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IMGT/V-QUEST and IMGT/JunctionAnalysis: The standardized approach for IG and TR rearrangement analysis

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IMGT®, the international ImMunoGeneTics information system® (http://imgt.cines.fr, Montpellier, France) is 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) [1]. The IMGT information system consists of databases, interactive tools and web resources. The accuracy and the consistency of the IMGT components are based on IMGT-ONTOLOGY [2], the first ontology in immunogenetics and immunoinformatics. IMGT-ONTOLOGY provides a semantic specification and definition of terms and rules which ensure the coherence of the IMGT tools and among them: IMGT/V-QUEST [3] and IMGT/JunctionAnalysis [4]. IMGT/V-QUEST is an integrated software which analyses the IG and TR rearranged nucleotide sequences and identifies the variable (V), diversity (D) and joining (J) genes and alleles by alignment with the IMGT reference directory. IMGT/V-QUEST also provides automatically the percentage of identity of the V regions of input rearanged IG sequences by comparison with the V region of the closest germline gene, the number and description of mutations per framework (FR-IMGT) and complementarity determining region (CDR-IMGT), and the identification and localization of the mutation hotspots in the closest germline gene. IMGT/V-QUEST includes IMGT/JunctionAnalysis, a tool specifically developed for the detailed analysis of the V-J or V-D-J JUNCTION(s). IMGT/JunctionAnalysis accurately identifies the D genes, delimits the palindromic P-REGION(s) and the N-REGION(s) and evaluates the number of somatic hypermutations for each gene, within the JUNCTION.
IMGT/V-QUEST and IMGT/JunctionAnalysis are the reference tools for the analysis of the IG and TR repertoires in biomedical studies and fundamental research [3,4]. They are part of the recommendation recently published by European Research Initiative on CLL (ERIC) [5]. It is widely accepted that the mutation status of IGHV genes is one of the most important prognostic factors in chronic lymphocytic leukemia (CLL) [6]. CLL patients whose tumour cells show a relatively high number of somatic mutations in their rearranged IGHV genes have a significantly increased mean survival time compared to patients with fewer mutations. IMGT/V-QUEST and IMGT/JunctionAnalysis are used in fundamental research for the analysis of the IG antibody sites and of the TR recognition sites in normal and pathological situations such as autoimmune diseases, infectious diseases, AIDS, leukemias, lymphomas, myelomas. Statistical analysis performed on the results of these tools provides a better charaterization of the mechanisms involved in the V-(D)-J rearrangements, as for example the trimming process of the V-REGION, D-REGION and J-REGION and the at random addition of N nucleotides [7].

To fit with users needs, IMGT/V-QUEST proposes two different appoaches for the sequence analysis: (i) a detailed view where the results are provided for each individual input sequence. (ii) a synthesis view where all sequences assigned to a same gene and allele are aligned together. For both approaches, the different tasks of IMGT/V-QUEST and IMGT/JunctionAnalysis are performed according to the IMGT Scientific chart rules, based on the IMGT-ONTOLOGY concepts, and more particularly on the DESCRIPTION and NUMEROTATION concepts.

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