The Homeodomain Resource: sequences, structures, DNA binding sites and genomic information

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ABSTRACT
The Homeodomain Resource is an annotated collection of non-redundant protein sequences, three-dimensional structures and genomic information for the homeodomain protein family. Release 3.0 contains 795 full-length homeodomain-containing sequences, 32 experimentally-derived structures and 143 homeobox loci implicated in human genetic disorders. Entries are fully hyperlinked to facilitate easy retrieval of the original records from source databases. A simple search engine with a graphical user interface is provided to query the component databases and assemble customized data sets. A new feature for this release is the addition of DNA recognition sites for all human homeodomain proteins described in the literature. The Homeodomain Resource is freely available through the World Wide Web at http://genome.nhgri.nih.gov/homeodomain.

INTRODUCTION
The homeodomain is a common DNA-binding structural motif found in many eukaryotic regulatory proteins (1,2). Homeodomain proteins are involved in the transcriptional control of many developmentally important genes, and 143 human loci have been linked to various genetic and genomic disorders. X-ray crystallographic and NMR spectroscopic studies (3–11) on several members of this family have revealed that the homeodomain motif is comprised of three α-helices that are folded into a compact globular structure. Helices I and II lie parallel to each other and across from the third helix. This third helix is also referred to as the ‘recognition helix’, as it confers the DNA-binding specificity of individual homeodomain proteins. The homeodomain has been evolutionarily conserved at the structural level (12); this is most evident upon examination of divergent members of the homeodomain family.

The Homeodomain Resource represents a comprehensive collection of information about the homeodomain family. The database contains all available full-length and homeodomain-only sequence data and structures as of October, 2000. The genetic data contained in this database includes information on human diseases in which homeodomain-containing proteins are implicated, cytogenetic map locations and specific mutation data underlying the disease condition. Since its last release (13), 27 new loci for genetic disorders have been identified. The sequence information within the database is automatically updated on a monthly basis, with each entry in the database rigorously selected to assure non-redundancy.

DATABASE DESCRIPTION
The current version of the database contains 795 full-length homeodomain protein sequences isolated from 83 different species (Table 1). The complete full-length sequence data as well as the homeodomain portion of the sequence is available in FASTA format. The database can be searched on the basis of SWISS-PROT ID, GenBank accession number, gene names (both common and alternative), protein description, sequence and organism name. The search engine also supports Boolean queries, allowing users to search on individual fields or on all fields at once. Search results are returned in a tabular format, with hyperlinks to the original records in GenBank and SWISS-PROT, respectively. Individual sequences can also be retrieved in FASTA format from a pop-up window.

Table 1. Homeodomain Resource statistics

<table>
<thead>
<tr>
<th>Category</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total sequences available</td>
<td>3796</td>
</tr>
<tr>
<td>Non-redundant full-length sequences</td>
<td>795</td>
</tr>
<tr>
<td>Genes/gene symbols</td>
<td>375</td>
</tr>
<tr>
<td>Distinct organisms</td>
<td>83</td>
</tr>
<tr>
<td>Three-dimensional structures</td>
<td>32</td>
</tr>
<tr>
<td>Homeobox loci implicated in human genetic disorders</td>
<td>143</td>
</tr>
</tbody>
</table>

The genetic information available for the homeodomain protein family has increased ~23% since the last release, with the inclusion of 27 new loci. The genetic data are compiled from both the literature and from the Online Mendelian Inheritance in Man (OMIM) database at NCBI (http://www.ncbi.nlm.nih.gov/Omim/). As before, a search engine is available for querying this genomic information. Search results are presented in a tabular format with hyperlinks to the original records and can be sorted by disease name, map location, gene symbol, protein name or OMIM identifier. This value-added format allows users easy access to related information.

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A new feature of the Homeodomain Resource is the inclusion of DNA binding sites for human homeodomain loci implicated in genetic or genomic disorders (Fig. 1). These data were obtained by extensive review of the published literature, citations in OMIM, and entries for DNA-bound homeodomain structures from the Protein Data Bank. The core regions of each of the DNA binding sites are shown in bold type. An expanded version of this table is available online (at http://genome.nhgri.nih.gov/homeodomain); the expanded version includes a listing of alternative gene names, as well as citation information.

A new feature of the Homeodomain Resource is the inclusion of DNA binding sites for human homeodomain loci implicated in genetic or genomic disorders (Fig. 1). These data were obtained by extensive review of the published literature, citations in OMIM, and entries for DNA-bound homeodomain structures from the Protein Data Bank. The online version of Figure 1 (available via http://genome.nhgri.nih.gov/homeodomain) includes alternate gene names and references to the primary citation from which the information was retrieved.

REFERENCES


