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Web Site Review

Review of the BRENDA Database

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1. Introduction

The rapid sequencing of a large number of genomes has made it imperative to organize the available data in ways that facilitate easy analysis. BRENDA (BRaunschweig ENzyme DAtabase) was created in 1987 at the German National Research Center for Biotechnology at Braunschweig and is currently being maintained at the University of Cologne. As of February 2003, it provides information on 40,000 different enzymes represented by 4,087 EC numbers, and present in more than 9000 different organisms as of February, 2003 (Schomburg et al., 2002a). The database is accessible at no charge at http://www.brenda.unikoeln.de for academic purposes.

2. The contents

The enzyme content of BRENDA can be accessed using the enzyme EC number, the enzyme name and the organism name. A search can also be conducted based on either the taxonomy tree of the organism in which the enzyme is present or the EC tree of the enzyme. The last classification categorizes enzymes into six different classes based on their functions. An advanced search can be performed for a combination of two fields, for instance, all enzymes which have glucose as their natural substrate and are stable above 50°C can be retrieved. Once a particular enzyme has been searched, information can be obtained for a large number of fields. These include not only the reaction catalyzed by the enzyme in terms of its substrates and products, but also the organisms and the tissues in which the enzyme is present. In addition to this primary information, functional parameters such as optimum pH range, optimum temperature range, and molecular properties of the enzyme can also be obtained. All information in the database is organized in the form of tables. For example, Figure 1 shows a table providing information on the activating compounds for the enzyme hexokinase. The second column in the table shows the name of the organism where the function of these activating compounds is observed. We also find links for a literature reference and for the 2D image of the activating compound in the last two columns.

Databases such as SWISSPROT/TREMBL (Bairoch et al., 2000) and PDB (Berman et al., 2000) can be accessed from the webpage for supplemental information on the encoding sequence and 3D structures of the participating compounds. Table 1 provides a list of all the fields for which information is provided in BRENDA.

A significant feature of the database is the information on the ligands with which the enzymes interact. As many as 320,000 enzyme–ligand relationships can be accessed. The inhibitors and activators of a particular enzyme, along with the cofactors essential for its activity, are listed in the section on enzyme–ligand interactions. These ligands are stored in three ways: first, as compound name and its synonyms, second, as SMILES (simplified molecular input line specification) strings (Weininger, 1988) which store structural information and third, as Molfiles (http://www.mdli.co.uk/downloads/literature/ctfile.pdf) which contain information on chemical connections and bonds in the ligand.

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ACTIVATING COMPOUND	ORGANISM	COMMENTARY	LITERATURE	IMAGE
Galactose	Candida maltosa H	activates isoenzyme Hex II	27	2D-image
Lyxose	Candida maltosa H	activates isoenzyme Hex II	27	2D-image
Mannose 6-phosphate	Candida maltosa H	activates isoenzyme Hex II	27	2D-image
Ribose	Candida maltosa H	activates isoenzyme Hex II	27	2D-image
Xylose	Candida maltosa H	activates isoenzyme Hex II	27	2D-image

Fig. 1. Table showing the activating compounds when a query was made for the enzyme hexokinase.

Table 1
Number of data entries for various information fields (parameters) in BRENDA as of February, 2003 (Schomburg et al., 2002a)

Information field	Entries	Information field	Entries
Enzyme nomenclature		*Functional parameters*	
EC number	4087	K_m value	28,134
Recommended name	3635	Turnover number	3986
Systematic name	3300	Specific activity	16,651
Synonyms	26,536	pH optimum	16,605
CAS Registry Number	3794	pH range	4492
Reaction	3655	Temperature optimum	6697
Reaction type	5155	Temperature range	1190
Enzyme structure		*Molecular properties*	
Molecular weight	15,524	pH stability	3535
Subunits	9228	Temperature stability	8293
Sequence links	44,479	General stability	5520
Post-translational modification	1555	Organic solvent stability	377
Crystallization	1258	Oxidation stability	386
3D-structure, specific PDB links	9671	Storage stability	7251
		Purification	13,069
Enzyme–ligand interactions		Cloned	3348
Substrates/products	1,29,651	Engineering	2373
Natural substrate	23,628	Renatured	247
Cofactor	8023	Application	1026
Activating compound	8703		
Metals/ions	14,471	*Organism-related information*	
Inhibitors	66,225		
		Organism	51,897
Bibliographic data		Source-tissue, organ	21,282
References	56,608	Localization	9195

BRENDA is currently being updated to include the representation of metabolic pathways (Introductory section at the BRENDA website). At present, direct links are provided to the KEGG (Kanehisa and Goto, 2000) and the TRANSFAC (Matys et al., 2003) databases for obtaining these pathways and also enzyme-regulating transcription factors. An aspect of BRENDA that is worth mentioning is the information on diseases associated with as many as 789 enzymes in the database (Schomburg et al., 2002b). Additionally, links to the OMIM (Online Mendelian Inheritance in Man, http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=OMIM) for finding pathological information on several other enzymes are available.

Crucial information for enzyme handling, preparation and application can also be acquired from the database. For instance, the field '*application*' cites information on the established and potential uses of an enzyme. The field '*protein engineering*' lists enzyme variants and helps to compare their properties with that of the wild-type enzyme. A number of links are provided to the NCBI website (http://www.ncbi.nlm.nih.gov/), ExPASy (http://us.expasy.org/, Boeckmann et al., 2003), IUBMB nomenclature (http://www.chem.qmul.ac.uk/iubmb/) and other sites to get further information on each enzyme. All data are connected to literature references which in turn are linked to PubMed (http://www.ncbi.nlm.nih.gov/PubMed).

3. Strengths and weaknesses

The BRENDA webpage provides a simple and user-friendly interface. The homepage lists all the fields for which information can be obtained on an enzyme. Each field is accessible directly from this page making it easy

for the reader to navigate the website. BRENDA is quite comprehensive in terms of both the number of enzymes included in the database and the broad range of properties on which information about an enzyme can be extracted. It also enables a user to get all the data compiled from different sources at the same place which is far more useful than retrieving data from a single reference at a time (http://emp.mcs.anl.gov/). Furthermore, with a single query, it is possible to retrieve the enzyme properties in all organisms where the enzyme is present. Thus, information is not limited to specific organisms, a feature lacking in most other databases such as BioCyc (http://biocyc.org/) and KEGG (http://www.genome.ad.jp/kegg/kegg2.html). This is essential because the properties of an enzyme may differ from one organism to another and a thorough comparison available at the same place is very convenient. However, one of the weaknesses of the site is the lack of a graphic interface for pathways involving the enzymes. This drawback may be eliminated once the addition of the metabolic pathways to the database is completed. In summary, BRENDA is a great tool for obtaining a wide range of information on enzymes and understanding their biological functions.

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