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WEBLEM 8

TO UNDERSTAND VARIOUS WEB-BASED TOOLS FOR VACCINE DESIGNING

Introduction:

Computational methods used in vaccine design have been changing drastically in recent years. In classical immunological research results could be recorded by pen and pencil or in a spreadsheet, but new experimental high throughput methods such as sequencing, DNA arrays, and proteomics have generated a wealth of data that are not efficiently handled and mined by these approaches. This has fueled the rapid growth of the field of Immunological Bioinformatics (or Immuno-informatics) that addresses how to handle these large amounts of data in the field of immunology and vaccine design. Many of the methods have been made available on the Internet and can be used by experimental researchers without expert knowledge of bioinformatics. This review attempts to give an overview over the methods currently available and to point out the strengths and weaknesses of the different methods.

Structural antibody database: (SAbDab; http://opig.stats.ox.ac.uk/webapps/sabdab)

It is an online resource containing all the publicly available antibody structures annotated and presented in a consistent fashion. The data are annotated with several properties including experimental information, gene details, correct heavy and light chain pairings, antigen details and, where available, antibody–antigen binding affinity. The user can select structures, according to these attributes as well as structural properties such as complementarity determining region loop conformation and variable domain orientation. Individual structures, datasetsand the complete database can be downloaded.

Computational analyses and tools are increasingly being employed to aid the antibody engineering process Many of these tools now use only the antibody data, as opposed to general protein data, because this has been shown to increase performance.

Structural Antibody Database (SAbDab), a database devoted to automatically collecting, curating and presenting antibody structural data in a consistent manner for both bulk analysis and individual inspection. SAbDab updates on a weekly basis and provides users with a range of methods to select sets of structures. For example, users can select by species, experimental details (e.g. method, resolution and r-factor), similarity to a given antibody sequence, amino-acid composition at certain positions and antibody–antigen affinity. Entries can also be selected using structural annotations including, for example, the canonical form of the complementarity determining regions (CDR), orientation between the antibody variable domains and the presence of constant domains in the structure. Structures can be inspected individually or downloaded en masse either as the original file from the PDB or as a structure that has been annotated using the Chothia numbering scheme. In all cases, a tab-separated file detailing heavy and light chain pairing, antibody–antigen pairing and all other annotations is generated.

Ag-Ab Interaction Database:

Antigen-Antibody Interaction Database (AgAbDb) is an immunoinformatics resource developed at the Bioinformatics Centre, University of Pune, and is available online at http://bioinfo.net.in/AgAbDb.htm. Antigen-antibody interactions are a special class of protein-protein interactions that are characterized by high affinity and strict specificity of antibodies towards their antigens. Several co-crystal structures of antigen-antibody complexes have been solved and are available in the Protein Data Bank (PDB). AgAbDb is

a derived knowledgebase developed with an objective to compile, curate, and analyze determinants of interactions between the respective antigen- antibody molecules. AgAbDb lists not only the residues of binding sites of antigens and antibodies, but also interacting residue pairs. It also helps in the identification of interacting residues and buried residues that constitute antibody-binding sites of protein and peptide antigens. The Antigen-Antibody Interaction Finder (AAIF), a program developed in-house, is used to compile the molecular interactions, viz. van der Waals interactions, salt bridges, and hydrogen bonds. A module for curating water-mediated interactions has also been developed. In addition, various residue-level features, viz. accessible surface area, data on epitope segment, and secondary structural state of binding site residues, are also compiled. Apart from the PDB numbering, Wu-Kabat numbering and explicit definitions of complementarity-determining regions are provided for residues of antibodies. The molecular interactions can be visualized using the program Jmol. AgAbDb can be used as a benchmark dataset to validate algorithms for prediction of B-cell epitopes. It can as well be used to improve accuracy of existing algorithms and to design new algorithms. AgAbDb can also be used to design mimotopes representing antigens as well as aid in designing processes leading to humanization of antibodies.

Immune Epitope Database (IEDB):

The Immune Epitope Database (IEDB) contains >1.6 million experiments representing the adaptive immune response to epitopes, gathered primarily from the literature . These experiments were manually curated following structured curation guidelines, as previously described . This data was obtained from 19 ,500 publications and includes all the literature available from the beginnings of PubMed until now. Historical curation of papers going back to 1952 was completed in 2011 and since, this database has focused on newly published papers. It perform a query of PubMed every two weeks to remain current with new content. The IEDB has approximately 300 unique visitors and 1220 page views per day. The IEDB exists as a free service with the goal of helping further immunological research. Thus, we routinely perform outreach activities to interact with our users to ascertain their needs and gather feedback on existing features. Here we present our efforts toward meeting user needs, as well as extending functionality to keep current with accepted web standards.

Significantly, research is ever-evolving; new experiments are continually created, expanding data quantity and complexity. As the cost of high throughput experiments is decreasing, scientists are publishing greater numbers of experiments per publication, leading to rapid increases in our data. This is reflected in the number of epitopes curated per publication year, which began rapidly increasing in 2015 Accordingly, the number of experiments captured in the IEDB has also increased by 140% since 2015, now surpassing 1.6 million.

Another factor leading to large amounts of new data is the addition of receptor sequence data to the IEDB schema. Previously, It's only captured full length antibody and T cell receptor (TCR) sequences whenever a 3D structure was available, but we now capture both full length and CDR sequences, as well as gene usage whenever authors provide this. To accommodate this new data, we added new database tables, search panes, results tabs, and details pages, as described in a separate publication.

Structural T–cell Receptor Database (STCRDab):

The Structural T–cell Receptor Database (STCRDab; http://opig.stats.ox.ac.uk/webapps/stcrdab) is an online resource that automatically collects and curates TCR structural data from the Protein Data Bank. For each entry, the database provides annotations, such as the α/β or γ/δ chain pairings, major histocompatibility complex details, and where available, antigen binding affinities. In addition, the orientation between the variable domains and the canonical forms of the complementarity-determining region loops are also provided. Users can select, view, and download individual or bulk sets of structures based on these criteria.

Where available, STCRDab also finds antibody structures that are similar to TCRs, helping users explore the relationship between TCRs and antibodies.

References:

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