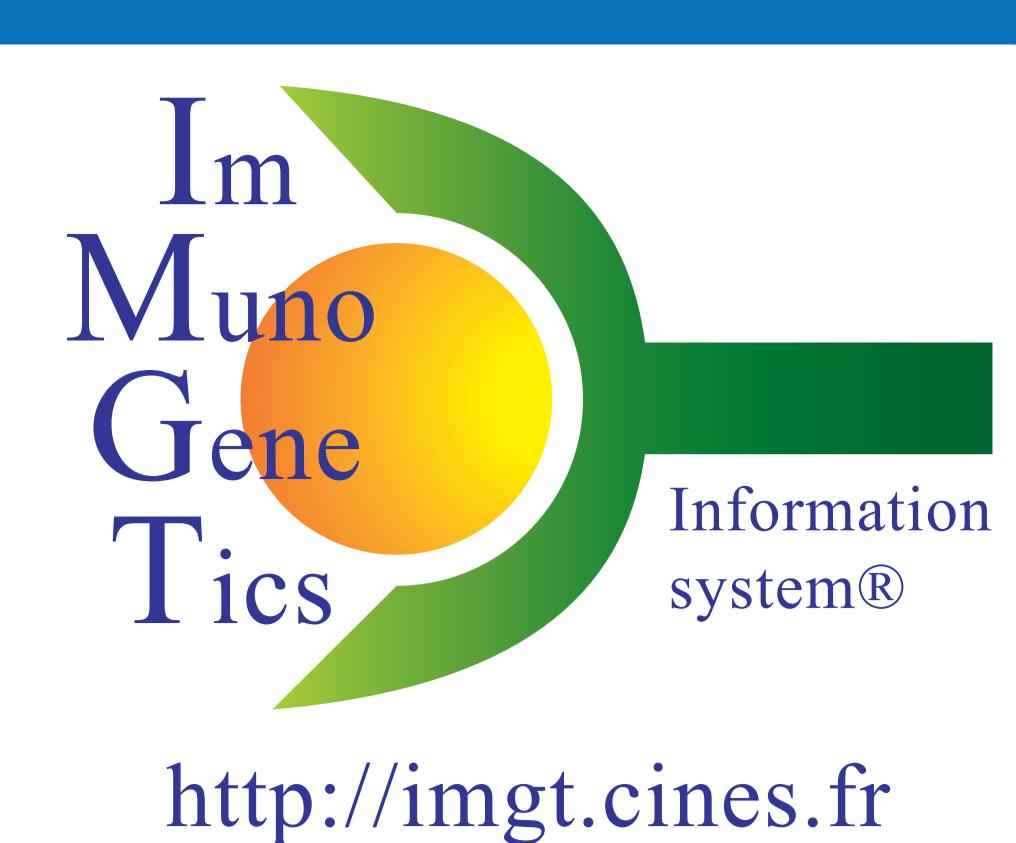


IMGT® resources for cancer research

Giudicelli V, Wu Y, Kaas Q, Brochet X, Lane J, Folch G, Jabado-Michaloud J, Regnier L, Ehrenmann F, Bellahcene F, Lucas O, Gemrot E, Ginestoux C, Lefranc G, Duroux P, Lefranc M-P

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<http://imgt.cines.fr>

IMGT®, the international ImMunoGeneTics information system® is the international reference in immunogenetics and immunoinformatics [1]. IMGT® provides a high quality integrated knowledge resource, specialized in immunoglobulins (IG), T cell receptors (TR), major histocompatibility complex (MHC) of human and other vertebrates, and related proteins of the immune system (RPI), which belong to the immunoglobulin superfamily (IgSF) and to the MHC superfamily (MhcSF). IMGT® includes six databases, Web resources which consist of more than 10,000 HTML pages, and fifteen interactive tools. The accuracy and the consistency of the IMGT® data are based on IMGT-ONTOLOGY, the first ontology for immunogenetics and immunoinformatics. IMGT® components are of a particular interest in cancer research as they provide international standards, for example in the analysis of IG and TR in lymphomas and leukemias, and standardized criteria for antibody humanization and engineering of therapeutic recombinant monoclonal antibodies.

1

IMGT/GENE-DB database

provides an easy and common access to the variable (V), diversity (D), joining (J) and constant (C) IG and TR genes and alleles [2]. Human IMGT gene names were approved in 1999 by the HUGO nomenclature committee (HGNC) and by the World Health Organization-International Union of Immunological Societies (WHO-IUIS) [3]. The IMGT gene nomenclature is based on the CLASSIFICATION axiom and concepts of IMGT-ONTOLOGY [4].

IMGT gene name and definition

IMGT gene name: Homo sapiens IGHV3-21
IMGT gene definition: Immunoglobulin heavy variable 3-21

Chromosomal localization

Locus name: Homo sapiens IGH locus
Chromosome: 14
Chromosomal localization: 14q32.33

Number of alleles: 2

IMGT reference alleles

| IGHV3-21 allele name | Gene functionality | R | T | Pr | IMGT/LIGM-DB reference sequences | | |
|----------------------|--------------------|---|---|----|----------------------------------|-------------------|---------------|
| | | | | | Clone names | Accession numbers | Molecule type |
| IGHV3-21*01 | F | + | + | + | - | AB019439 | gDNA |
| IGHV3-21*02 | F | | | | V3-21 | M99658 | gDNA |

IMGT/GENE-DB reference sequences (in FASTA format) for the allele(s): IGHV3-21*01, IGHV3-21*02

- Nucleotide sequences with gaps according to the IMGT unique numbering
- Amino acid sequences with gaps according to the IMGT unique numbering
- Nucleotide sequences without gaps
- Amino acid sequences without gaps

Other sequences from the literature (compiled in IMGT Gene tables, IMGT Repertoire)

| IGHV3-21 allele names | Gene functionality | R | T | Pr | IMGT/LIGM-DB sequences from the literature | | |
|-----------------------|--------------------|---|---|----|--|-------------------|---------------|
| | | | | | Clone names | Accession numbers | Molecule type |
| IGHV3-21*01 | F | + | + | + | WLG16 | X62127 | gDNA |
| | | | | | HKG4 | X62129 | gDNA |
| | | | | | DP-77 | Z14073 | gDNA |

IMGT Repertoire links

| Locus and genes | Proteins and alleles | 2D and 3D structures | Probes and RFLP | Gene regulation and expression | Genes and clinical entities |
|---|---|--|-----------------|--------------------------------|--|
| Gene table Chromosomal localization Protein display | Alignment of alleles Table of alleles Protein numbering | FR-IMGT and CDR-IMGT lengths Collier de Perles (IMGT) | Phages | cDNA | Translocations and inversions Translocations and inversions |

Known IMGT/LIGM-DB cDNA sequences for *Homo sapiens* IGHV3-21

D83686 L02260 L02260 L28051 L28051 L28051 L28051 L00508 U00572 U06787 U21270 U43754 U64497 U77372 U81383 U95238 X61023 X61235 X79168 X97554 X96932 X98933 X98934 X98935 X98936 X98937 X98938 X98939 X98944 X98945 X98946 X98947 X98948 X98950 X98952 X98954 X99354 X99362 Y19334 ...

External links

HGNC Genew: 5586 NCBI Entrez Gene: 28444 GDB: GDB:9931690 GenAtlas: 26448 GeneCards: IGHV3-21

An IMGT/GENE-DB entry provides a full characterization of a gene and of its alleles with expertly annotated data (definition, localization, reference sequences, functionality...) and external links to HGNC Genenew, Entrez Gene, GDB, GenAtlas, GeneCards, and OMIM.

3 IMGT/Collier-de-Perles tool

can display the V-DOMAIN [9] according to the IMGT unique numbering [10] on one or two layers, colored with the VH or VL coloring of the CDR-IMGT, and with the IMGT amino acid physicochemical classes [8] for the FR-IMGT.

Domain type: Variable (V)

Number of layers: 1

CDR-IMGT color type: 2 (GKJLRLTRG)

Background color: IMGT 80% basic classes

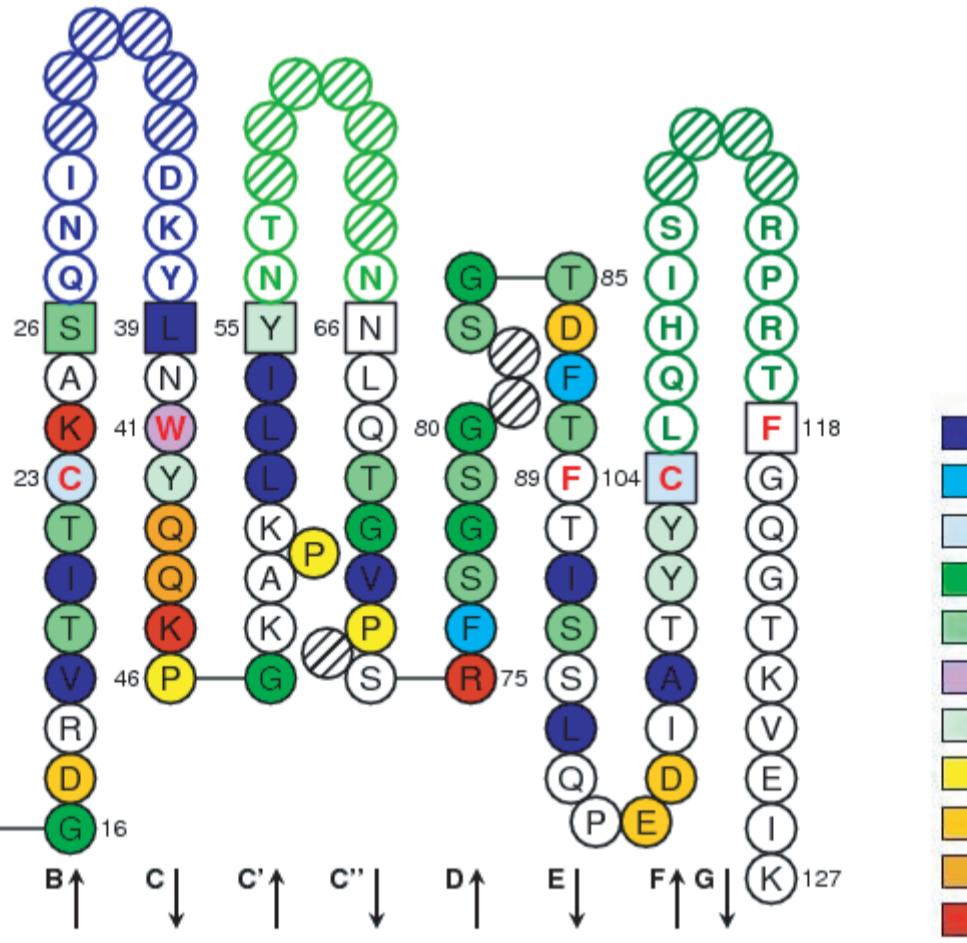
Domain sequence: D1Q1P1S1S1L1S1A1V1R1Y1K1N1D1M1Y1L1V1C1S1P1T1W1F1

Amino acid insertions: Position, Length, Numbering labels

CDR-3-IMGT length: 9

Your domain title:

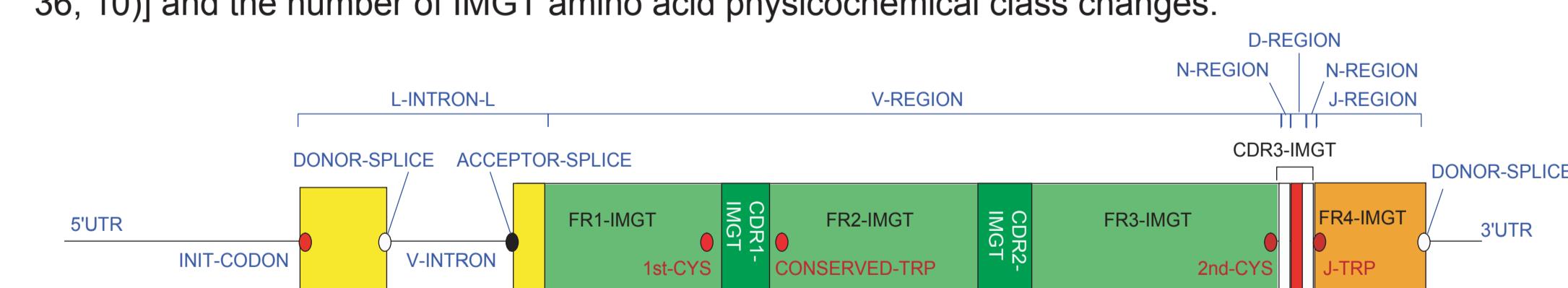
Domain:



5 The IMGT unique numbering

allows the standardized comparison of V domain sequences for antibody humanization [12].

A standardized comparison of V domain sequences for antibody humanization includes the delimitation of the FR-IMGT and CDR-IMGT, the determination of the CDR-IMGT lengths (e.g. [8.8.13]), the percentage of identity between FR-IMGT [calculated on 91 amino acids for VH (FR1-, FR2-, FR3-, FR4-IMGT: 25, 17, 38, 11) and 89 for V-Kappa (FR1-, FR2-, FR3-, FR4-IMGT: 26, 17, 36, 10)] and the number of IMGT amino acid physicochemical class changes.



| V-DJ-REGION | FR1-IMGT | FR2-IMGT | FR3-IMGT | FR4-IMGT | Total |
|-------------------|----------|----------|----------|----------|-------|
| VH (V-D-J-REGION) | 25 | 17 | 38 | 11 | 91 |
| VL (V-J-REGION) | 26 | 17 | 36 | 10 | 89 |

Humanized antibodies used in oncology [12]

| Humanized antibody | CDR-IMGT antibody | Closest <i>Homo sapiens</i> gene and allele | FR-IMGT identity | AA with IMGT class change |
|--------------------|-----------------------|---|------------------|---------------------------|
| VH | alemtuzumab [8.10.12] | IGHV4-59*01 | 84.61% (77/91) | 2 |
| | bevacizumab [8.8.16] | IGHV7-4-1*02 | 74.72% (68/91) | 1 |
| | trastuzumab [8.8.13] | IGHV3-66*01 | 90.10% (82/91) | 0 |
| VL | alemtuzumab [6.3.9] | IGKV1-33*01 | 97.75% (87/89) | 1 |
| | bevacizumab [6.3.9] | IGKV1-33*01 | 92.13% (82/89) | 2 |
| | trastuzumab [6.3.9] | IGKV1-39*01 | 93.25% (83/89) | 1 |

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