dictyBase, the model organism database for Dictyostelium discoideum

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ABSTRACT
dictyBase (http://dictybase.org) is the model organism database (MOD) for the social amoeba Dictyostelium discoideum. The unique biology and phylogenetic position of Dictyostelium offer a great opportunity to gain knowledge of processes not characterized in other organisms. The recent completion of the 34 MB genome sequence, together with the sizable scientific literature using Dictyostelium as a research organism, provided the necessary tools to create a well-annotated genome. dictyBase has leveraged software developed by the Saccharomyces Genome Database and the Generic Model Organism Database project. This has reduced the time required to develop a full-featured MOD and greatly facilitated our ability to focus on annotation and providing new functionality. We hope that manual curation of the Dictyostelium genome will facilitate the annotation of other genomes.

INTRODUCTION
dictyBase (http://dictybase.org) is the model organism database (MOD) for the social amoeba Dictyostelium discoideum. Like other MODs such as FlyBase (1), WormBase (2,3), Mouse Genome Informatics (4) and the Saccharomyces Genome Database (SGD) (5), dictyBase (6) uses the organism’s genome sequence to organize the biological knowledge resulting from experimental studies using Dictyostelium. Dictyostelium is a model organism widely used for biomedical research. An amoeba during most of its life, starvation induces a very interesting developmental program during which individual cells stream together by chemotaxis to form a multicellular tissue (7). A morphogenetic process involving cell migration and cellular morphogenesis transforms a simple mound of cells into a slug or pseudoplasmodium establishing a relatively simple developmental pattern. This structure then develops into a fruiting body consisting of multiple cell types including spores and terminally differentiated stalk cells. These features together with the efficient genetic manipulation by gene targeting and replacement as well as insertional mutagenesis and suppressor screens have made Dictyostelium a popular experimental system. Research using Dictyostelium has been critical in understanding fundamental processes such as cell migration (8), cell signaling (9,10), phagocytosis and morphogenesis. Recently Dictyostelium has also been used to help establish the mechanisms of action of medically important drugs such as cisplatin (11–14), used to treat various cancers, and lithium and valproic acid (15), used to treat depressive disorders. The recently completed Dictyostelium genome sequence is housed at dictyBase and has been integrated with other experimental data to provide investigators with a rich new resource that will facilitate future studies using Dictyostelium experimentally and for comparative genomics.

GENOME SEQUENCE COMPLETED
In May 2005 the sequence of the complete genome of Dictyostelium was reported (16). The A + T rich genome (77.6%) consists of 34 million bases of DNA sequence that are predicted to encode 13 573 genes—a number of genes comparable with Drosophila. dictyBase houses and maintains the genome sequence produced by the International Sequencing Consortium. As the first free living protozoan to be completely sequenced, the predicted proteome supports the hypothesis that Dictyostelium represents an early branch in the Eukaryotic Tree of Life that diverged after the split between animals, plants and fungi, with Dictyostelium and other amoebae more closely related to animals. Many Dictyostelium proteins are more similar to human orthologs than are those of Saccharomyces cerevisiae. The genome has several notable features. The sequence is very gene dense with an average gene spacing of 2.5 kb. The abundance of short sequence

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repeats produces unusual runs of amino acids, such as polyasparagine and polyglutamine tracts of 20 residues or more. These amino acid repeats occur in >2000 of the predicted proteins. The genome also contains a surprisingly large number of polyketide synthases, which may produce a previously unanticipated large complement of natural products. Consistent with this apparently large secondary metabolism, the genome contains many ABC transporters that may be involved in export of these natural products. Also encoded are a large number of proteins containing multiple EGF repeats that have been postulated to play roles in adhesion or cell recognition.

These fascinating genomic features together with the unique biology of Dictyostelium and the rich body of Dictyostelium literature (nearly 8000 publications) provide a valuable opportunity to annotate many of the genes with functional information that will widen the spectrum of characterized proteins in public databases. This emphasizes the need for a well-curated database for Dictyostelium—a need that dictyBase strives to fulfill.

dictyBase LINKS GENOME SEQUENCE TO FUNCTIONAL INFORMATION

As the MOD for D.discoideum, dictyBase provides highly curated information that facilitates research by providing a searchable, structured repository of Dictyostelium experimental results. In addition to the complete genome sequence, groups performing high-throughput experiments such as large-scale mutagenesis and microarray-based gene expression studies are depositing their data in dictyBase for integration and distribution to the research community. dictyBase uses the genomic DNA sequence as a scaffold on which to organize and display the biological knowledge and experimental evidence derived from Dictyostelium research. dictyBase is the most comprehensive source of information regarding Dictyostelium, and the database presents the highest quality annotations of Dictyostelium genes. Table 1 presents the data content of dictyBase as of September 2005. Nearly all of the data in dictyBase is available for bulk download through our download center (http://dictybase.org/downloads/).

The heart of dictyBase is the Gene Page. A Gene Page is available for each gene that has been shown or predicted to exist in the genome. The Gene Page collects and organizes all of the available information related to that gene into several sections. Figure 1 shows an example of a typical Gene Page. A General Information section provides the official gene name together with any other names that have been used to refer to that gene. This assures that a search of the database will allow retrieval of a gene using any name that has been used to refer to that gene. Scientific curators verify published and proposed gene names to encourage use of the Dictyostelium Nomenclature Guidelines (http://dictybase.org/nomenclatureguidelines.htm) and to ensure that names are not duplicated. When appropriate, curators communicate with authors to discuss and modify gene names. Also in this section, gene product names and a brief description of the gene product are presented, as is the unique dictyBaseID. Next, the Chromosomal Coordinates section presents a graphical view of the gene and associated sequences such as expressed sequence tags (ESTs), cDNAs and other GenBank entries. An Associated Sequences section provides links to sequences corresponding to each of the sequence features known for that gene, including gene predictions as well as ESTs, cDNAs and genomic sequences submitted by individual researchers to other public databases. The Protein Information section contains the size, molecular weight and protein domains of the predicted protein.

Functional information is presented in sections for Gene Ontology (GO) annotations and phenotypes whenever this information is available. Phenotypic data is represented using a restricted vocabulary that describes the consequences of mutations reported for that gene. The Gene Ontology section lists terms from each of the function, process and component ontologies associated with the gene (17,18). Following links in each of these sections display additional details for these annotations. Clicking on a GO term or a phenotype will list all of the other genes annotated with the same term. The Expression section leads to developmental profiles for the gene that have been generated by large-scale microarray based studies performed at the Baylor College of Medicine and the University of California, San Diego. The Links section on the Gene Page provides links to GenBank, UniProt, GeneDB at the Sanger Institute and, where appropriate, to signaling pathways at the Signal Transduction Knowledge Environment at Science (19,20). This section also links to researchers in our colleague database who are investigating that gene or gene product. A Literature Section lists the most recent publications referring to the gene and a link to a Literature Guide that contains a complete listing of papers relevant to that gene. As of the fall of 2005, >500 Gene Pages had a Summary paragraph written by a dictyBase curator that contains the current knowledge regarding that gene. dictyBase curators are in the process of manually reviewing all of the automated gene predictions in light of available data such as ESTs and cDNAs. Manually reviewed genes are indicated by the presence of a ‘Curated Model’ on the Gene Page. As of September 2005 dictyBase curators have reviewed nearly 2500 genes, which corresponds to ~20% of the total number of genes.

Table 1. Data and annotations in dictyBase (September 2005)

- 13,573 Automated Gene Predictions
- 1387 GenBank records
- 155,032 ESTs
- 6,011 PubMed references
- 1,131 Colleagues
- 2,445 Curated Models
- Nine alternative transcripts
- Gene products for 5,228 genes
- Brief descriptions for 1,657 genes
- Mutant phenotypes for 322 genes
- GO annotations for 5,097 genes
- Summary paragraphs for 502 genes
- External data:
  - 6,801 Microarray expression profiles (BCM and UCSD)
  - In situ hybridization: 150 images (Tsukuba Atlas)
  - Insertional mutants: 817 links (BCM)
  - DSC:
    - 728 strains
    - 153 plasmids

| Data and annotations in dictyBase (September 2005) | Number of Entries |
|-----------------------------------------------|-------------------|
| Automated Gene Predictions                    | 13,573            |
| GenBank records                               | 1,387             |
| ESTs                                          | 155,032           |
| PubMed references                             | 6,011             |
| Colleagues                                    | 1,131             |
| Curated Models                                | 2,445             |
| Alternative Transcripts                        | 9                  |
| Gene Products                                 | 5,228             |
| Brief Descriptions                            | 1,657             |
| Mutant Phenotypes                             | 322               |
| GO Annotations                                | 5,097             |
| Summary Paragraphs                            | 502               |
| External Data                                 |                   |
| Microarray Expression Profiles                | 6,801             |
| In situ Hybridization images                  | 150               |
| Insertional Mutants                           | 817               |
| DSC                                           |                   |
| Strains                                       | 728               |
| Plasmids                                      | 153               |
Figure 1. A typical dictyBase Gene Page. This sample Gene Page shows the types of information that are displayed on a dictyBase Gene Page.
GENERAL RESOURCES FOR DICTYOSTELIUM
dictyBase also serves as a clearinghouse for resource materials for students, researchers and educators using Dictyostelium in a wide range of classroom and laboratory settings. We maintain archives of the dictyNews, a weekly electronic newsletter that presents abstracts of papers available upon acceptance for publication, as well as a growing collection of protocols for working with Dictyostelium.

DICTY STOCK CENTER (DSC)
dictyBase also provides a direct portal to the DSC maintained at Columbia University. This resource provides access to Dictyostelium strains, including natural isolates, targeted mutants and GFP labeled strains. The collection also contains plasmids used to manipulate gene expression or create targeted gene disruptions. Currently the DSC has >700 strains and >150 plasmids all available to researchers. A shopping cart system allows Stock Center users to add strains and proceed to a checkout system familiar to any user of online ordering systems. For users who are also registered as colleagues in the dictyBase colleagues database, addresses for delivery and contact information are populated directly from the database. dictyBase holds all of the Stock Center data and provides the informatics support for the DSC. This will enable increased integration between gene information and strains available through the DSC.

DICTYBASE INCORPORATES SOFTWARE DEVELOPED BY OTHER MODS AND THE GENERIC MODEL ORGANISM DATABASE (GMOD) PROJECT
dictyBase was initially established as a clone of the software developed and generously provided by SGD. dictyBase developers have subsequently integrated several software packages from the GMOD project (http://gmod.org). These include the GBrowse tool for chromosome and map displays and, most recently, the Chado database schema for storing sequence and sequence feature information. This entailed porting of the Chado schema to Oracle since both dictyBase and SGD are implemented in Oracle. dictyBase has developed new code that separates communication with the database from code that generates the HTML interfaces. This object layer facilitated adoption of the Chado schema without significant impact on the presentation interface and enables good software practices such as unit testing.

CONCLUSION AND FUTURE DIRECTIONS
dictyBase strives to present a comprehensive, reliable, carefully curated dataset that integrates sequences, functional annotation, phenotypes, expression data and the research literature, while retaining the flexibility to integrate new data types as they become available. Our goal is to assure that the information in dictyBase is accessible in an effective and intuitive interface useful for biologists, while also maximizing its utility for the bioinformatics community to use computationally. Our operating principles are to respond to users’ needs, to capitalize on the vast efforts of the Dictyostelium research community, and to provide an important link in the network of MODs. As additional amoeba genome sequences become available dictyBase hopes to implement, and where necessary, develop interfaces and tools that facilitate comparative genomics of this diverse group of organisms.

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