IMGT databases (IMGT/3Dstructure-DB, IMGT/mAb-DB...) and IMGT tools (IMGT/DomainGapAlign and IMGT/Collier-de-Perles for amino acid sequences, IMGT/V-QUEST for nucleotide sequences) provide a standardized way to compare immunoglobulin sequences and to delimit the FR-IMGT and CDR-IMGT in the process of antibody humanization and engineering, whatever the chain type (heavy and light) and whatever the species (e.g. murine and human) [1-3]. Indeed these databases and tools, as the IMGT Web resources, are based on the IMGT-ONTOLOGY concepts of classification (IMGT gene and allele nomenclature approved by HGNC and WHO-IUIS), of description (IMGT labels), and of numerotation (IMGT unique numbering for V-DOMAIN). The comparison between V domain sequences includes determination of the CDR-IMGT lengths (shown between brackets and separated with dots, e.g. [8.8.13]), percentage of identity between FR-IMGT and evaluation of the number of IMGT physicochemical class changes. The IMGT information system, based on the IMGT-ONTOLOGY concepts of CLASSIFICATION and DESCRIPTION, provides an invaluable help for the analysis of recombinant antibody sequences and further characterization of specificity or potential immunogenicity.

1] Lefranc M.-P. Mol. Biotechnol. 40, 101-111 (2008) 2] Lefranc M.-P. et al. Nucleic Acids Res 37, D1006-1012 (2009) 3] Ehrenmann F. et al. Nucleic Acids Res 38: January Database issue (2010)

The IMGT unique numbering and IMGT tools provide the delimitations of the FR-IMGT and CDR-IMGT for the analysis of antibody paratope or loop grafting in antibody engineering.

The IMGT databases and tools based on the IMGT-ONTOLOGY concepts bridge the gap between sequences and 3D structures facilitating the analysis of antibody/antigen interactions.

IMGT/3Dstructure-DB and IMGT/DomainGapAlign for antibody engineering and humanization

François Ehrenmann, Yan Wu, Chantal Ginestoux, Véronique Giudicelli, Patrice Duroux and Marie-Paule Lefranc

IGKV1-33*01

V-REGION alignment according to the IMGT unique numbering

IMGT/V-QUEST

IMGT®, the international ImMunoGeneTics information system®, LIGM, Université Montpellier 2 CNRS UPR1142, IGH, 141 rue de la Cardonille, 34396 MONTPELLIER cedex 05, France Marie-Paule.Lefranc@igh.cnrs.fr



http://www.imgt.org

IMGT® is funded by the Centre National de la Recherche Scientifique (CNRS), the Ministère de l'Enseignement Supérieur et de la Recherche,
Université Montpellier 2. Agence Nationale de la Recherche BIOSYS (ANR-06-BYOS-0005-01) and the European ImmunoGrid project (IST-2004-0280069

MGT founder and director: Marie-Paule Lefranc (Marie-Paule, Lefranc@igh, cnrs.fr)

V-REGION most frequently occurring AA per position and per FR-IMGT and CDR-IMGT

Analysis of antibody amino acid sequences:

Paste your domain sequences in FASTA format. Select "V" for sequences of the variable domains of the light and heavy chains. Select "C" for sequences of the constant domains of the light and heavy chains. To defirnt the domains (CH1, CH2, CH3) of the heavy chains, an easy way is to check with IMCT Alignments of alleties (in IMCT Repetroles). Select the number of alignments to displays.



asize name of the closed sequence(s) from the IMC i reference directory is (sele) provided with a peticentage of identity. For instance, the VFGCIMON of the alterium/and bornals are identified as having 7.3 via 468.25.2 visiteffly with the Homo aspiens IGHV4-9501 and IGKV1-3301, respectively. The constant domain of the light drash has 100% identify with Homo aspiens IGKC*01. The combined results of CH1 and CH3 of the heavy chain identifies the Homo aspiens IGHS*011 (CH1: K120, CH3: CH2, CH4) (there is no amino acid difference with IGHS*1'02). IGHS*0112 with other been characterized by CH1: K120, CH2, ETM, M1.

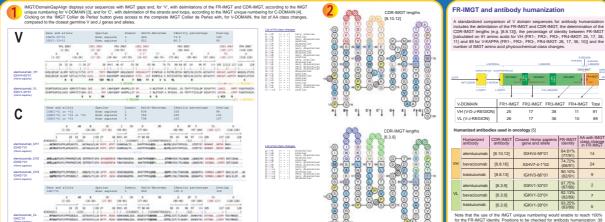
were approved by the HUGO Nomenclature Committee (HGNC) and by the WHO-IUIS Nomenclature Committee [2]. They are used by Entrez Gene (NCBI), GDB, GeneCards, Ensembl (EBI)...

IMGT/DomainGanAlinn identifies the closest nermine V-REGION (for 'V') and the closest C-DOMAIN (for 'C'). The IMGT gene and

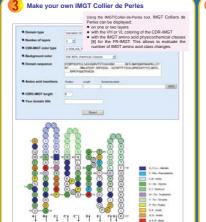
IMGT nomenclature is based on the CLASSIFICATION axiom and concepts of IMGT-ONTOLOGY [1]. IMGT gene and allele names

Dur One Nature

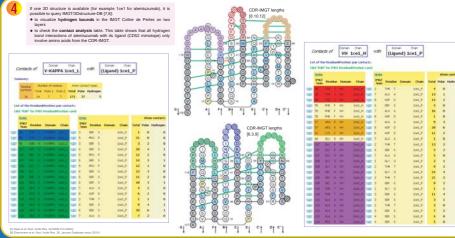
IMGT/DomainGapAlian



IMGT/Collier-de-Perles



IMGT/3Dstructure-DB contact analysis



Analysis of antibody nucleotide sequences:

The nucleotide sequences are analysed with IMGT/V-QUEST and IMGT/.hunctionAnalysis ne mulcebooks sequences are analyses with not in Y-QUES i and not in Indianovalysis.

MIGTIV-QUES indentifies the sequences with the closest gene and siles in the MIGT seference directory, displays the nucleotide and protein alignments according to the MIGT unique numbering and provides an extensive analysis analysis and residence of the mutations [9].

MIGT/JunctionAnalysis analyses accurately the junctions of artibody rearranged sequences (IGF) genes and afelies, N- and

IMGT/V-QUEST QUERY 12 C Separate of V. V.L. or V.D.L. SERION Of and Mrivellings in FASTS Access to MITH Transfers to 2 FESSION OF Your relection: Human Nucleotide requences





1. Result summary

B. Synthesis for the IMGT/V-QUEST analysed sequences

- Alignment for V-GENE V-REGION alignment according to the IMGT unique numbering - V-REGION translation @ - V-REGION protein display 6 · V-REGION protein display (with color) Other requite include: - V-REGION most frequently occurring AA 6 · Results of IMGT/JunctionAnalysis 6

IMGT/JunctionAnalysis

