



MOLECULAR BASES OF HUMAN DISEASES

IMGT[®] - the international ImMunoGeneTics information systems[®]

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Our research activities are focused on molecular immunogenetics, immunoinformatics, bioinformatics and rare human genetic diseases. We are studying the genetics, structures, functions and repertoires of the immunoglobulins (IG) of B lymphocytes and plasmocytes, and of the T cell receptors (TR) on T lymphocytes, which are essential components of the adaptive (specific) immunity in humans and other vertebrates.

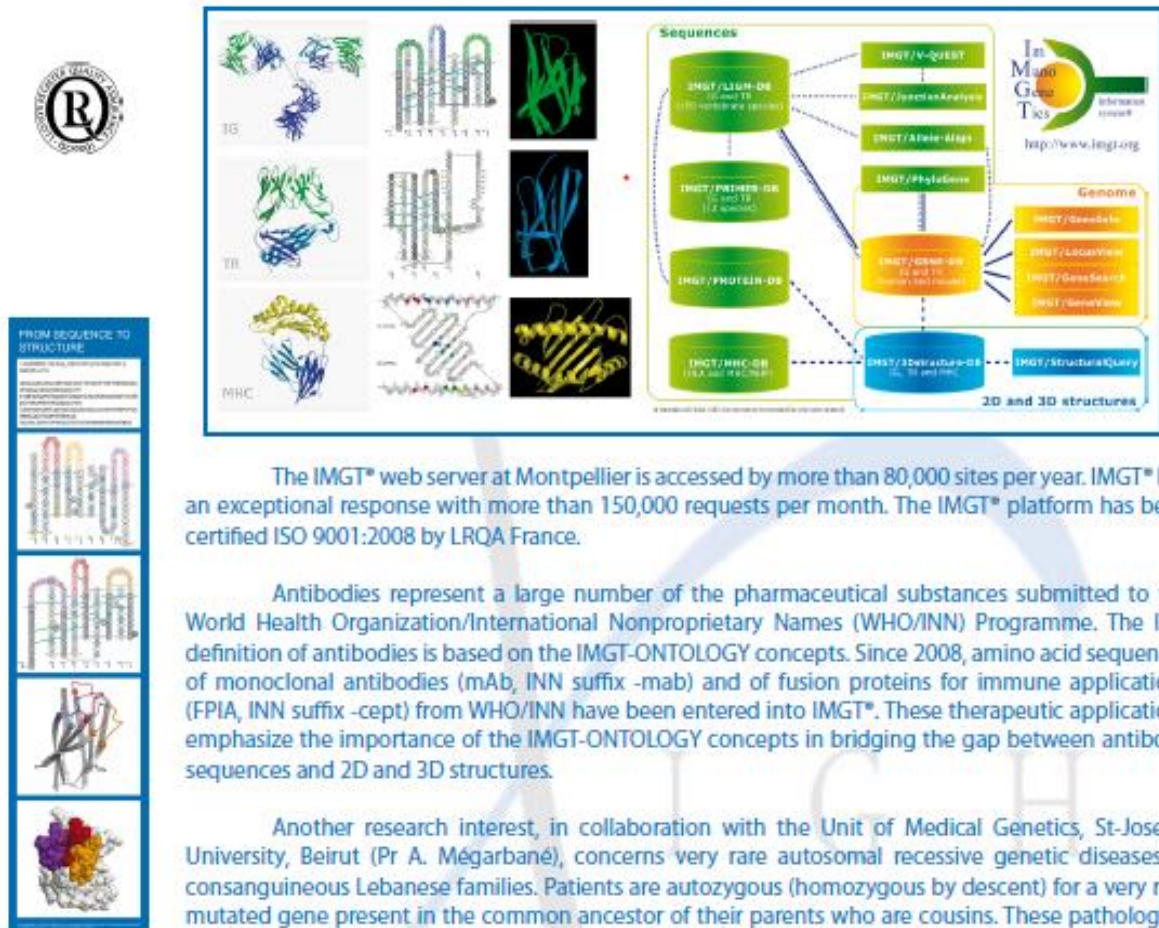
In 1989, we created IMGT[®], the international ImMunoGeneTics information system[®] (Montpellier 2 University and CNRS). IMGT[®], a CNRS registered trademark (EU, Canada and USA), is the global reference in immunogenetics and immunoinformatics.

This high-quality integrated knowledge resource is specialized in the IG, TR and major histocompatibility (MH) proteins of vertebrate species, and in the immunoglobulin superfamily (IgSF), MH superfamily (MhSF) and related proteins of the immune system (RPI) of any species. IMGT[®] provides a common access to expertly annotated nucleotide and protein sequences, structural data and genetic information. IMGT[®] includes six databases (IMGT/LIGM-DB, a comprehensive database of more than 150,000 IG and TR sequences from human and 260 other vertebrate species in November 2010; IMGT/GENE-DB, IMGT/PRIMER-DB, IMGT/2Dstructure-DB, IMGT/3Dstructure-DB and IMGT/mAb-DB), fifteen interactive tools and more than 15,000 pages of web resources. IMGT/HighV-QUEST analyses Next-Generation Sequencing (NGS) High-throughput IG and TR sequencing data by batch of up to 150,000 sequences.

IMGT/DomainGapAlign is widely used for antibody engineering and design of humanized antibodies as it allows the precise definition of FR-IMGT and CDR-IMGT and the easy comparison of amino acid sequences between the nonhuman (mouse, rat...) V domains and the closest human germline genes. Since July 1995, IMGT[®] is available on the web at <http://www.imgt.org>. IMGT[®] is used by academic and industrial scientists involved in fundamental research, medical research (autoimmune and infectious diseases, AIDS, leukemia, lymphoma, myeloma), veterinary research, genomics (genome diversity and evolution of the adaptive immune system), biotechnology related to antibody engineering for humanization of therapeutic antibodies, diagnostics (detection of minimal residual diseases) and therapeutic approaches (grafts, immunotherapy, vaccinology).

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The IMGT® web server at Montpellier is accessed by more than 80,000 sites per year. IMGT® has an exceptional response with more than 150,000 requests per month. The IMGT® platform has been certified ISO 9001:2008 by LRQA France.

Antibodies represent a large number of the pharmaceutical substances submitted to the World Health Organization/International Nonproprietary Names (WHO/INN) Programme. The INN definition of antibodies is based on the IMGT-ONTOLOGY concepts. Since 2008, amino acid sequences of monoclonal antibodies (mAb, INN suffix -mab) and of fusion proteins for immune applications (FPIA, INN suffix -cept) from WHO/INN have been entered into IMGT®. These therapeutic applications emphasize the importance of the IMGT-ONTOLOGY concepts in bridging the gap between antibody sequences and 2D and 3D structures.

Another research interest, in collaboration with the Unit of Medical Genetics, St-Joseph University, Beirut (Pr A. Mégarbané), concerns very rare autosomal recessive genetic diseases in consanguineous Lebanese families. Patients are autozygous (homozygous by descent) for a very rare mutated gene present in the common ancestor of their parents who are cousins. These pathologies, almost unknown in panmictic populations, are invaluable starting points from which to identify unknown genes, their products and functions as well as unsuspected links with cell physiology. For examples, the ICF (Immunodeficiency, Centromeric region instability and Facial anomalies) syndrome results from mutations in the DNA methyltransferase 3B (DNMT3B) gene in most cases (type 1); a recessive form of Hyper-IgE syndrome is due to mutations in the Dedicator Of CytoKinesis 8 (DOCK8) gene; many candidate genes for adaptive and innate immunodeficiencies have been investigated; recessive infantile osteopetrosis, a bone disease with neural involvement in the most severe form, results from mutations of the TCIRG1 (Atp6a3), CLCN7 or OSTM1 (grey lethal) genes. The genome evolution (Alu sequences, mtDNA, Y chromosome) is analyzed in Lebanon and in Tunisia, along the paths of human expansion out of Africa. We study also markers of positive selection or, conversely, of susceptibility towards infectious diseases. In these cases also, consanguineous families are powerful and time-saving sources of information.