NCBI FieldGuide

NCBI Molecular Biology Resources

Sept. 2004

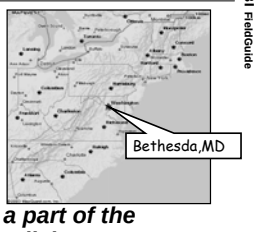
NCBI FieldGuide

NCBI Resources

- About NCBI
- NCBI Databases
- Tools
- Entrez
- Examples

NCBI FieldGuide

The National Center for Biotechnology Information



Created in 1988 as a part of the National Library of Medicine at NIH

- Establish public databases
- Research in computational biology
- Develop software tools for sequence analysis
- Disseminate biomedical information

Molecular Databases

- Sequence
- Structure
- Expression

Types of Databases

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- Primary Databases
  - Original submissions by experimentalists
  - Content controlled by the submitter
    - Examples: GenBank, SNP, GEO
- Derivative Databases
  - Built from primary data
  - Content controlled by third party (NCBI)
    - Examples: Refseq, TPA, RefSNP, UniGene, NCBI Protein, Structure, Conserved Domain

GenBank: NCBI's Primary Sequence Database

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Release 143	August 2004
37,343,937	Records
41,808,045,653	Nucleotides
>140,000	Species
160 Gigabytes	*658 files*

- full release every two months
- incremental and cumulative updates daily
- available only through internet

ftp://ftp.ncbi.nih.gov/genbank/

Traditional GenBank Divisions

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- Direct Submissions (Sequin and BankIt)
- Accurate
- Well characterized

BCT	Bacterial and Archeal
INV	Invertebrate
MAM	Mammalian (ex. ROD and PRI)
PHG	Phage
PLN	Plant and Fungal
PRI	Primate
ROD	Rodent
SYN	Synthetic (vectors, synth. genes)
VRL	Viral
VRT	Other Vertebrate

Bulk Divisions

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- Batch Submission and htg (email and ftp)
- Inaccurate
- Poorly Characterized
- Largest component of GenBank

- Expressed Sequence Tag
  - 1st pass single read cDNA
- Genome Survey Sequence
  - 1st pass single read gDNA
- High Throughput Genomic
  - incomplete sequences of genomic clones
- Sequence Tagged Site
  - PCR-based mapping reagents

GenBank Records

NCBI FieldGuide

```
LOCUS       AY198415                4675 bp    mRNA    linear   PRI 11-AUG-2003
DEFINITION  Homo sapiens PR domain-containing protein 1 beta (PRDM1) mRNA,
            complete cds.
ACCESSION   AY198415
VERSION     AY198415.1  GI:28630982
```

Primate division (traditional)

```
LOCUS       AI588321                 482 bp    mRNA    linear   EST 07-JUN-2001
DEFINITION  fb99c12.x1 Zebrafish WashU MPIMG EST Danio rerio cDNA clone
            IMAGE:3720022 3', mRNA sequence.
ACCESSION   AI588321
VERSION     AI588321.1  GI:4597368
KEYWORDS    EST.
```

EST division (bulk)

```
LOCUS       AC027700               229988 bp    DNA     linear   HTG 19-MAR-2004
DEFINITION  Mus musculus chromosome 10 clone RP23-145G7 map 10, *** SEQUENCING
            IN PROGRESS ***, 3 unordered pieces.
ACCESSION   AC027700
VERSION     AC027700.7  GI:45593019
KEYWORDS    HTG; HTGS_PHASE1; HTGS_FULLTOP; HTGS_ACTIVEFIN.
SOURCE      Mus musculus (house mouse)
```

HTG division (bulk)

```
LOCUS       AADN01000358           53718 bp    DNA     linear   VRT 29-FEB-2004
DEFINITION  Gallus gallus chromosome 3 Cont0.358, whole genome shotgun
            sequence.
ACCESSION   AADN01000358 AADN01000000
VERSION     AADN01000358.1  GI:44803930
KEYWORDS    WGS.
SOURCE      Gallus gallus (chicken)
```

Vertebrate division (chicken WGS)

RefSeq: NCBI's Derivative Sequence Database

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- **Curated transcripts and proteins**
  - reviewed
  - human, mouse, rat, fruit fly, zebrafish, arabidopsis microbial genomes (proteins)
- **Model transcripts and proteins**
- **Assembled Genomic Regions (contigs)**
  - human genome
  - mouse genome
- **Chromosome records**
  - Human genome
  - microbial
  - organelle

`srcdb_refseq[Properties]`

ftp://ftp.ncbi.nih.gov/refseq/release/

RefSeq Records

NCBI FieldGuide

```
LOCUS       NM_007548               5281 bp    mRNA    linear   ROD 25-AUG-2004
DEFINITION  Mus musculus PR domain containing 1, with ZNF domain (Prdm1), mRNA.
ACCESSION   NM_007548
VERSION     NM_007548.1  GI:6680783
```

Curated transcript

```
LOCUS       NT_039492           23191165 bp    DNA     linear   CON 31-AUG-2004
DEFINITION  Mus musculus chromosome 10 genomic contig, strain C57BL/6J.
ACCESSION   NT_039492
VERSION     NT_039492.3  GI:51765603
KEYWORDS    .
SOURCE      Mus musculus (house mouse)
```

RefSeq contig

```
LOCUS       XP_228320                1022 aa            linear   ROD 23-OCT-2003
DEFINITION  similar to Blimp-1 [Rattus norvegicus].
ACCESSION   XP_228320
VERSION     XP_228320.2  GI:34853200
DBSOURCE    REFSEQ: accession XM_228320.2
KEYWORDS    .
SOURCE      Rattus norvegicus (Norway rat)
```

RefSeq gene model

```
LOCUS       NC_000006          170975699 bp    DNA     linear   CON 24-AUG-2004
DEFINITION  Homo sapiens chromosome 6, complete sequence.
ACCESSION   NC_000006
VERSION     NC_000006.9  GI:51511722
KEYWORDS    HTG.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
```

RefSeq chromosome

Third Party Annotation (TPA) Database

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- Annotations of existing GenBank sequences
- Allows for community annotation of genomes
- Direct submissions
  - BankIt

`tpa[Properties]`

NCBI's SNP Database

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- Primary Database and Derivative (RefSNP)
- Single Nucleotide Polymorphism
- Repeat polymorphisms
- Insertion-Deletion Polymorphisms
- 19 Species
- Over 11 million submissions

RefSNP HFE

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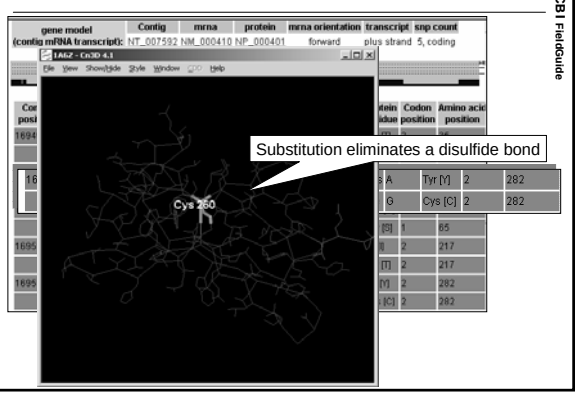

What is UniGene?

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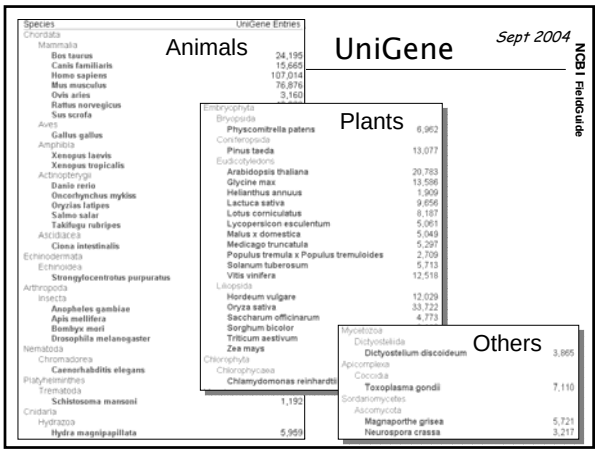
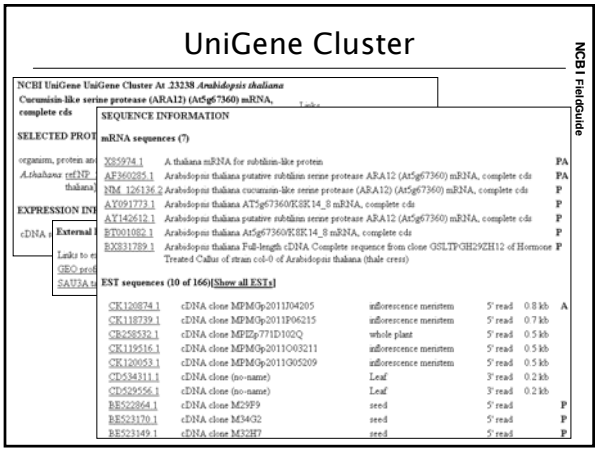
A gene-oriented view of sequence entries

- **MegaBlast based automated sequence clustering**
- **Now informed by genome hits *New!***
- **Nonredundant set of gene oriented clusters**
- **Each cluster a unique gene**
- **Information on tissue types and map locations**
- **Includes known genes and uncharaterized ESTs**
- **Useful for gene discovery and selection of mapping reagents**





Gene Expression Omnibus

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- Expression Data Repository
  - microarray
    - protein
    - nucleotide
  - SAGE
  - Mass Spec

Current holdings:

Number of:	Public	Unreleased	Total
Platforms:	834	74	908
Samples:	23072	5410	28482
Series:	1192	305	1497

MMDB: Molecular Modeling Data Base

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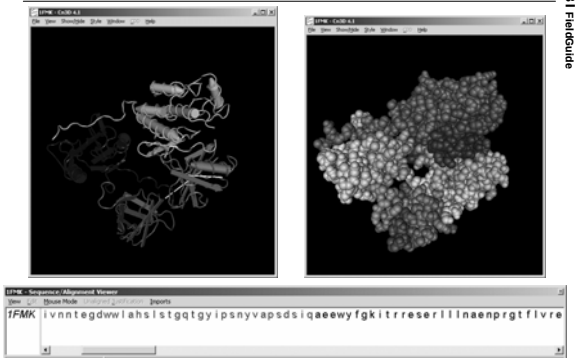
- Derived from experimentally determined PDB records
- Value added to PDB records including:
  - Addition of explicit chemical graph information
  - Validation
  - Inclusion of Taxonomy, Citation, and other information
  - Conversion to ASN.1 data description language
- Structure neighbors determined by Vector Alignment Search Tool (VAST)

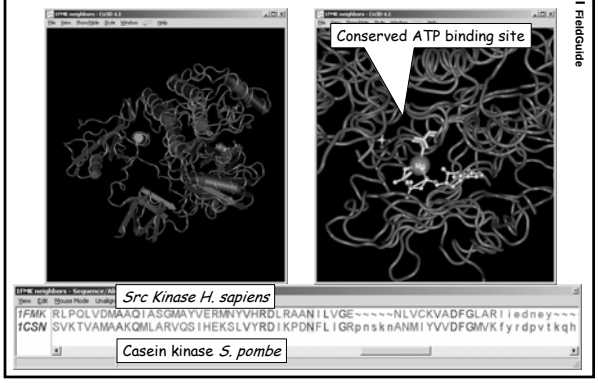
Cn3D 4.1: C-SRC

NCBI FieldGuide



Cn3D 4.1: Structural Alignment

NCBI FieldGuide



Cn3D: Simple Homology Modeling

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NCBI's Conserved Domain Database

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- Multiple sequence alignments
- PSI-BLAST –based score matrices
- Sources SMART, PFAM, COGs
- New NCBI curated domains
  - structure informed alignments
- Stats:
  - COGS 4,873
  - Pfam 5,193
  - Smart 653
  - NCBI CDD 316

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NCBI Tools

BLAST
VAST

Basic Local Alignment Search Tool

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- Calculates similarity for biological sequences
- Finds best local alignments
- Heuristic approach based on Smith-Waterman algorithm
- Searches for matching “words” rather than individual residues
- Uses statistical theory to determine if a match might have occurred by chance

The Flavors of BLAST

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- Standard BLAST
  - traditional contiguous word hit
  - position independent scoring
  - nucleotide, protein and translations
- Megablast
  - optimized for large batch searches
  - can use discontiguous words
- PSI-BLAST
  - constructs PSSMs automatically
  - searches protein database with PSSMs
- RPS BLAST
  - searches a database of PSSMs
  - basis of conserved domain database

WWW BLAST

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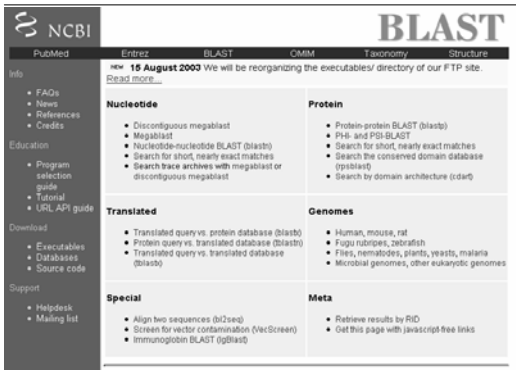

BLAST Search

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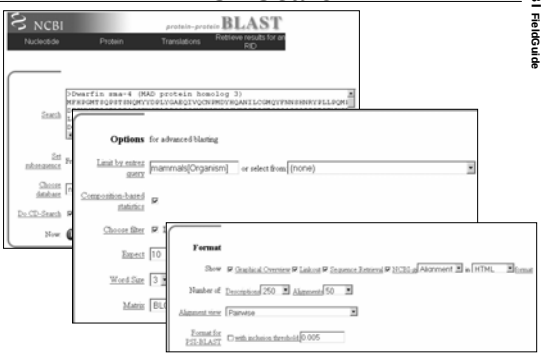
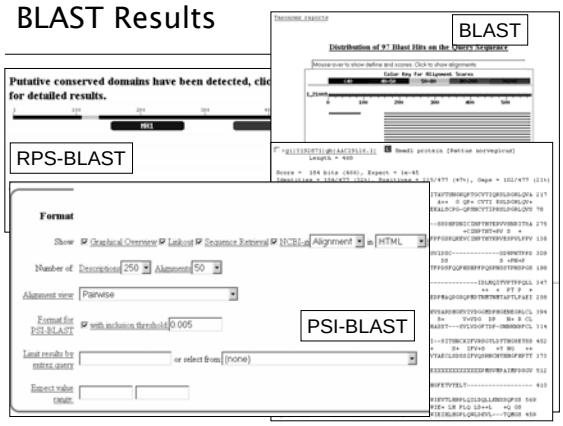
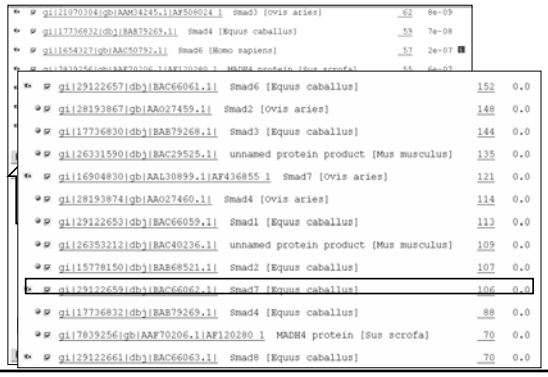


BLAST Results



PSI-BLAST

NCBI FieldGuide



VAST: Structure Neighbors

Vector Alignment Search Tool

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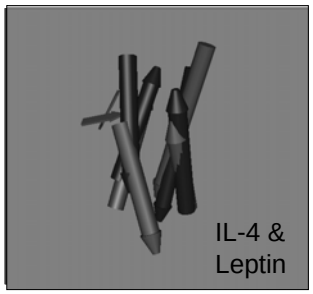
For each protein chain,

locate SSEs (secondary structure elements),

and represent them as individual vectors.

align the vectors



Human IL-4

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Finding a human PR domain RefSeq

- Finding PRDM1
- Links and Neighbors with PRDM1

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WWW Access

Entrez & BLAST

Entrez: Database Integration

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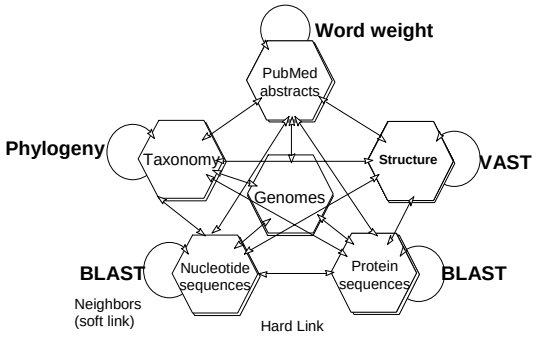
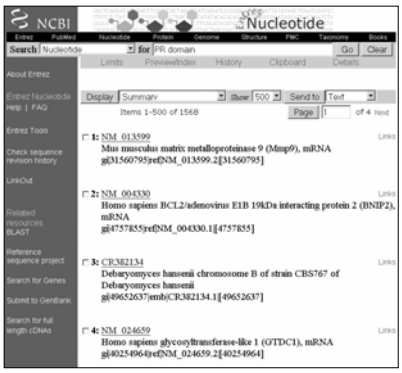


PR Domain Global Search

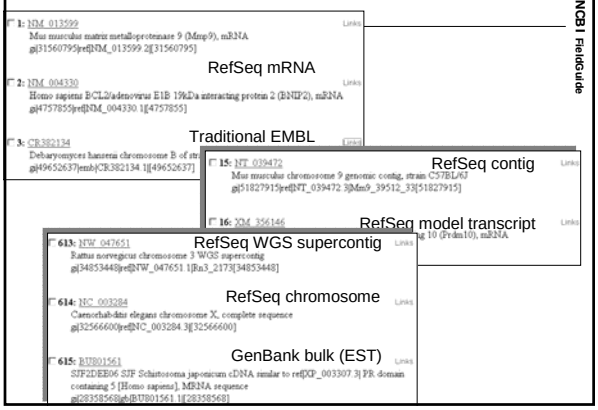
NCBI FieldGuide

PM Domain search results

NCBI FieldGuide



PM Domain search results



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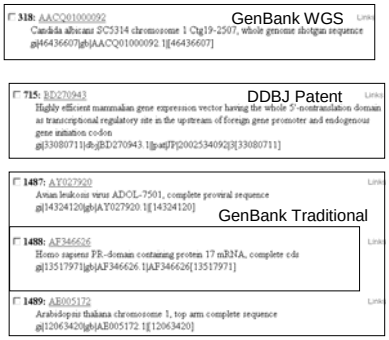
PM Domain search results (continued)



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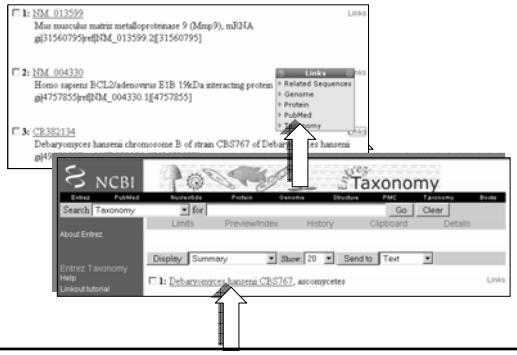
What is *Debaryomyces*?



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Debaryomyces: Taxonomy Browser

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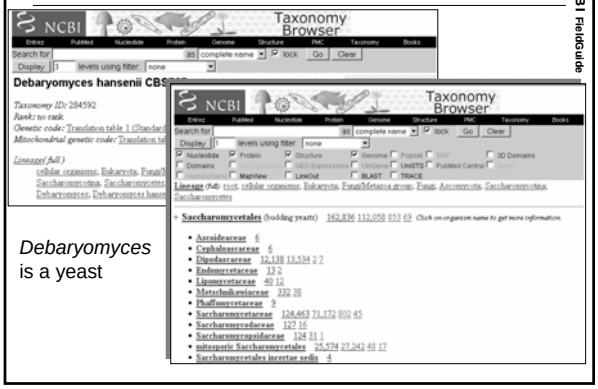

Debaryomyces is a yeast

Refining Search

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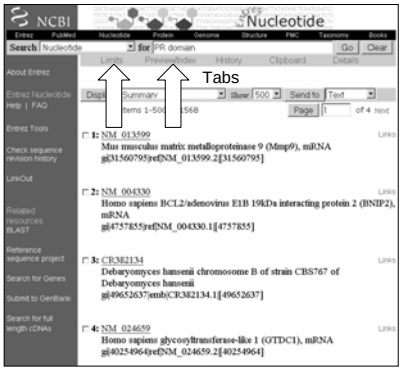
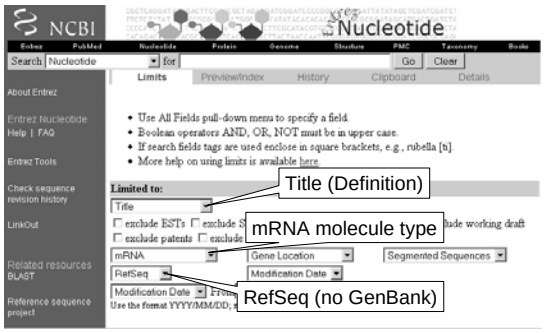


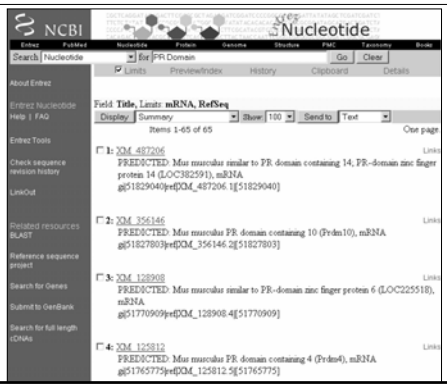
Limits

NCBI FieldGuide



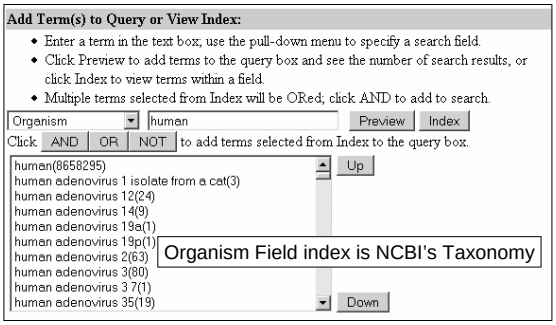
Limited Search Results

NCBI | FieldGuide



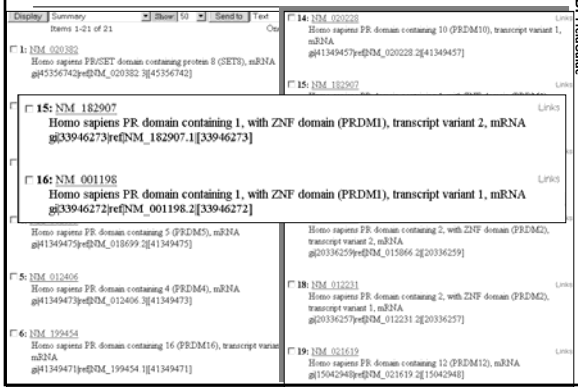
Preview / Index: Adding Terms

NCBI | FieldGuide



Human PR domain RefSeqs

NCBI | FieldGuide



PRDM Reviewed RefSeq

NCBI FieldGuide

1: NM_001198. Homo sapiens PR d...[gi:33946272]

```
LOCUS       NM_001198                5165 bp    mRNA    linear   PRI 23-AUG-2004
DEFINITION  Homo sapiens PR domain containing 1, with ZNF domain (PRDM1),
            transcript variant 1, mRNA.
ACCESSION   NM_001198
VERSION     NM_001198.2  GI:33946272
KEYWORDS
COMMENT     REVIEWED REFSEQ: This record has been curated by NCBI staff. The
            reference sequence was derived from AY198414.1.
            On Aug 20, 2003 this sequence version replaced gi:4557362.

            Summary: This gene encodes a protein that acts as a repressor of
            beta-interferon gene expression. The protein binds specifically to
            the PRDI (positive regulatory domain I element) of the beta-IFN
            gene promoter. Transcription of this gene increases upon virus
            induction. Two alternatively spliced transcript variants that
            encode different isoforms have been reported.

            Transcript Variant: This variant (1), also known as PRDM1alpha,
            encodes the longer isoform (1). The protein encoded by this
            transcript has also been named PRDI-BF1alpha.
            COMPLETENESS: complete on the 3' end.
            lines
  JOURNAL   J. Immunol. 170 (6), 3125-3133 (2003)
   PUBMED   12626569
  REMARK    GeneRIF: PRDI-BF1 beta is abundantly expressed in myeloma cell
            lines through alternative transcription initiation, has a disrupted
            PR domain and a significantly impaired transcription repressor
            function on multiple target genes.
REFERENCE   3  (bases 1 to 5165)
```

Links Menu

NCBI FieldGuide

1: NM_001198. Homo sapiens PR d...[gi:33946272]

```
LOCUS       NM_001198                5165 bp    mRNA    linear
DEFINITION  Homo sapiens PR domain containing 1, with ZNF doma
            transcript variant 1, mRNA.
ACCESSION   NM_001198
VERSION     NM_001198.2  GI:33946272
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata
            Mammalia; Eutheria; Primates; Catarrhini; Hominida
REFERENCE   1  (bases 1 to 5165)
  AUTHORS   Gyory,I., Wu,J., Fejer,G., Seto,E. and Wright,K.L.
  TITLE     PRDI-BF1 recruits the histone H3 methyltransferase
            transcriptional silencing
  JOURNAL   Nat. Immunol. 5 (3), 299-308 (2004)
   PUBMED   14985713
  REMARK    GeneRIF: PRDI-BF1 mediates silencing of interferon-beta gene
            transcription via recruitment of the histone H3 methyltransferase
            G9a.
REFERENCE   2  (bases 1 to 5165)
  AUTHORS   Gyory,I., Fejer,G., Ghosh,N., Seto,E. and Wright,K.L.
  TITLE     Identification of a functionally impaired positive regulatory
            domain I binding factor 1 transcription repressor in myeloma cell
            lines
  JOURNAL   J. Immunol. 170 (6), 3125-3133 (2003)
   PUBMED   12626569
  REMARK    GeneRIF: PRDI-BF1 beta is abundantly expressed in myeloma cell
            lines through alternative transcription initiation, has a disrupted
            PR domain and a significantly impaired transcription repressor
            function on multiple target genes.
REFERENCE   3  (bases 1 to 5165)
```

Links
- Gene
- HomoloGene
- Master
- Related Sequences
- Map Viewer
- OMIM
- Protein
- PubMed
- SNP
- Taxonomy
- UniGene
- UniSTS
- LinkOut

Online Mendelian Inheritance in Man

NCBI FieldGuide

NCBI

MIM *603423
Cloning
Mapping
Animal Model
References
Contributors
Creation Date
Edit History

Gene map

Entrez Gene
Nomenclature
RefSeq
GenBank
Protein
UniGene

LinkOut

*603423
PR DOMAIN-CONTAINING PROTEIN 1; PRDM1

Alternative titles; symbols

B LYMPHOCYTE-INDUCED MATURATION PROTEIN 1; BLIMP1
POSITIVE REGULATORY DOMAIN I-BINDING FACTOR 1; PRDI-BF1

Gene map locus 6q21-q22.1

TEXT

CLONING

The DNA sequences that are required for the transient induction of the beta-interferon gene (147640) by virus are located within the beta-interferon promoter in a region containing both positive and negative regulatory sequences, including an element designated the 'positive regulatory domain I' (PRDI). By screening a human cDNA expression library with a probe containing multiple PRDI sites, Keller and Maniatis (1 isolated a cDNA encoding a novel repressor of human beta-interferon gene expression which they designated PRDI-BF1 for 'PRDI-binding factor-1.' The deduced 789-amino acid PRDI-BF1 protein has a predicted molecular mass of 88 kD and contains 5 zinc fingers of the TFIIIA (600520) type near the C terminus. Northern blot analysis detected 5.7- and 3.5-kb PRDI-BF1 messages in a human osteosarcoma cell line. The authors demonstrated that transcription of the PRDI-BF1 gene increases upon virus induction. They showed that PRDI-BF1 binds specifically to the PRDI element and is a repressor of PRDI-dependent transcription; repression was highly dependent on the location of the PRDI site.

Huang (1994) determined that PRDI-BF1 is the human homolog of the mouse Blimp1 gene, the expression of which drives the terminal differentiation of B lymphocytes. The author also identified a novel stretch of 100 amino acids, which he named the PR domain, that is conserved between PRDI-BF1 and RIZ (601196).

- Zn Finger domains
- PR Domain
- Homologs
  - BLIMP1 Mouse
  - U-boot Zebrafish
- Genomic context

Protein Link -> Related Sequences

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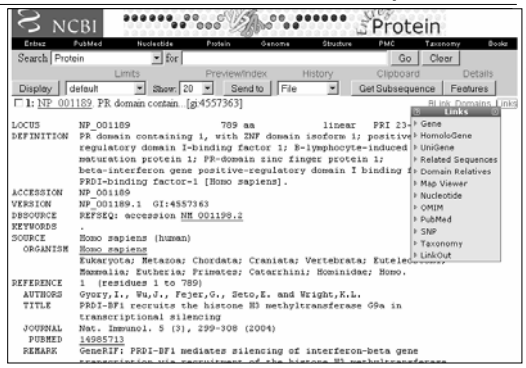
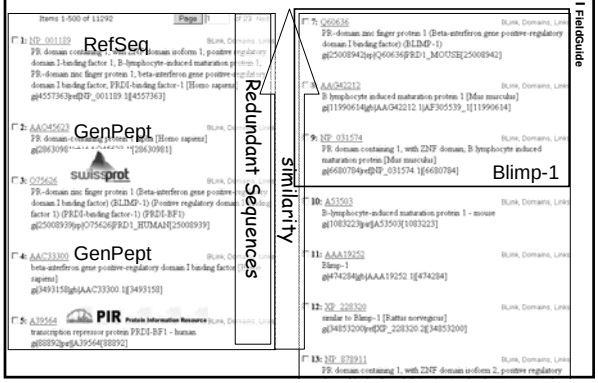


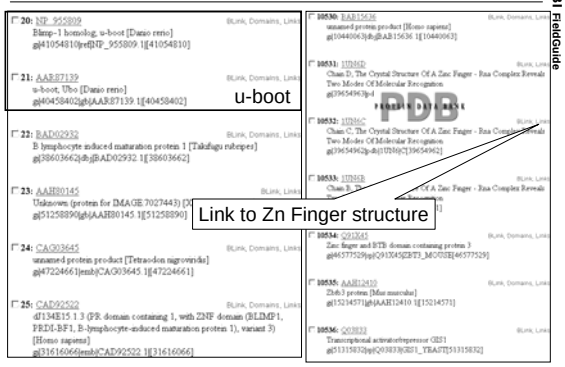
Protein Neighbors: Redundancy and homologs

NCBI FieldGuide



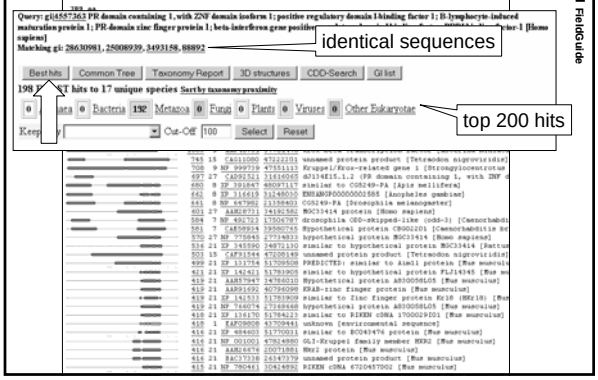
Homologs (cont.)

NCBI FieldGuide



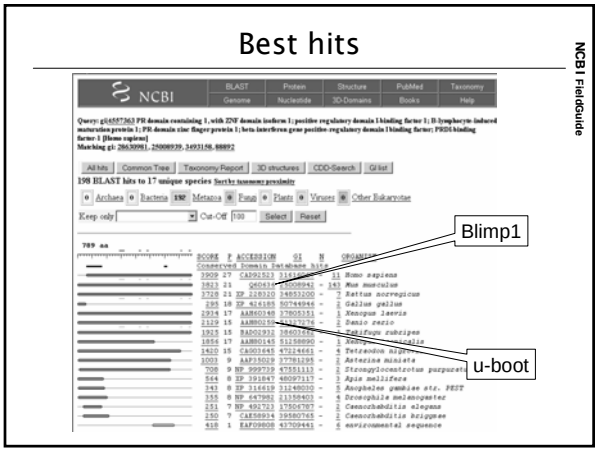
BLink: Non-redundant neighbors

NCBI FieldGuide



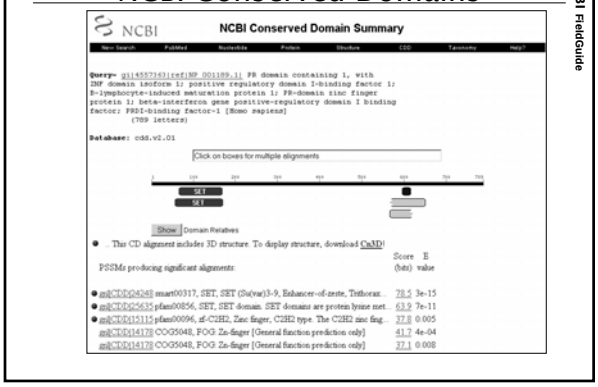
Best hits

NCBI FieldGuide

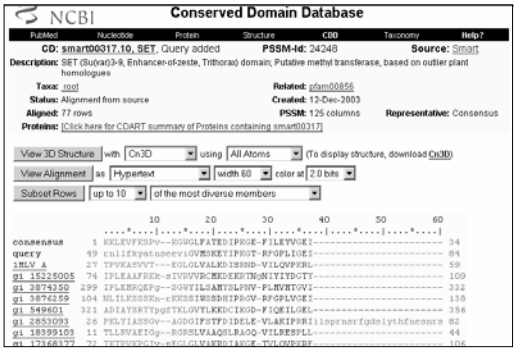


NCBI Conserved Domains

NCBI FieldGuide

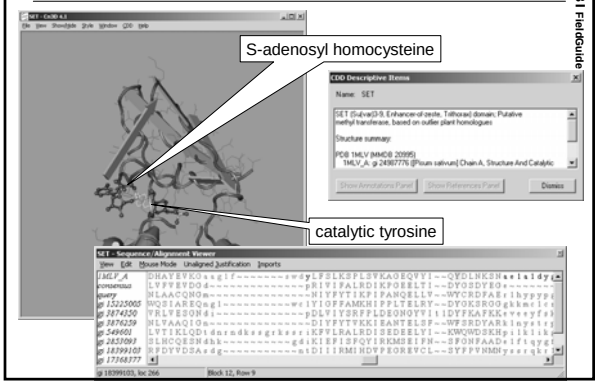


The SET Domain



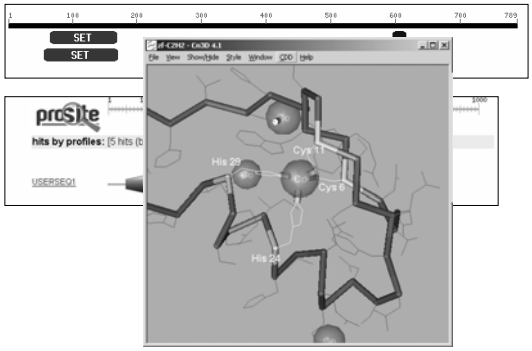
NCBI FieldGuide

SET Domain Structural Model



NCBI FieldGuide

Zn finger: a DNA binding motif



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Entrez Gene: One stop shopping

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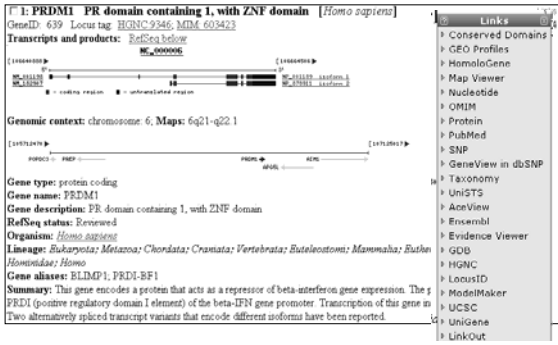

HomoloGene: homologs in complete genomes

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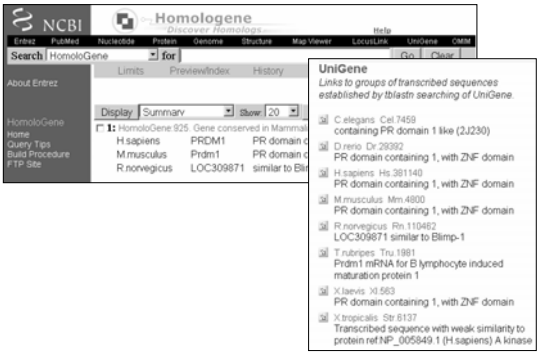

Map Viewer: PRDM1

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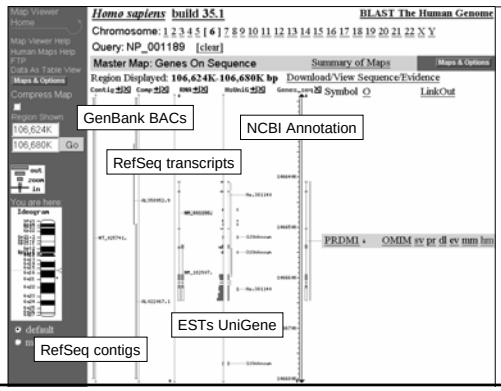
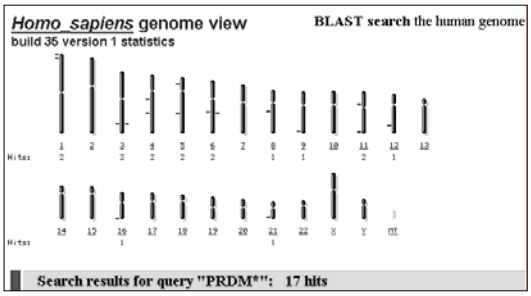


PRDM1: Potential Paralogs



NCBI FieldGuide