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KDBI: Kinetic Data of Bio-molecular Interactions database

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ABSTRACT

Understanding of cellular processes and underlying molecular events requires knowledge about different aspects of molecular interactions, networks of molecules and pathways in addition to the sequence, structure and function of individual molecules involved. Databases of interacting molecules, pathways and related chemical reaction equations have been developed. The kinetic data for these interactions, which is important for mechanistic investigation, quantitative study and simulation of cellular processes and events, is not provided in the existing databases. We introduce a new database of Kinetic Data of Bio-molecular Interactions (KDBI) aimed at providing experimentally determined kinetic data of protein–protein, protein-RNA, protein-DNA, protein-ligand, RNA-ligand, DNA-ligand binding or reaction events described in the literature. KDBI contains information about binding or reaction event, participating molecules (name, synonyms, molecular formula, classification, SWISS-PROT AC or CAS number), binding or reaction equation, kinetic data and related references. The kinetic data is in terms of one or a combination of the following quantities as given in the literature of a particular event: association/dissociation or on/off rate constant, first/second/third/... order rate constant, equilibrium rate constant, catalytic rate constant, equilibrium association/dissociation constant, inhibition constant and binding affinity constant. Each entry can be retrieved through protein or nucleic acid or ligand name, SWISS-PROT AC number, ligand CAS number and full-text search of a binding or reaction event. KDBI currently contains 8273 entries of biomolecular binding or reaction events involving 1380 proteins, 143 nucleic acids and 1395 small molecules. Hyperlinks are provided for accessing references in Medline and available 3D structures in PDB and NDB. This database can be accessed at http://xin.cz3.nus.edu.sg/group/kdbi/kdbi.asp.

INTRODUCTION

Cellular processes and underlying molecular events involve complex interactions and cross talks between individual molecules, pathways and networks of pathways (1,2). Quantitative as well as mechanistic understanding of these interactions is important for exploration and engineering of cell behavior and for the development of novel therapeutics to combat diseases. A number of databases of molecular interactions (3,4), pathways (5–8) and enzyme reactions (9) have been developed. These databases provide comprehensive information about interacting molecules, molecular complexes, pathways, chemical reactions and conformation changes. The kinetic data for these interactions, important for mechanistic investigation, quantitative study and simulation of cellular processes and events (10–12), is not provided in the existing database.

A new database, Kinetic Data of Bio-molecular Interactions (KDBI), is introduced as a resource of experimentally determined kinetic data for protein–protein, protein-DNA, protein-RNA, protein-ligand, DNA-ligand and RNA-ligand interactions. KDBI provides detailed description about binding or reaction event, participating molecules, binding or reaction equation, kinetic data and related references. To facilitate the search of data and potential cross-links to and from related biomolecular interaction and pathway databases, a variety of molecular descriptions are also provided which include name of molecule, synonyms, SWISS-PROT AC for a protein or CAS number for a small molecule ligand, molecular formula, classification, protein function and tissue distribution. The kinetic data is in terms of one or a combination of kinetic quantities as given in the literature of a particular event. These quantities include association/dissociation rate constant, on/off rate constant, first/second/third/... order rate constant, catalytic rate constant, equilibrium association/dissociation constant, inhibition constant and binding affinity constant.

DATABASE STRUCTURE AND ACCESS

KDBI has a web interface at http://xin.cz3.nus.edu.sg/group/kdbi/kdbi.asp, which is shown in Figure 1. The entries of this database are generated from a search of published literature

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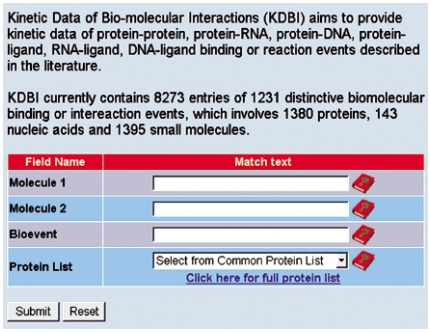

Figure 1. Web interface of KDBI. Four types of search mode are supported. This database is searchable by molecule name, SWISS-PROT AC number for a protein, CAS number for a small molecule and key word description about a Bioevent. A partial protein list is also provided to facilitate the access of relevant kinetic data.

about experimentally measured kinetic data of biomolecular binding or reaction events. The kinetic data of an event is searchable by several methods. One method is via the name of participating molecules (protein, nucleic acid, small peptide, ligand or ion) in an event. In some events described in the literature, a participating entity is an unidentified molecule located in the membrane of a cell or on the surface of a virus. In these entries, only the name of the cell or virus is given. An entry can also be searched through a SWISS-PROT AC number for a protein or the CAS number for a small molecule ligand. Moreover, keyword-based text search is also supported. To facilitate convenient access of relevant data, a partial list of proteins is provided. Searches involving combination of these methods or selection fields are also supported.

The search is case insensitive and wildcards are supported. In a query, a user can specify full name or any part of the name in a text field. Wild character of '*' and '?' is allowed in text field. Here, '?' represents any one character and '*' represents a string of characters of any length. For example, input of 'reductase' in the molecule field finds entries containing 'reductase' in their name, such as NADPH-adrenoferredoxin reductase, NADH-CoQ recuctase, cytochrome P450 reductase, 5-alpha reductase, thiol-disulfide oxidoreductase, etc. On the other hand, input of NAD^+ reductase finds all the reductase start their names with 'NAD'. In this case, '*' represents 'PH-adrenoferredoxin' and 'H-CoQ' respectively.

The result of a search is illustrated in Figure 2, in which all events that satisfy the search criteria are listed. This list includes the name of the participating molecules as well as the description about the corresponding event. The related kinetic data can be obtained by clicking the 'Kinetic data' button of a selected event. The page of kinetic data, as shown in Figure 3, provides detailed description about the reaction equation (while available), the kinetic data given in the literature and the source of the literature. Further information about the participating molecules can be obtained by clicking the name of the respective molecules. As shown in Figure 4, the corresponding molecular information page provides the name, synonym, SWISS-PROT access number for a protein or CAS number for a small molecule ligand, classification and formula for a small molecule ligand (while available), and the function,

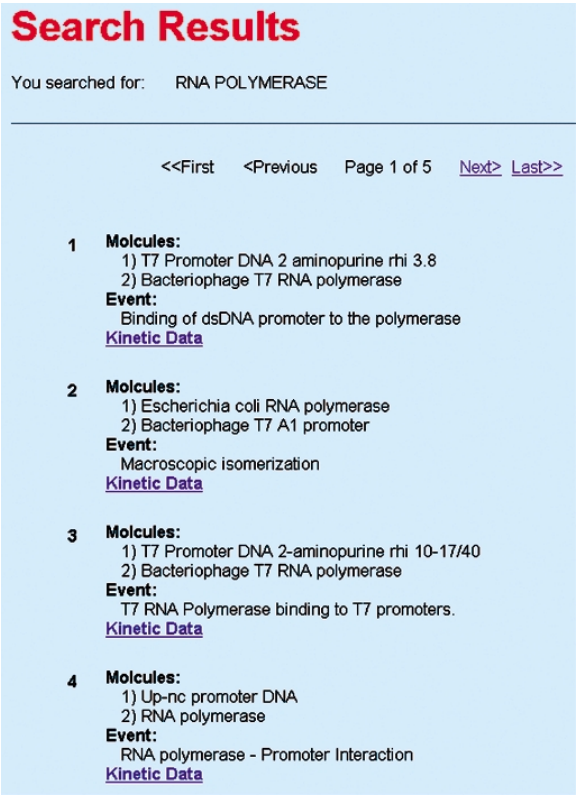

Figure 2. The interface for a search in KDBI. All entries that satisfy the search criteria are listed. This list includes the name of participating molecules, description of an event and links to the kinetic data page.

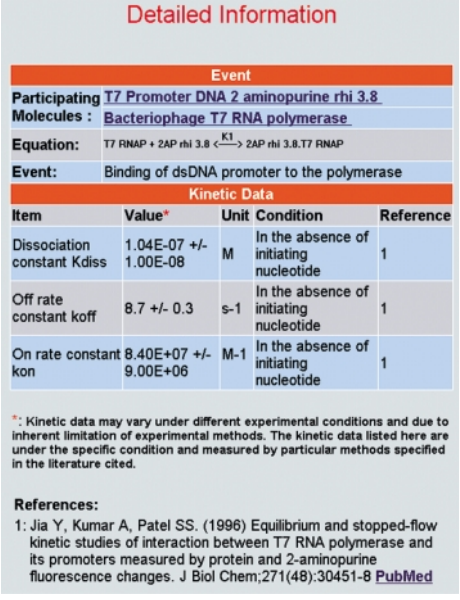

Figure 3. The kinetic data page. This page provides kinetic data and reaction equation (while available) as well as the name of participating molecules and description of event. Further information about the participating molecules can be obtained by clicking the name of these molecules.

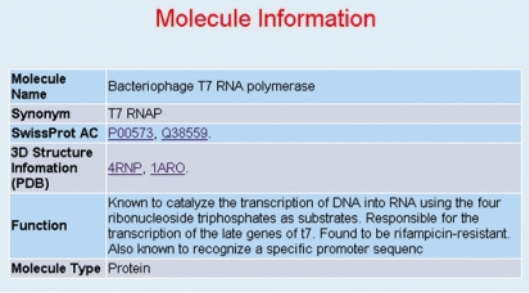

Figure 4. Molecular information page. Information provided includes molecular name, synonyms, SWISS-PROT AC number for a protein or CAS number for a small molecule, molecular formula for a small molecule, protein function, tissue distribution and cross-link to SWISS-PROT database and PDB database for a protein.

tissue distribution and cross-link to SWISS-PROT database (13) for a protein. Moreover, hyperlinks are provided to facilitate access to the relevant reference in Medline and available 3D structural entries in PDB (14). For a nucleic acid, hyperlink to its available 3D structural entries in NDB is also provided (15).

REMARKS

KDBI currently contains 8273 entries of biomolecular binding or reaction events. There are a total of 1380 proteins, 143 nucleic acids and 1395 small molecules included in the database. Work is underway to collect kinetic data published in earlier years, which is expected to significantly increase the number of entries in the database. Rapid advances in proteomics (16) pathways (17) and networks (18) are expected to stimulate more interest in the quantitative aspects of biomolecular interactions including kinetic data (10–12). The availability of increasing amount of kinetic data can better serve the need for mechanistic investigation, quantitative study and simulation of cellular processes and events.

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