Correlation between IMGT® Biocuration, IMGT/LIGM-DB and IMGT/GENE-DB

Géraldine Folch*, Joumana Michaloud*, Marine Peralta, Mélanie Arrivet, Imène Chentli, Mélissa Cambon, Pascal Bento, Patrice Duroux, Véronique Giudicelli, Marie-Paule Lefranc* and Sofia Kossida*

*Equal contribution

Université Montpellier and CNRS, Laboratoire d'ImmunoGénétique Moléculaire (LIGM), Institut de Génétique Humaine (IGH), UPR CNRS 1142, Montpellier (France)

http://www.imgt.org

IMGT®, the international ImMunoGeneTics information system®, http://www.imgt.org, has developed a biocuration pipeline for immunoglobulin (IG) and T cell receptor (TR) sequence annotation. The expert annotation and added standardized knowledge are based on the seven IMGT-ONTOLOGY axioms: IDENTIFICATION, CLASSIFICATION, DESCRIPTION, NUMEROTATION, LOCALIZATION, ORIENTATION and OBTENTION [1-3]. IMGT/LIGMotif is the tool for genomic DNA sequences analysis [4], and IMGT/Automat is the tool for automatic annotation of rearranged cDNA sequences [5, 6].

IMGT expert biocurators check the annotation tool results for consistency, both manually and by using IMGT® tools (IMGT/NtiToVald, IMGT/V-QUEST, IMGT/BLAST…). These annotated sequences are integrated in IMGT/LIGM-DB, the comprehensive and largest IMGT® database of IG and TR nucleotide sequences from human and other vertebrate species. For a given entry, nine types of display are available, including the IMGT flat file, the translation of the coding regions and the analysis by the IMGT/V-QUEST tool. They include the sequence identification, the gene and allele classification, the constitutive and specific motif description, the codon and amino acid numbering and the sequence obtaining information. IMGT/LIGM-DB annotations allow data retrieval not only from IMGT/LIGM-DB, but also from other IMGT® databases. The main source of IG and TR gene and allele knowledge is stored in IMGT/GENE-DB [7], the comprehensive IMGT® genome database and in the IMGT reference directory. IMGT/GENE-DB provides a search of IG and TR genes by locus, group and subgroup. An IMGT/GENE-DB entry displays accurate gene data related to genome, allelic polymorphisms, gene expression, proteins and structures. IMGT/GENE-DB manages the IMGT reference directory used by the IMGT tools for gene and allele comparison and assignment, and by the IMGT databases for gene data annotation. IMGT/GENE-DB is the official repository of all IG and TR genes and alleles, IMGT® gene and allele names have been approved by HGNC and endorsed by WHO/IUIS, the World Health Organization (WHO)/International Union of Immunological Societies (IUIS) Nomenclature Subcommittee for IG and TR. Reciprocal links exist between IMGT/GENE-DB and HGNC, NCBI, VEGA, GeneCards and GenAtlas.

IMGT® is used in very diverse domains: fundamental and medical research, veterinary research, repertoire analysis, biotechnology related to antibody engineering, diagnostics and therapeutical approaches.

[1] Giudicelli, V. and Lefranc, M.-P., Bioinformatics, 15, 1047-1054 (1999), [2] Giudicelli, V. and Lefranc, M-P, Front Genet, 3:79 (2012), [3] Giudicelli, V. and Lefranc, M.-P., Encycl Systems Biology, 964-972 (2013), [4] Lane L., Duroux P.,and Lefranc M.-P. BMC Bioinformatics, 11:223 (2010), [5] Giudicelli, V.et al. Stud. Health Technol. Inform, 116, 3-8 (2008), [6] Giudicelli V, Protat C, Lefranc M-P. Data and Knowledge Bases, Poster DKB_31, ECCB pp. 103–104 (2003), [7] Giudicelli V. et al. Nucleic Acids Res, 33, D256-261 (2005).

IMGT® Expert Biocuration Pipeline

IMGT Tools

Internally developped, proprietary IMGT® research tools:

IMGT/LIGMotif
Annotation of **genomic sequences** of immunoglobulin (IG) and T cell receptor (TR) loci.

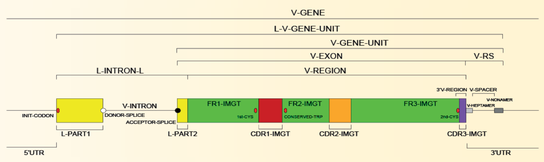
IMGT/Automat
Annotation of **cDNA sequences** of immunoglobulin (IG) and T cell receptor (TR) loci.

IMGT/NtiToVald
Automatical control of data for **consistency** and **relevance**

optimization — *efficiency/accuracy* — **IMGT expert biocurators** — *optimization* — *standardization*

IMGT-ONTOLOGY & Prototypes

1. IDENTIFICATION
2. DESCRIPTION
3. CLASSIFICATION
4. NUMEROTATION
5. LOCALIZATION
6. ORIENTATION
7. OBTENTION



Left: IMGT-ONTOLOGY axioms and concepts, bridge the gap between genes, sequences and three-dimensional structures. The concepts include the IMGT® standardized keywords (identification), labels (description) and nomenclature (classification), as well as IMGT unique numbering and IMGT Colliers de Perles (numerotation). IMGT-ONTOLOGY includes a controlled vocabulary and annotation rules which are indispensable to ensure accuracy, consistency and coherence in IMGT®.
Right: IMGT standardized labels for the description of prototypic V-GENEs.

IMGT/LIGM-DB

177 049 sequences
351 species

IMGT/LIGM-DB includes all germline (non-rearranged) and rearranged IG and TR genomic DNA and complementary DNA sequences published in generalist databases. IMGT/LIGM-DB allows searches from the Web interface according to biological and immunogenetic criteria. For a given entry, nine types of display are available including the IMGT flat file, the translation of the coding regions and the analysis by the IMGT/V-QUEST tool.
The annotations hugely enhance the quality and the accuracy of the distributed detailed information.

IMGT/GENE-DB

3 570 genes
5267 alleles
22 species

IMGT/GENE-DB Query Page allows the search of IG/TR genes according to IMGT-ONTOLOGY's seven axioms.
IMGT/GENE-DB entry displays accurate gene data related to genome (gene localization), allelic polymorphisms (number of alleles, IMGT reference sequences, functionality, etc.) gene expression (known cDNAs) and proteins structures (IMGT Colliers de Perles, IMGT/3Dstructure-DB). It provides internal links to the IMGT sequence databases and the IMGT Web resources as well as external links to genome and generalist sequence databases.

Web Resources

1 IMGT flat file

1 **IDENTIFICATION: Keywords**
genomic DNA=MoleculeType
germline=ConfigurationType
regular=StructureType
functional=Functionality
Homo sapiens=Taxon
Ig-Heavy-Mu=ChainType
variable=GeneType

2 **DESCRIPTION: Labels**
V-GENE=Entity
V-REGION=CoreRegion
FR1-IMGT=SubRegion
…

3 **CLASSIFICATION: Nomenclature**
IGHV=Group
IGHV3=Subgroup
IGHV3-66=Gene
IGHV3-66*04=Allele

4 **NUMEROTATION**
[8.7.2]=V-REGION CDR lengths
1 to 26, AA 10 is missing=AA IMGT numbering

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ID   X70208; SV 1; linear; gDNA; STD; HUM; 830 BP.
XX
AC   X70208; X68844;
XX
DT   15-MAY-1995 (Rel. 199520-1, arrived in LIGM-DB)
DT   31-MAR-2015 (Rel. 201514-2, Last updated, Version 19)
XX
DE   H.sapiens DNA for IgM heavy chain (MTGLa)                    1
XX
KW   antigen receptor; Immunoglobulin superfamily (IgSF); immunoglobulin (IG);
KW   IG-Heavy; IG-Heavy-Mu; variable; lymphoma; IMGT reference sequence;
KW   regular; gDNA; germline; functional; V-gene.
-----------------------------------------------------------------------
CC   IMGT/LIGM-DB annotation level: by annotators
XX
FH   Key             Location/Qualifiers
FH
FT   V-GENE      2   1..830
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FT                   /IMGT_gene="IGHV3-66"          3
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FT                   /mol_type="genomic DNA"
FT                   /organism="Homo sapiens"
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FT   L-PART1         292..337
FT                   /translation="MEFGLSWVFLVAILK"
FT   INIT-CODON      292..294
FT   DONOR-SPLICE    337..339
FT   V-INTRON        338..438
FT   ACCEPTOR-SPLICE 436..440
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FT                   R"
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FT                   /IMGT_gene="IGHV3-66"
FT   FR1-IMGT        450..524
FT                   /translation="EVQLVESGGGLVQPGGSLRLSCAAS"
FT                   /AA_IMGT="1 to 26, AA 10 missing"          4
-----------------------------------------------------------------------
FT   3'UTR           741..830
XX
SQ   Sequence 830 BP; 203 A; 202 C; 237 G; 188 T; 0 other;
     cctaaatgaa tatcaaggca caatcacata atataaaatt atatttcct gaatgatagg       60
     aatactacca atctcccccc aggagacttt catctgcact gggcccggcc ctctcctcag      120
     ctgtgtatta ctgtgcgaga cacacagtga gggaaggcca ttgtgcgccc agacacaaac      780
     cctcccctgca ggaacgctgg ggaaatcagc ggcagggggc gctcaggagc                830
//
```

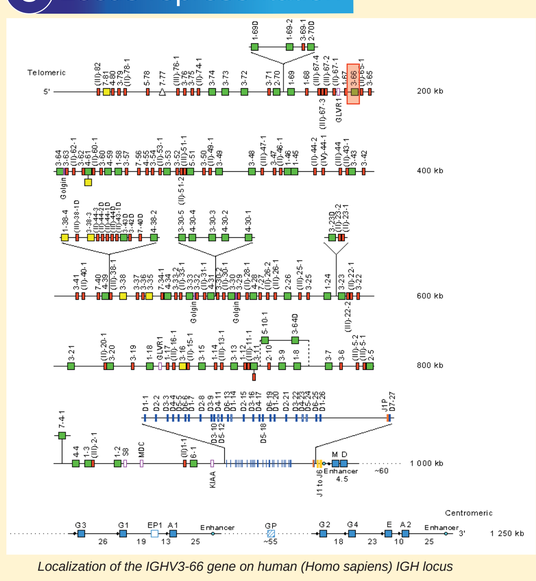
*Extracts from the IMGT Flat File X70208 with the IGHV3-66 gene and the IGHV3-66*04 allele.*

2 Gene table

IMGT/LIGM-DB reference sequences											IMGT/LIGM-DB sequences from the literature			
IMGT subgroup	IMGT gene name	IMGT allele name	Fct	Chromosomal localization	R	T	Pr	Positions in the locus	Clone names	Accession numbers	Positions in the sequence (from INIT-CODON to the end of V-REGION)	Secondary accession numbers	Clone names	Accession numbers	Positions in the sequence (from INIT-CODON to the end of V-REGION)
IGHV3	IGHV3-66	IGHV3-66*01	F	14q32.33	+	+	+		8-1B MAP	X92218 [6]					
		IGHV3-66*02	F	14q32.33	+				YAC-5 MAP	Z27504 [12]					
		IGHV3-66*03	F	14q32.33				155001-165000		AB019437 [61]	153482-158510		DP-86	Z27455 [65]	
													DA-9	Z29984 [12]	
		IGHV3-66*04	F	14q32.33						X70208 [50]					

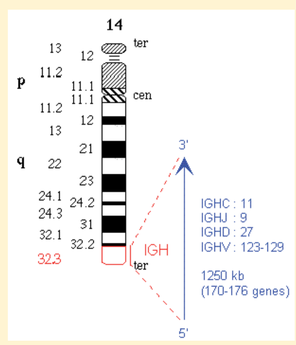
*Extract from IMGT Gene Table: human (Homo sapiens) IGHV. View on the IGHV3-66 gene and the IGHV3-66*04 allele.*

3 Locus representation



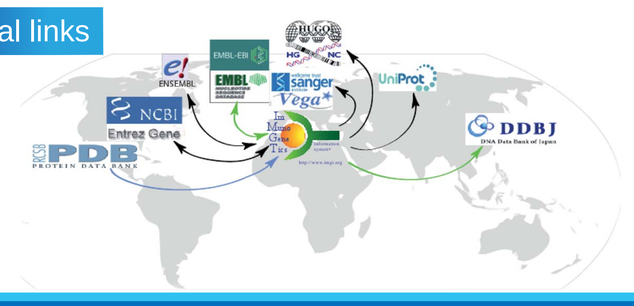
Localization of the IGHV3-66 gene on human (Homo sapiens) IGH locus

4 Chromosomal localization

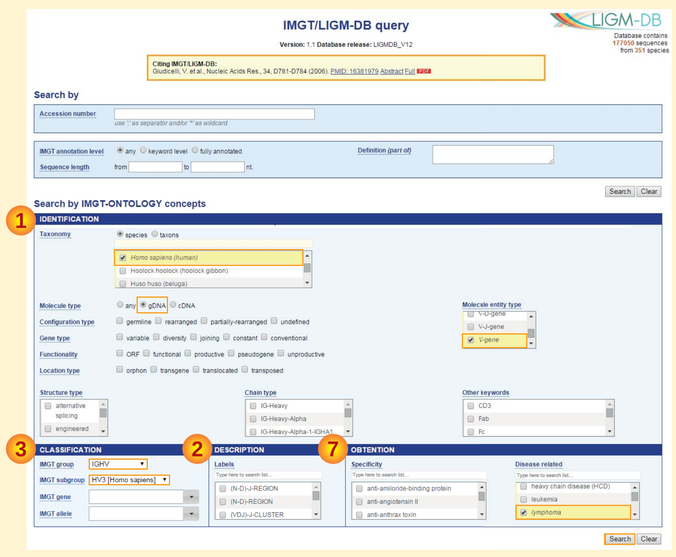


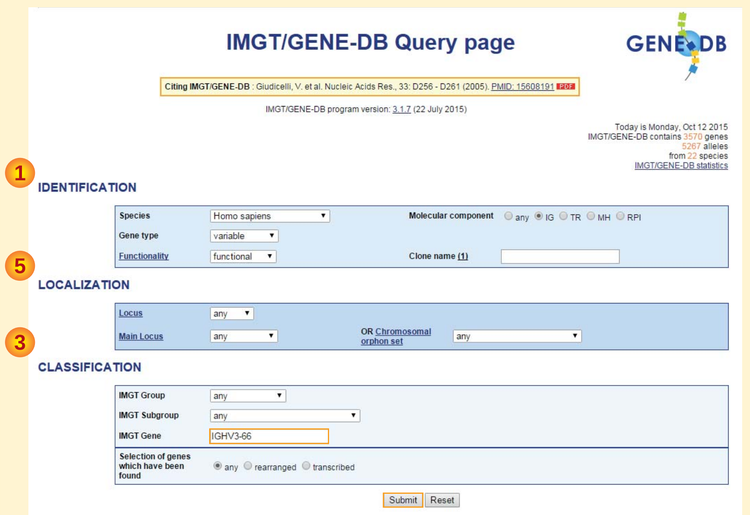
Localization of the human (Homo sapiens) IGH locus on chromosome 14 (14q32.33)

5 External links

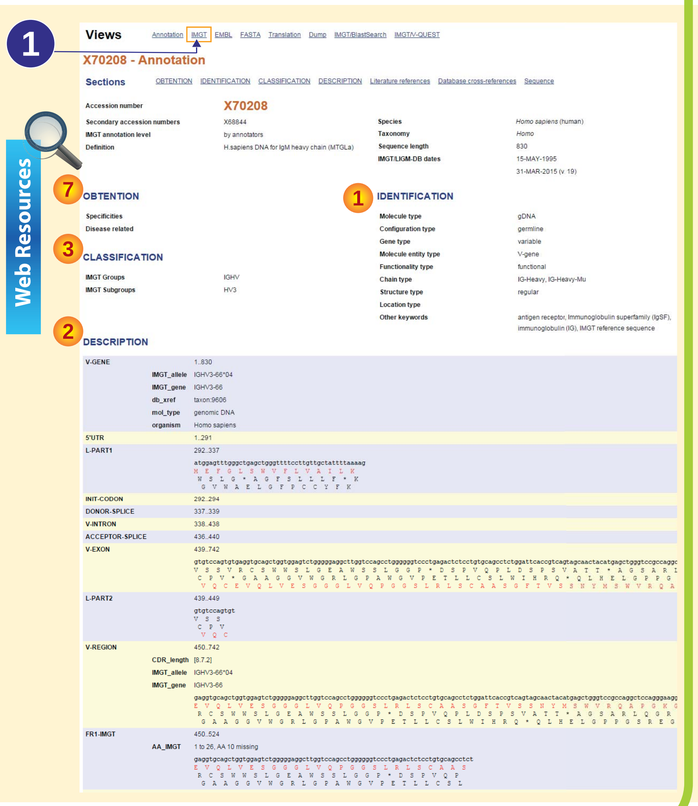


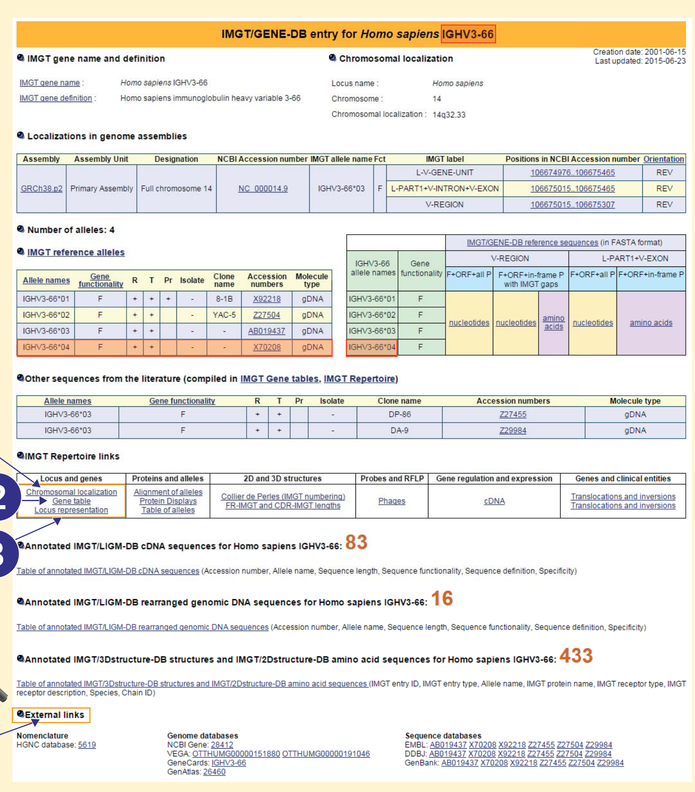
INTEROPERABILITY





WEB INTERFACE





APPLICATIONS

- Fundamental and medical research
- Genome diversity and genome evolution
- Structural evolution of the IgSF and MhcSF
- Veterinary research
- Biotechnologies related to antibody engineering
- Diagnostics
- Therapeutical approaches

IMGT® director: Sofia Kossida (Sofia.Kossida@igh.cnrs.fr)
IMGT® founder and executive director emeritus: Marie-Paule Lefranc (Marie-Paule.Lefranc@igh.cnrs.fr)
Bioinformatics manager: Véronique Giudicelli (Veronique.Giudicelli@igh.cnrs.fr)
Computer manager: Patrice Duroux (Patrice.Duroux@igh.cnrs.fr)