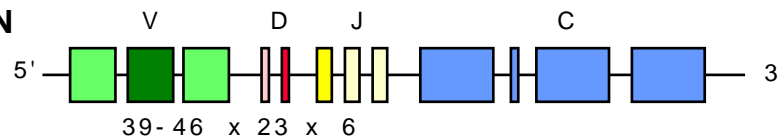
Chromosome 2p11.2



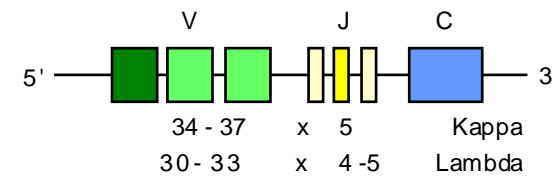
Immunoglobulin (IG) synthesis

150
FUNCTIONAL IG GENES

HEAVY CHAIN



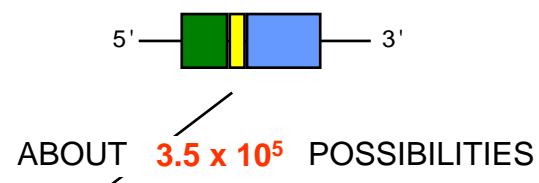
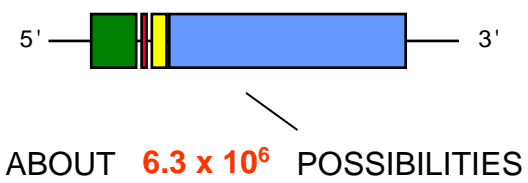
LIGHT CHAIN



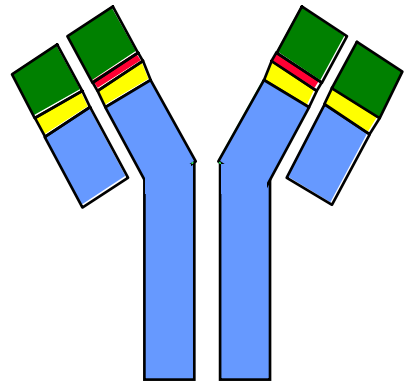
6300 **POTENTIAL RECOMBINATIONS**

185 + 165 **POTENTIAL RECOMBINATIONS**

**N-DIVERSITY
SOMATIC MUTATIONS
x 1000**



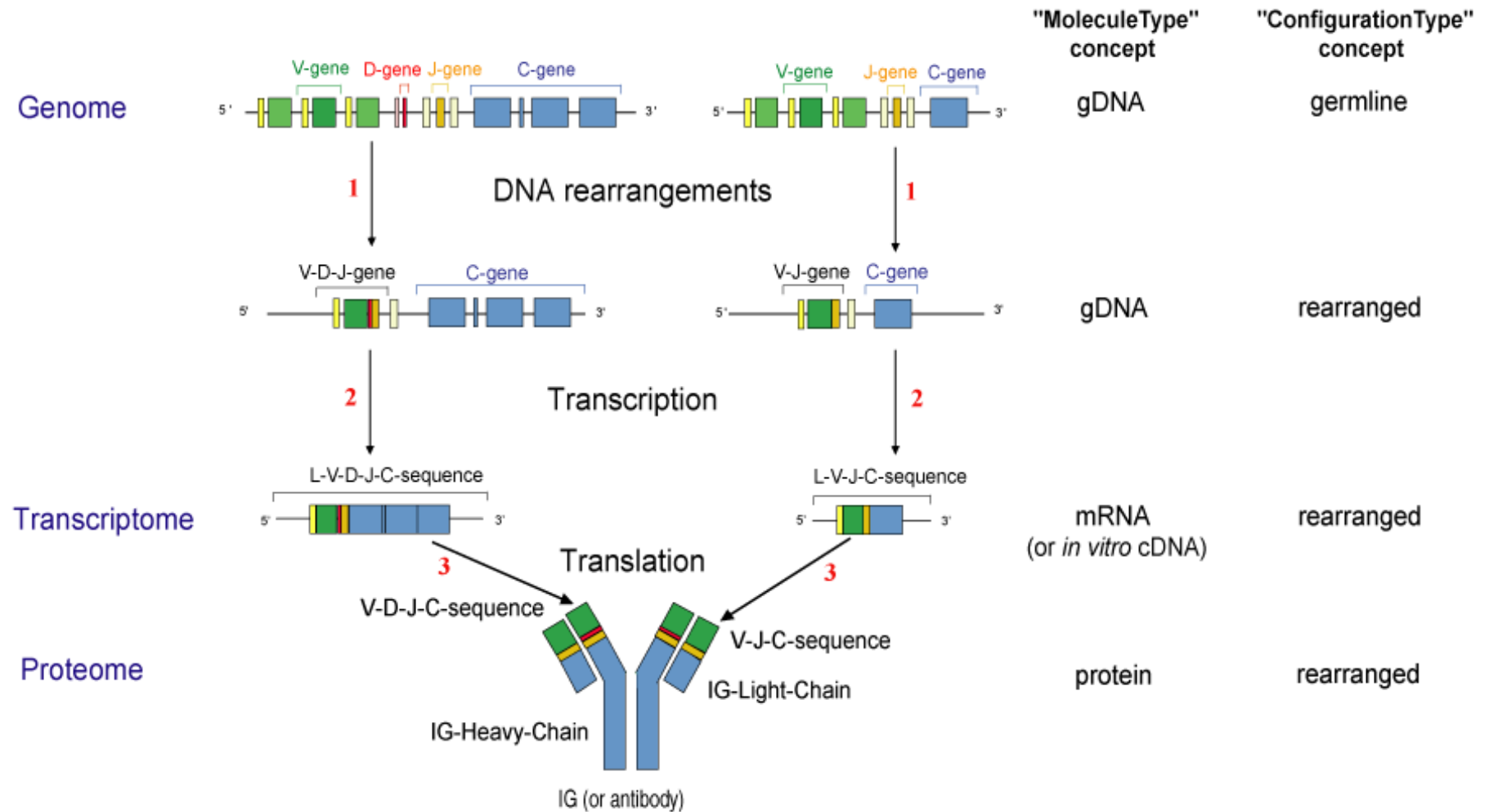
2×10^{12}
DIFFERENT ANTIBODIES



(IMGT label)

Immunoglobulin (IG) synthesis

IMGT-ONTOLOGY



Structure des Gènes



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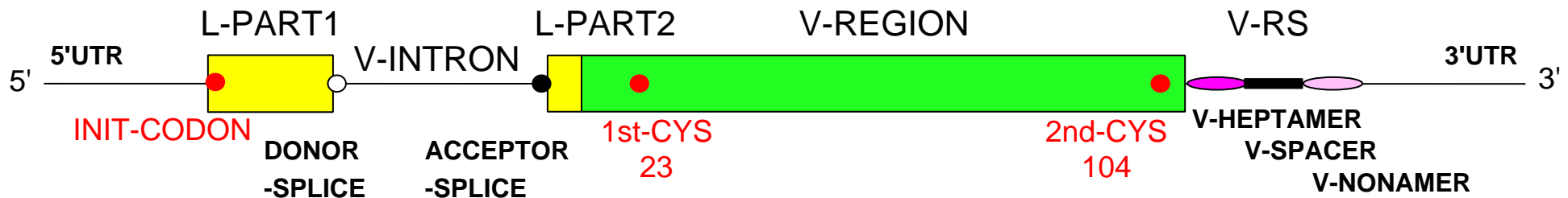
Genomic DNA in germline configuration

V-GENE

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

```

tgagagctcc gttcctcacc atggactgga cctggaggat cctcttcttg gtggcagcag      60
ccacaggaa gaggctcctt agtcccagtg atgagaaaga gattgagtcc agtccagggg      120
gatctcatcc acttctgtgt tctctccaca ga ggagcccact ccaggtgca gctggtgcag      180
tctggggctg aggtgaagaa gcctggggcc tcagtgaagg tctcctgcaa ggcttctgga      240
tacaccttca ccggctacta tatgcactgg gtgcgacagg ccctggaca agggcttgag      300
tggatgggat ggatcaacc taacagtggg ggcacaaact atgcacagaa gtttcagggc      360
agggtcacca tgaccagggg cacgtccatc agcacagcct acatggagct gagcaggctg      420
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tgagggtgtc agaaacccaa gggaggaggg ag
    
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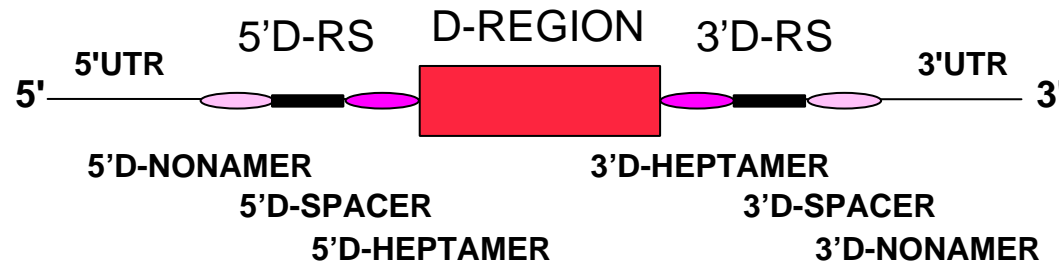
Genomic DNA in germline configuration

D-GENE

>J00256|IGHD7-27*01|*Homo sapiens* D-GENE

ccagccgcag ggtttttggc tgagctgaga ac cactgtgc taactgggga cacagtgatt
ggcagctcta caaaaaccat gctccccgg g

60



J-GENE

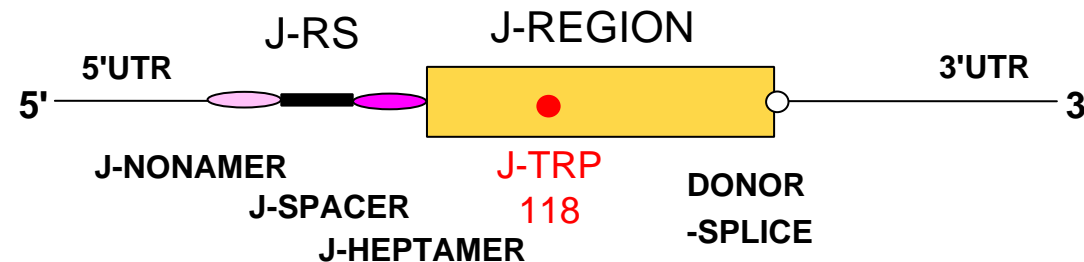
>J00256|IGHJ1*01|*Homo sapiens* J-GENE

accccggtt gtgggtttct gtgccctgg ctcagggtg actcaccgtg gctgaatact
tccagcactg gggccagggc accctgggtca ccgtctcctc aggtgagtct gctgtactgg
ggatagcggg gagccatgtg tactgggcca agcaagggtc ttggcttcag

60

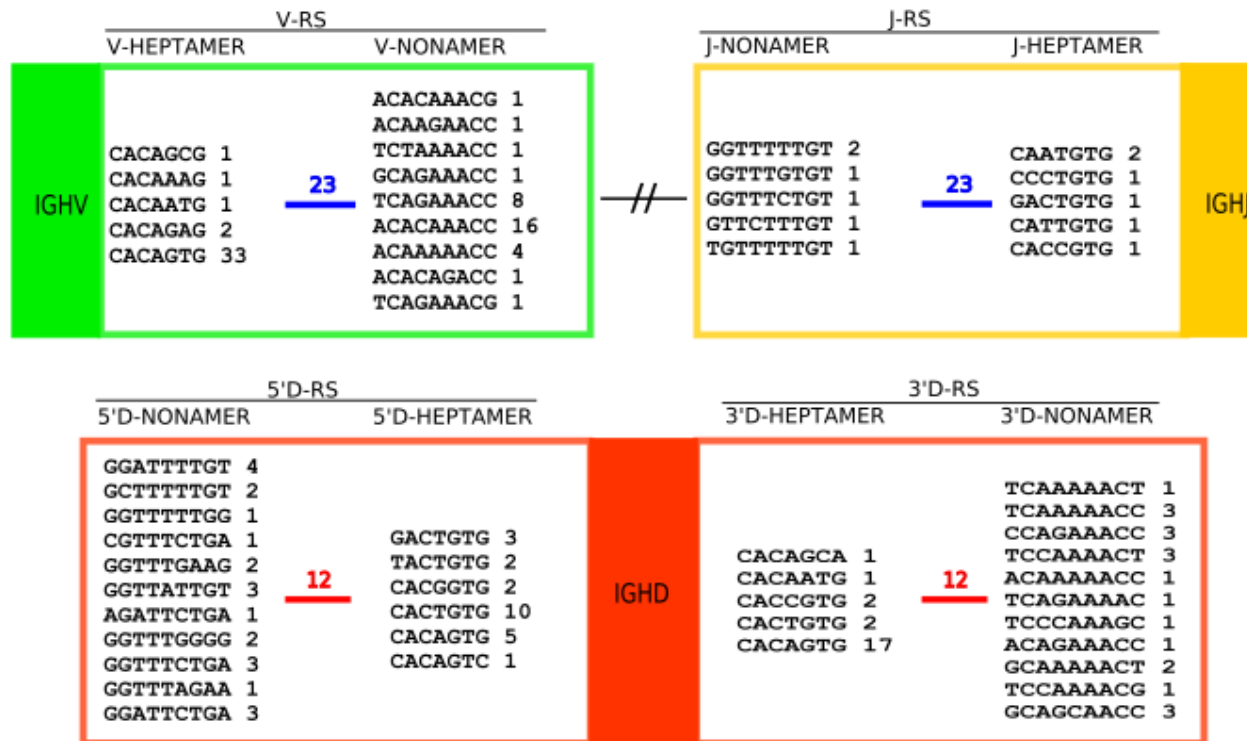
120

170

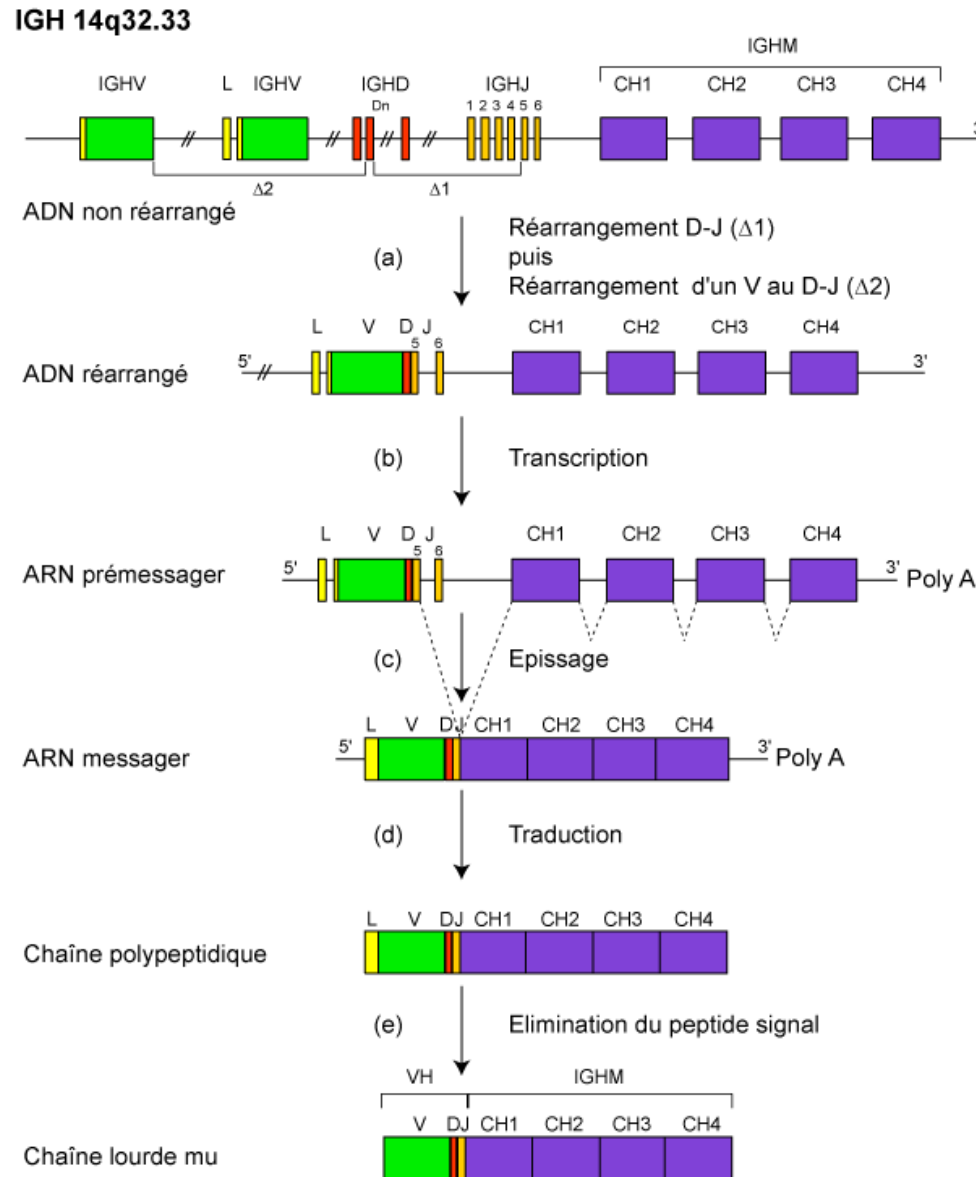


Signaux de recombinaison des IGH

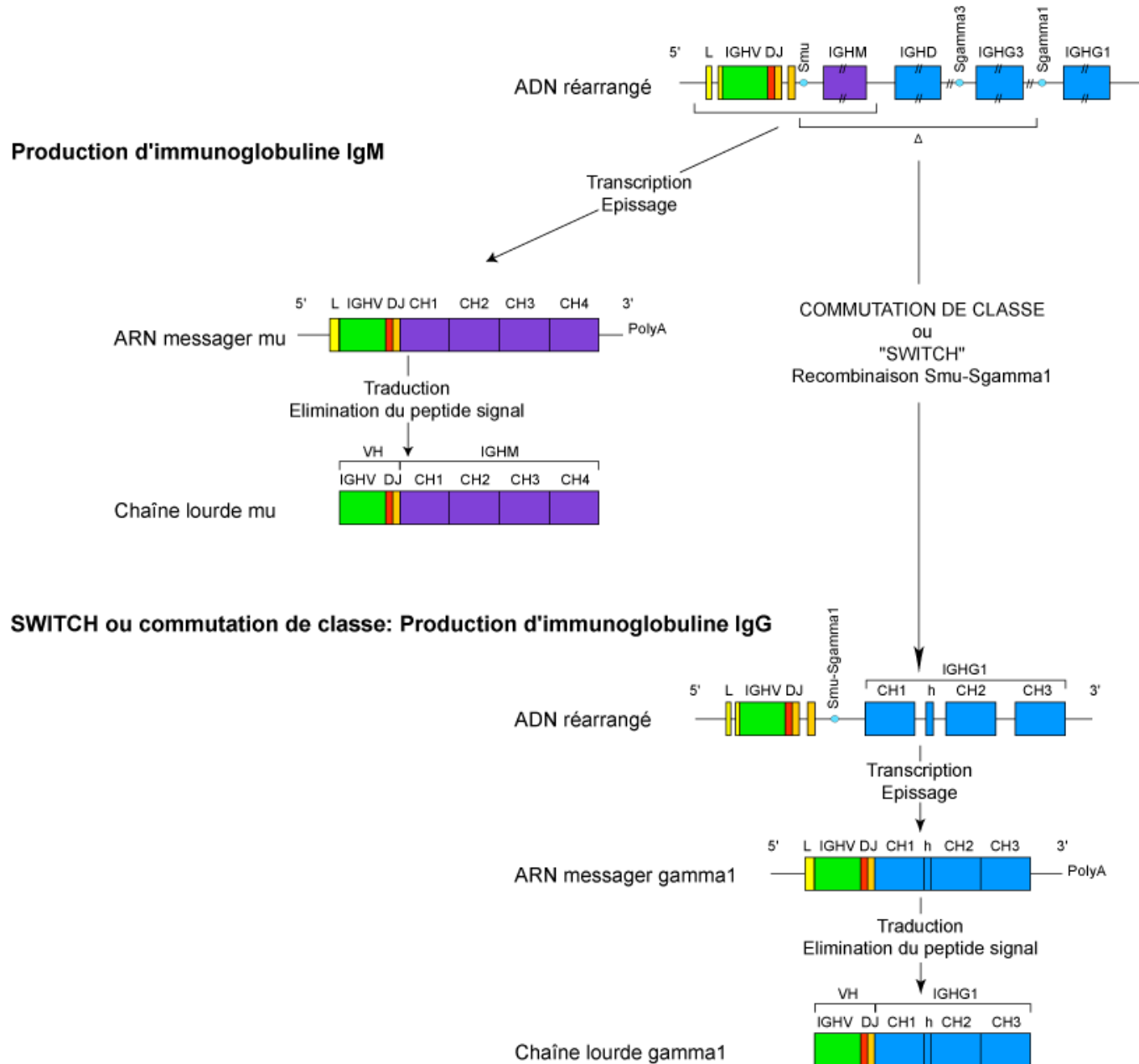
IGH (14q32.33)



Synthèse d'une chaîne lourde mu d'immunoglobuline



Commutation de classe IgM-IgG : recombinaison Smu-Sgamma



Sites de polyadenylation (ou Poly(A))

Poly(A) signal : POLYA_SIGNAL (IMGT label)

Motif conservé : AATAAA

Les signaux de polyadenylation sont localisés en aval des exons 3'.

Poly(A) site : POLYA_SITE (IMGT label)

The POLYA_SITE est le site of clivage où le POLYA_TAIL is rajouté dans l'ARNm. Il peut être déterminé en comparant l'ADNc et l'ADNg.

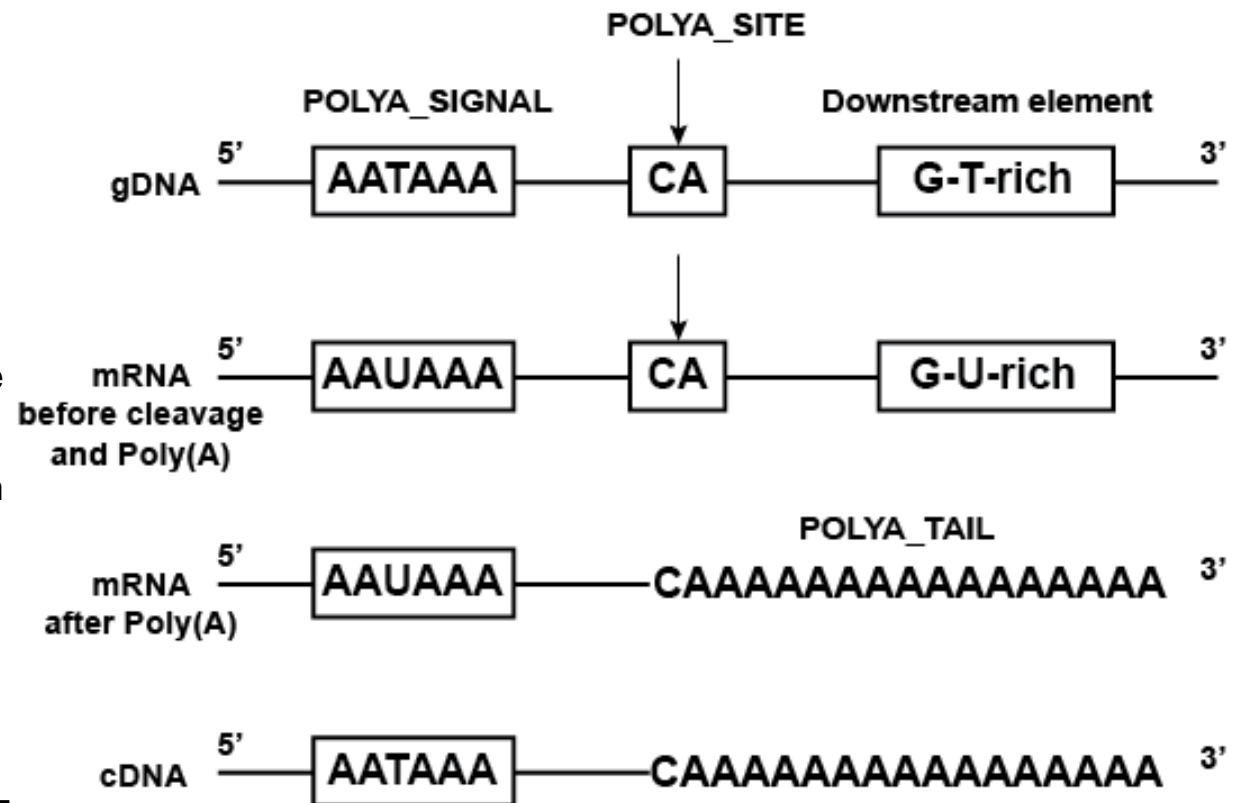
La séquence en 5' du site de clivage sur l'ARNm est souvent CA.

Poly(A) queue : POLYA_TAIL (IMGT label)

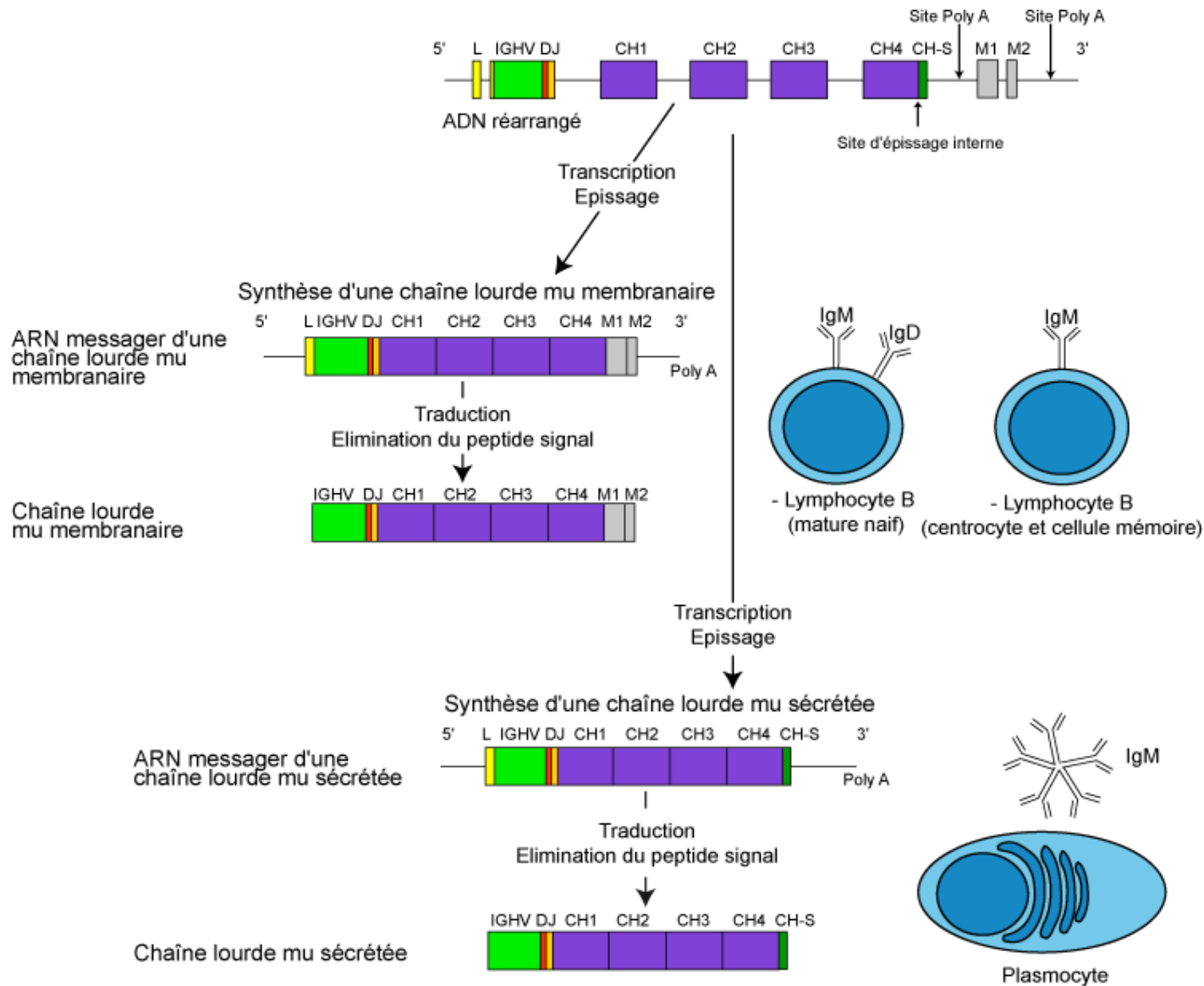
Stretch d'adenosine monophosphate en 3'

Un POLYA_SIGNAL situé en aval de l'exon **CH3-CHS** de l'IGHG3 humain est utilisé pour la transcription des chaînes sécrétées.

Un POLYA_SIGNAL situé en aval de l'exon **M2** de l'IGHG3 humain est utilisé pour la transcription des chaînes membranaires.



Synthèse d'une chaîne lourde mu membranaire (lymphocyte B) et d'une chaîne lourde mu sécrétée (plasmocyte)



cDNA

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..... .gagga ttcaccatgg aactggggct ccgctgggtt ttccttggtg cttttttaga 120
aggtgtccag tgtgaggtgc aactgggtgga gtctggggga ggctgggtca agccgggggg 180
gtccctgaga ctctctgtg cagcctctgg attaagcttc agtacctatg cdatgaadtg 240
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