

AngioDB: database of angiogenesis and angiogenesis-related molecules

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ABSTRACT

Angiogenesis is the formation of new capillaries sprouting from pre-existing vessels. Angiogenesis occurs in a variety of normal physiological and pathological conditions and is regulated by a balance of stimulatory and inhibitory angiogenic factors. The control of this balance may fail and result in the formation of a pathologic capillary network during the development of many diseases. Therefore, we developed the angiogenesis database (AngioDB), which can provide a signaling network of angiogenesis-related biomolecules in human. Each record of AngioDB consisted of 12 fields and was developed by using a relational database management system. For the retrieval of data, Active Server Page (ASP) technology was integrated in this system. Users can access the database by a query or imagemap browsing program. The retrieving system also provides a list of angiogenesis-related molecules classified by three categories, and the database has an external link to NCBI databases. AngioDB is available via the Internet at <http://angiodb.snu.ac.kr/>.

INTRODUCTION

Biological databases provide organized information to biology researchers and facilitates the efficient set up of experimental protocols by biologists. Biological databases are divided into two groups by source of information. First, a primary database, which brought data sources from literature resources about broad topics. Secondly, a secondary database, which brought data sources for a specific topic from the primary database and additional literature resources (1).

The angiogenesis database (AngioDB) is useful to researchers seeking appropriate experimental models for studying angiogenesis in humans or for the identification of new factors that control the balance of angiogenesis. Angiogenesis is the formation of new capillaries sprouting from pre-existing vessels, which is different from vasculogenesis by which endothelial cells arise from progenitor cell types (2). The angiogenic response is composed of the triads of protease secretion to facilitate basement

membrane remodeling, proliferation of endothelial cells and endothelial migration to form capillary sprouts and lumen closure (3). Angiogenesis occurs in physiological states such as embryonic development, wound healing, tissue regeneration and neovascularization (4). Angiogenesis is strictly limited and finely tuned by a balance of stimulatory and inhibitory angiogenic factors (5–7). These controls may fail and result in formation of a pathologic capillary network during the development of many diseases including malignant tumors, diabetic retinopathy, rheumatoid arthritis, intraocular vascular syndromes, psoriasis and other disorders (8,9). Currently, there is a considerable interest in the molecular regulation of angiogenesis because it is a prerequisite for tumor growth and metastasis.

AngioDB can be classified to a secondary database. It was remodelled with the integrated information according to the specific categories. The most important principle for the construction of AngioDB is how to efficiently organize the mechanisms of angiogenesis, which is controlled by a balance of related factors such as activators and inhibitors. Diverse information related to angiogenesis can be linked to a database record, including information on cellular location, synonym, DNA sequence, protein sequence, classification, angiogenic overview and references. Therefore, AngioDB can be useful to relevant researchers who are seeking appropriate experimental models and new factors that control the balance of angiogenesis. AngioDB has been available as a Web-accessible database since July 2000. In the first release of AngioDB, we have focused on several areas of database development including data acquisition, imagemap based-retrieving and database-derived information summaries for the type of data in AngioDB. In this article, we describe the details listed above and the current data status of the database.

DATA ACQUISITION

Raw data were extracted and information was collected for AngioDB from a primary database such as GenBank (10) and off-line data resources. Then, researchers corrected and reprocessed the integrated data. The published scientific literature and the information in primary databases served as the primary source for data in AngioDB. Journal articles identified as containing information appropriate for the database by our laboratory

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workers were subsequently categorized according to the molecule name. The principal focus for AngioDB currently is on angiogenic function of biomolecules. Data entry is prioritized based on the previously reported angiogenesis-related biomolecules observed in humans.

QUERIES AND VISUALIZATION

The records of AngioDB consisted of angiogenesis-related biomolecules. Each record of AngioDB contained 12 fields, including information on cellular location, DNA sequence, angiogenic overview, references and many other features. Users can retrieve the data in accordance with gene name, sequence, cellular location, accession number and keyword, and also by imagemap. When a user clicks on a particular image of a molecule in imagemap, the data on chosen molecule are displayed. Moreover, the database provides a list of molecules sorted by angiogenesis-related diseases and category.

DATA FIELDS

Structure of data is constituted with 12 fields: 'Symbol', 'Name', 'Synonym', 'Cellular location', 'Keyword', 'Nucleotide number', 'Nucleotide sequence', 'Protein number', 'Protein sequence', 'Classification', 'Angiogenic overview' and 'Reference'. The 'Cellular location' field represents the functional area of the molecule in a cell. For example, data for the cellular location field in Vascular Endothelial Growth Factor Receptor-1 (VEGFR-1) indicates 'cell membrane'. It means that the molecule VEGFR-1 is localized and activated on the cell membrane. The 'Classification' field represents the category or the type of molecule. The 'Angiogenic overview' field represents a short description or comment on a functional contribution to angiogenesis. Among those 12 fields, the 'Nucleotide number' and 'Protein number' fields are hyper-linked with NCBI databases (10). These fields are also linked to Entrez (10) cross-reference database for any additional information.

IMAGEMAP-BASED RETRIEVING

AngioDB has two imagemaps, one is a protein-protein interacting network, and another is VEGF signal pathway. Each protein in imagemap was linked with AngioDB. In imagemap, users can probe information by clicking an image of a molecule. Each click event creates accession of the database. So, this effort can contribute to the field of angiogenesis research with a special focus on the mechanism of angiogenesis linked with a complex interaction network of molecules.

CURRENT STATUS OF AngioDB

To date, AngioDB holds 234 records of proteins and chemicals. The molecules were classified into three groups. The first group is angiogenic activators that have been reported to induce angiogenesis *in vivo* and/or *in vitro*. The second group is angiogenic signalling molecules that are involved in the angiogenesis-signaling pathway. The third group is angiogenic inhibitors that inhibit angiogenesis *in vivo* and/or *in vitro*. Each group has 94, 84 and 56 records, respectively. However, it will

be expanded in the next release. The public version of AngioDB will be updated monthly.

SUMMARIES AND FUTURE DIRECTIONS

AngioDB is a biological database using ASP technology in which the data comes from a primary database. Users can efficiently retrieve data with various options. In addition, AngioDB efficiently provides angiogenesis researchers with information that they will need in real-time Internet access. Moreover, AngioDB can be used for understanding of angiogenesis itself, angiogenesis-related molecules and their regulatory network. Hence, AngioDB information primarily supports pure and applied research. Drug industries increasingly need to know the expected effect of their drug candidates, and this is largely governed by points of drug action in an angiogenesis pathway and/or structure of molecule candidates. The AngioDB can also be used to predict a functional effect of angiogenic factor candidates.

The current goal of AngioDB is acquisition of data that is as comprehensive as possible and visualization of data in AngioDB by imagemap. To accomplish this goal, we will add data fields and categories about angiogenesis, and integrate more heterologous information such as medical information, angiogenesis processes and species-comparative information.

The next goal will be to use this information to predict molecular candidates for angiogenesis that AngioDB does not contain. Thus, we will newly integrate information about promoter regions of genes and motifs of proteins in AngioDB, this information will be helpful in predicting signaling networks and protein-protein interactions between molecules in AngioDB. Furthermore, we will supplement experimental data from cDNA microarray and two-dimensional gel electrophoresis to build the expression profiles from various cells, tissues and extracellular environments.

DATABASE ACCESS

AngioDB is available at <http://angiodb.snu.ac.kr/>. We appreciate feedback from our users. Any correspondence, including requests and corrections for AngioDB, should be mailed to tkson21@hotmail.com or the address of the corresponding author.

CITATION OF AngioDB

Authors wishing to make use of the information provided by AngioDB should cite this article as a general reference for access to and content of AngioDB.

SUPPLEMENTARY MATERIAL

Supplementary Material is available at NAR Online. This information includes links to web pages and to screen shots showing the results of specific AngioDB queries.

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