Editorial

State of the art immunogenetics and immunoinformatics

Eleni Papakonstantinou and Dimitrios Vlachakis

Laboratory of Genetics, Department of Biotechnology, School of Food, Biotechnology and Development, Agricultural University of Athens, Athens, Greece

Correspondence should be addressed to Dimitrios Vlachakis; Tel:+30 210 5294323, Email: dimvl@aua.gr

Antibodies, or immunoglobulins, belong to the 'gamma globulin' protein group and can be found mainly in the blood of vertebrates. Antibodies constitute the major serological line of defense of the vertebrates with jaws (gnathostomata) by which the immune system identifies and neutralizes threatening invaders, such as viruses, fungi, parasites, bacteria. The contrivance underlying the reaction efficiency of our immune system to specifically recognize and fight invading organisms or to trigger an autoimmune response and disease still remains to be elucidated.

The efficient reaction of our immune system against all kinds of intruders is highly dependent on the number, condition and availability of antibodies, as reaction times are 'key' to the successful elimination of the foreign pathogen (Filntisi *et al.* 2013). In reference to autoimmune diseases, antibodies can be described as an inappropriate and offensive response of the immune system against normal tissues of the body. In essence the immune system mistakenly recognizes its own cells as potential pathogens and attacks them (Filntisi *et al.* 2013). In most cases this reaction may be localized on just parts of certain organs or include a specific type of tissue that can be found in more than one organ in the human body. Up until now, the most commonly practiced clinical treatments for diseases of the immune system involve immunosuppression, which aims to lessen the reactive immune response.

IMGT/3Dstructure-DB in one of the largest open-source structure related databases available and together with its query, has a great appeal on immunogenetics and immunoinformatics. The database is active and updated frequently. The query tool for the database is also updated frequently (version 4.10.0, 2014-04-09). The IMGT/3Dstructure-DB query tool can seek data among the 5439 entries of the database, but can also seek data from three other external databases. First and foremost, from the Protein Data Bank (PDB), which hosts 4596 entries, moreover, from the World Health Organization's Non Proprietary Names (WHO/INN) database, which hosts 507 entries and last but not least, from the Kabat Sequence Database, which hosts 336 entries. In spite of having such large quantity of information, which makes it not so user-friendly for the novice user, it will reward the professional user with its detailed and precise adjustability of every different inquiry needed (Ehrenmann & Lefranc 2011). The criteria of the inquiry can be set separately or can be combined diminishing the results. IMGT/3Dstructure-DB allows searching the database by specific structural characteristics, by experimental data or bibliographical references, by molecule name or entry code. In addition, the query tool of the IMGT/3Dstructure-DB can search for structures with criteria such as the complex type (selecting between: IG/Ag, TR/pMH1, TR/pMH2, RPI/pMH1, RPI/pMH2, pMH1 and pMH2), the local structure at position, specifying the presence of a specific amino acid, the type of the secondary structure, amino acid φ and ψ angles in degrees, the accessible surface area (ASA) in angstrom^2 (Å2) and the type of atom contacts between two positions (Giudicelli *et al.* 2005).

As mentioned above, currently there are 4596 antibody structures that are expertly annotated in IMGT/3Dstructure-DB, with gene and allele identification, CDR-IMGT lengths, contact analysis. These are all X-ray crystallography, NMR or electron microscopy determined three dimensional structures of antibodies (Vlachakis *et al.* 2014a). A set of in-house developed filters and tools were applied to select and identify the best candidate template structure of each of the aforementioned groups of antibodies (Vlachakis *et al.* 2014b, c). The filters were mainly based on the simultaneous satisfaction of the exact CDR length required for each group, the percentage coverage, percentage identity and similarity score (Maltezos *et al.* 2014).

The IMGT curated database of the 3D structures of antibodies has been optimized to include keys or metadata for the description of a series of crucial antibody characteristics (Filntisi *et al.* 2013). Some of them include the number of chains in the PDB entry, the resolution of the X-ray crystallography, the date it was released, the species (Homo sapiens, Mus musculus), the variable domain type (e.g. VH or VL, and for VL, V-KAPPA, V-LAMBDA), and for those that are dimers, a description of their dimeric type (e.g. VH:VL).

From the user's point of view, the query tool for the IMGT/3Dstructure-DB as a GUI (Graphical User Interface) is lacking of adaptability to each specified query processes, making it more difficult to understand how it is operated. While for example, at the HIV Molecular Immunology Database we can see how easily the graphical interface is adapted to the inquiry taking place (Filntisi *et al.* 2013). Moreover, it could be improved in the aspects of practicality, for example having a quick search tool, like the AbMiner database (Major *et al.* 2006). In addition, the graphical interface could enhance the ease of use and learning of the tool, guiding the user step-by-step, like the pop-up boxes the Abysis query tool has (Swindells *et al.* 2017).

In conclusion, the IMGT/3Dstructure-DB is a powerful tool to search and obtain information about the appropriate antibody structures. Combined with IMGT/DomainGapAlign and IMGT/Collier-de-Perles tool, which are also freely available, they greatly contribute to the development of antibody engineering.

References

Ehrenmann F & Lefranc MP 2011 IMGT/3Dstructure-DB: querying the IMGT database for 3D structures in immunology and immunoinformatics (IG or antibodies, TR, MH, RPI, and FPIA). *Cold Spring Harbor Prot* **6** prot5637

Filntisi A, Vlachakis D, Matsopoulos G & Kossida S 2013 3D structural bioinformatics of proteins and antibodies: state of the art perspectives and challenges. *Int J Syst Biol Biomed Tech* **2** 67-74

Giudicelli V, Chaume D & Lefranc MP 2005 IMGT/GENE-DB: a comprehensive database for human and mouse immunoglobulin and T cell receptor genes. *Nucleic Acids Res* **33** 256-261

Major SM, Nishizuka S, Morita D, Rowland R, Sunshine M, Shankavaram U, Washburn F, Asin D, Kouros-Mehr H, Kane D & Weinstein JN 2006 AbMiner: a bioinformatic resource on available monoclonal antibodies and corresponding gene identifiers for genomic, proteomic, and immunologic studies. *BMC Bioinformatics* **7** 192

Maltezos A, Platis D, Vlachakis D, Kossida S, Marinou M & Labrou NE 2014 Design, synthesis and application of benzyl-sulfonate biomimetic affinity adsorbents for monoclonal antibody purification from transgenic corn. *J Mol Recognit* **27** 19-31

Swindells MB, Porter CT, Couch M, Hurst J, Abhinandan KR, Nielsen JH, Macindoe G, Hetherington J & Martin AC 2017 abYsis: Integrated Antibody Sequence and Structure-Management, Analysis, and Prediction. *J Mol Biol* **429** 356-364

Vlachakis D, Armaos A, Kasampalidis I, Filntisi A & Kossida S 2014a ASSP; the Antibody Secondary Structure Profile search tool in *ICABD* 2014

Vlachakis D, Champeris Tsaniras S, Ioannidou K, Papageorgiou L, Baumann M & Kossida S 2014b A series of Notch3 mutations in CADASIL; insights from 3D molecular modelling and evolutionary analyses. *J Mol Biochem* **3** 97-105

Vlachakis D, Champeris Tsaniras S, Tsiliki G, Megalooikonomou V & Kossida S 2014c 3D structural analysis of proteins using electrostatic surfaces based on image segmentation. *J Mol Biochem* **3** 27-33