Informatics in Biological Research

Agenda for Informatics in the Biological Sciences

University of Chicago *13 Jan 2003*

Peter Cooper
National Center for Biotechnology Information

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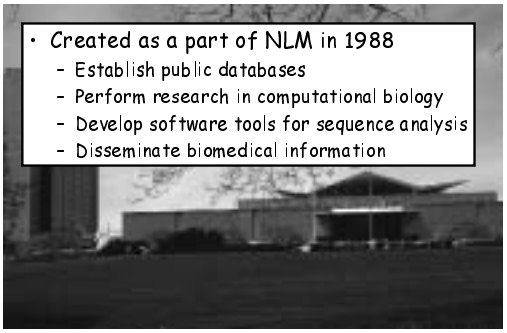
The National Center for Biotechnology Information



- Created as a part of NLM in 1988
  - Establish public databases
  - Perform research in computational biology
  - Develop software tools for sequence analysis
  - Disseminate biomedical information

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The Revolutions

- Biology
  - DNA sequencing
  - High throughput methodologies
  - Improvements in cloning techology
  - PCR
  - Microarray techniques
- Computer Science
  - CPU speed
  - Storage devices
  - The Internet and the WWW

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The Selection Pressure

"It's sink or swim as a tidal wave of data approaches"

Nature 399:517 10 June 1999

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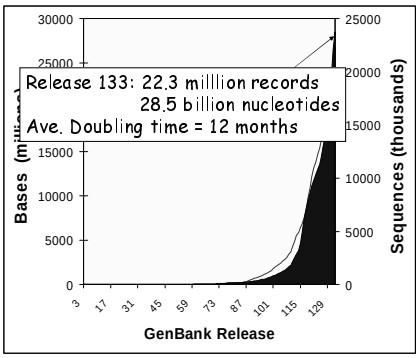
The Growth of GenBank



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The Genome Sequencing Era

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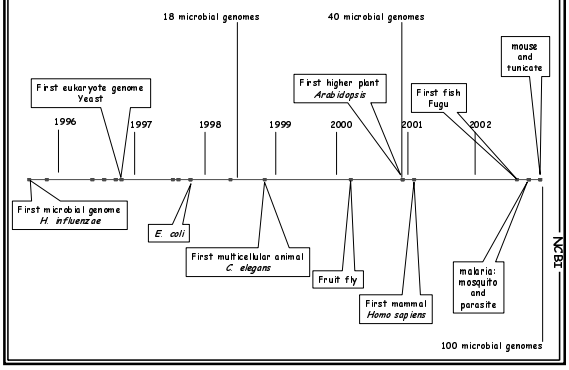
The Genome Sequencing Era



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Coming soon …

- Nearly done
  - rat
  - purple sea urchin
  - zebrafish
- NHGRI's Priority Organisms
  - Chicken
  - Cow
  - Dog
  - Chimpanzee
  - Honeybee
  - *Tetrahymena*
  - *Oxytichia*
  - Several fungi
- Over 100 bacterial genomes

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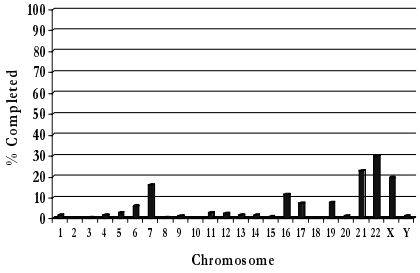
Human Genome Sequencing Progress

June 1998



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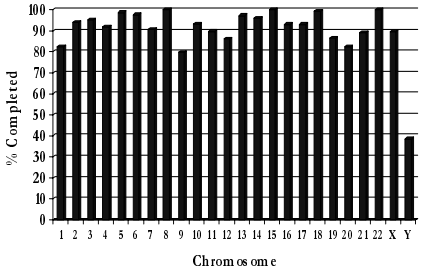
Human Genome Sequencing Progress

Dec. 2002



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The Rapid Evolution of Resources

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Web Access

Text

Entrez

Sequence

BLAST

Structure

VAST

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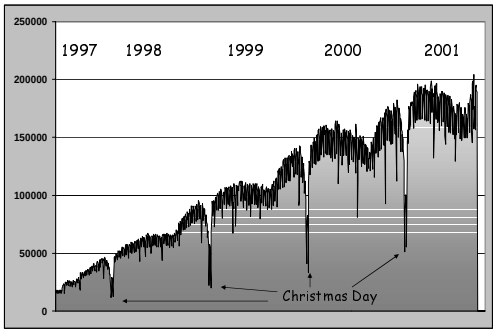
Users per day



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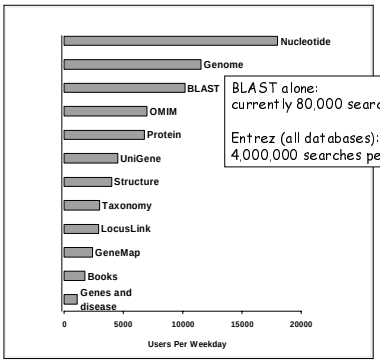
Some Web Statistics



BLAST alone:
currently 80,000 searches per day

Entrez (all databases):
4,000,000 searches per day

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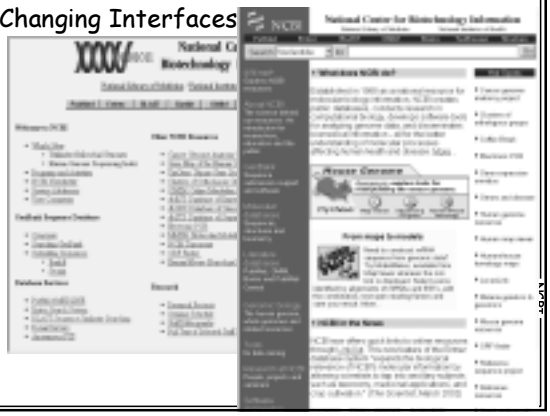
Changing Interfaces



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Changing Interfaces

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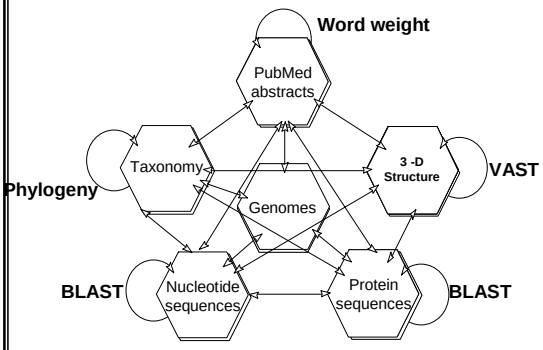
Entrez: Database Integration



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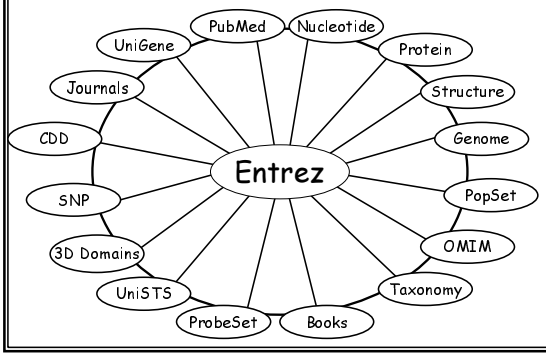
The (ever) Expanding Entrez System



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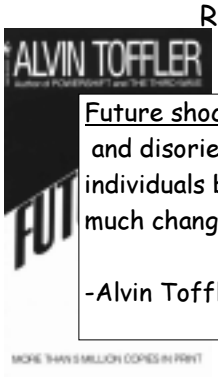
Revolution



Future shock: the shattering stress and disorientation that we induce in individuals by subjecting them to too much change in too short a time.

-Alvin Toffler

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The Promise of Computational Biology

Gene

```
> DNA sequence
AATTCATGAAAATCGTATACTGGTCTGGTACCGGCAACAC
TGAGAAAATGGCAGAGCTCATCGCTAAAGGTATCATCGAA
TCTGGTAAAGACGTCAACACCATCAACGTGTCTGACGTTA
ACATCGATGAACTGCTGAACGAAGATATCCTGATCCTGGG
TTGCTCTGCCATGGGCGATGAAGTTCTCGAGGAAAGCGAA
TTTGAACCGTTCATCGAAGAGATCTCTACCAAAATCTCTG
GTAAGAAGGTTGCGCTGTTCGGTTCTTACGGTTGGGGCGA
CGGTAAGTGGATGCGTGACTTCGAAGAACGTATGAACGGC
TACGGTTGCGTTGTTGTTGAGACCCCGCTGATCGTTCAGA
ACGAGCCGGACGAAGCTGAGCAGGACTGCATCGAATTTGG
TAAGAAGATCGCGAACATCTAGTAGA
```

Structure & Function

```
> Protein sequence
MKIVYWSGTGNTEKMAELIAKGIIESGKDVNTINVSDVNI
DELLNEDILILGCSAMGDEVLEESEFEPFIEEISTKISGK
KVALFGSYGWGDGKMRDFEERMNGYGCVVVETPLIVQNE
PDEAEQDCIEFGKKIANI
```

The power of computing on the data

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The Cross-over to "Functional Genomics"

"In the past we have had functions in search of sequences. In the future, pathology and physiology will become 'functionators' *for the sequences*."

Daniel C. Tosteson, Dean
Harvard Medical School
March 26, 1997

The future is NOW.

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Comparative Analysis of Genomes

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"What is true for *E. coli* is also true for elephant." Jacques Monod, c. 1961

"What is true for yeast is also true for human." David Botstein, 1988

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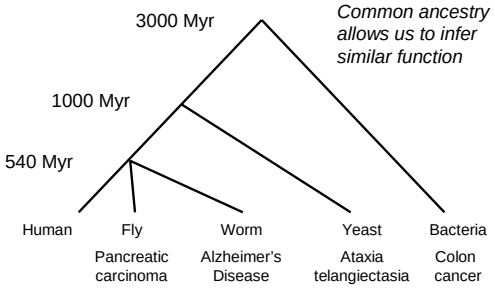
Molecular Evolution



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"Homology...

... is the central concept for *all* of biology. Whenever we say that a mammalian hormone is the 'same' hormone as a fish hormone, that a human gene sequence is the 'same' as a sequence in a chimp or a mouse, that a HOX gene is the 'same' in a mouse, a fruit fly, a frog, and a human -- even when we argue that discoveries about a worm, a fruit fly, a frog, a mouse, or a chimp have relevance to the human condition -- we have made a bold and direct statement about homology. The aggressive confidence of modern biomedical science implies that we know what we are talking about."

David B. Wake

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Application:
MLH1 Homolog in *Anopheles gambiae*

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Annotation on the fly: mosquito genome

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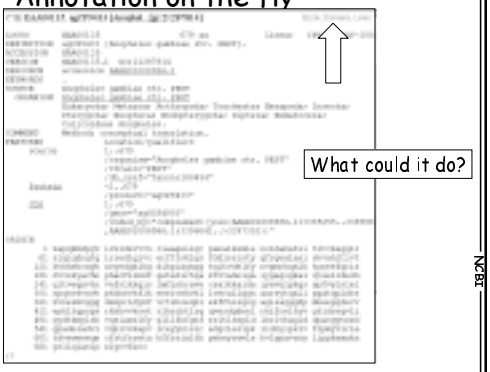
Annotation on the fly



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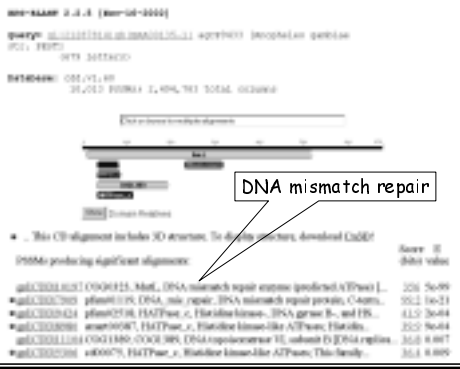
Conserved Domains



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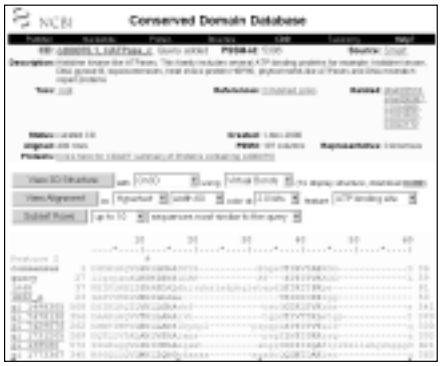
NCBI Curated CD



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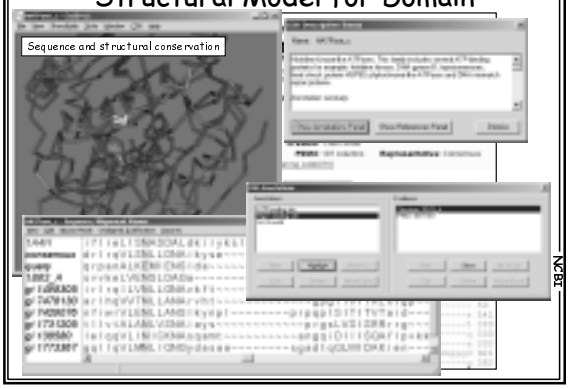
Structural Model for Domain



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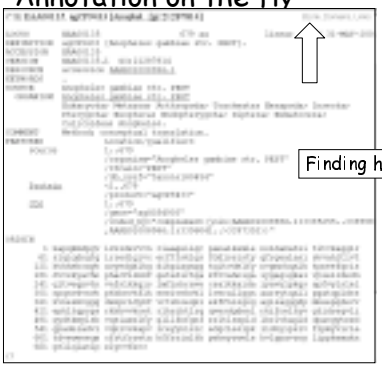
Annotation on the fly



Finding homologues

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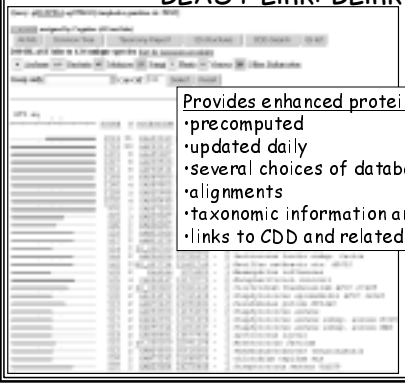
BLAST Link: BLink



Provides enhanced protein BLAST output
- precomputed
- updated daily
- several choices of database
- alignments
- taxonomic information and sorting
- links to CDD and related structures

NCBI

BLAST Link: BLink

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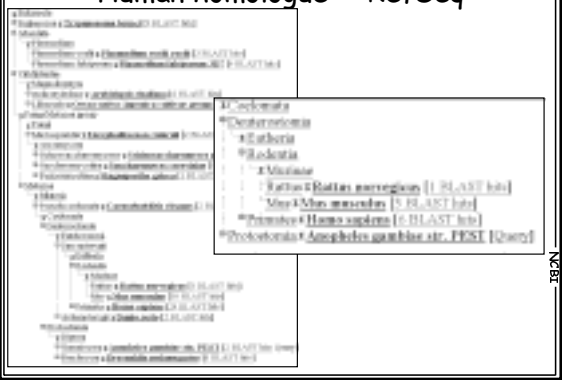
Human homologue -> RefSeq



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NCBI Curated Proteins

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NCBI Curated Proteins

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NCBI Curated Proteins

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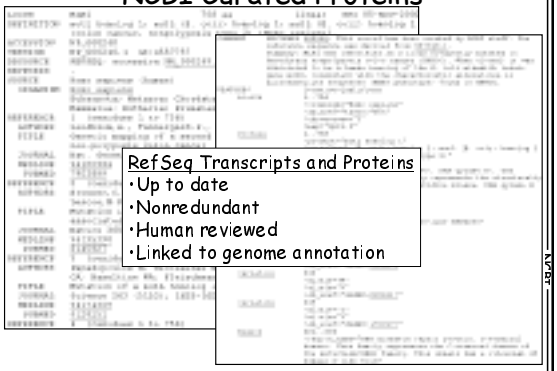

RefSeq Transcripts and Proteins
- Up to date
- Nonredundant
- Human reviewed
- Linked to genome annotation

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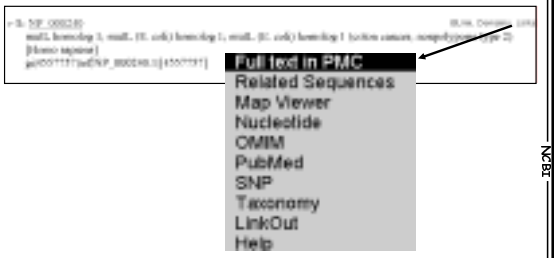
Links and Neighbors Human mutL



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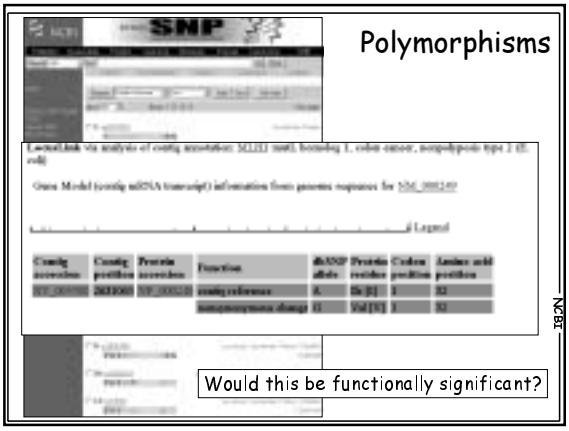
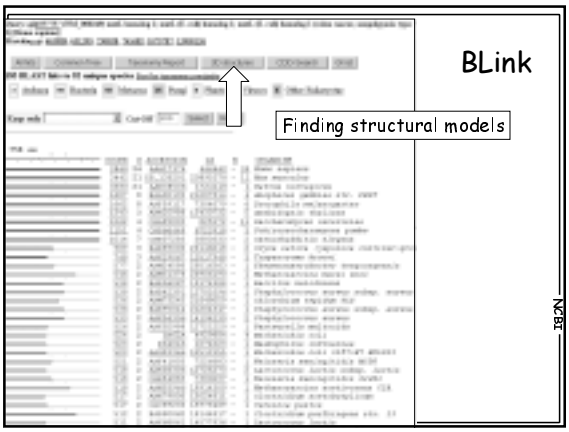
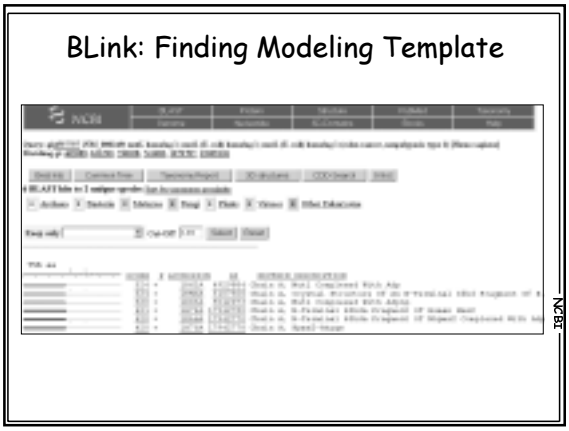
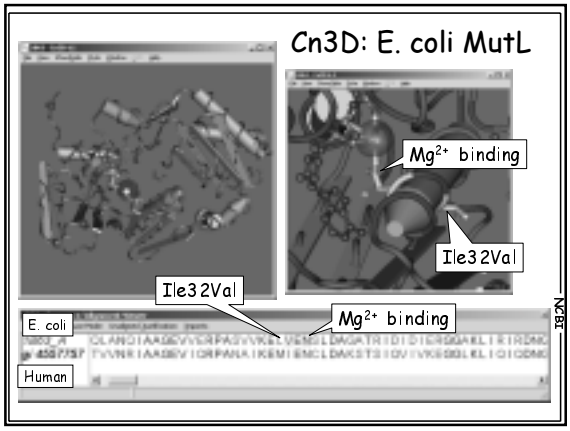
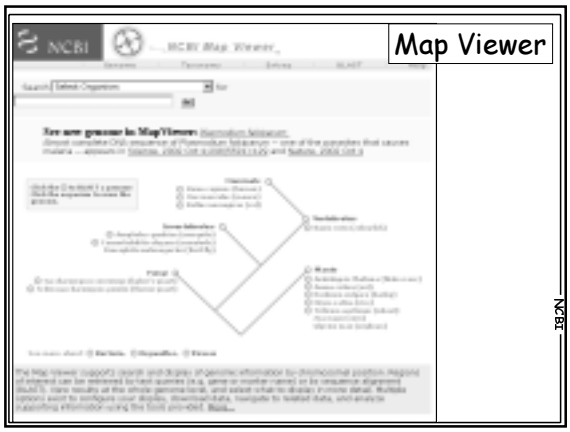
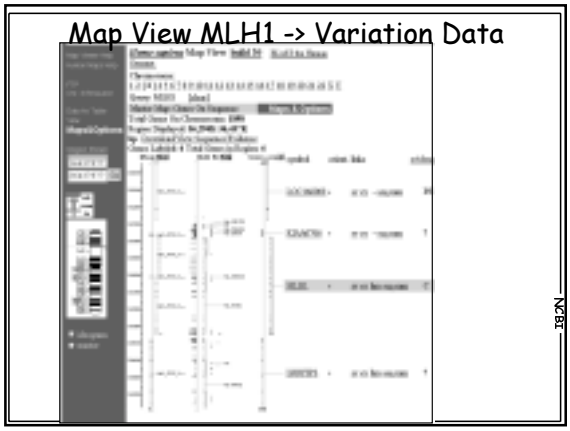

Polymorphisms
Would this be functionally significant?
NCBI


BLink
Finding structural models
NCBI

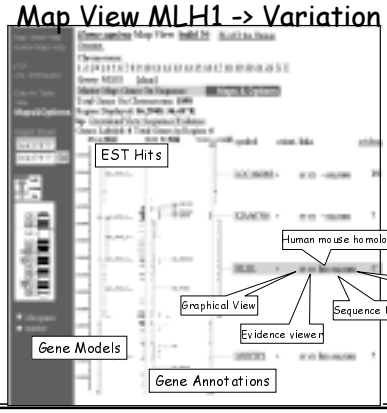

BLink: Finding Modeling Template
NCBI


Cn3D: E. coli MutL
Mg2+ binding
Ile32Val
Ile32Val
Mg2+ binding
E. coli
Human
NCBI


NCBI
Map Viewer
NCBI


Map View MLH1 -> Variation Data
NCBI

Map View MLH1 -> Variation Data



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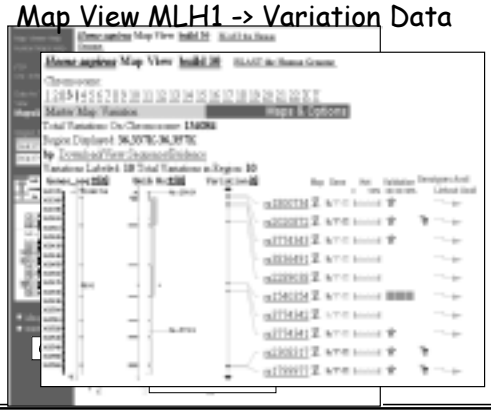
Map View MLH1 -> Variation Data



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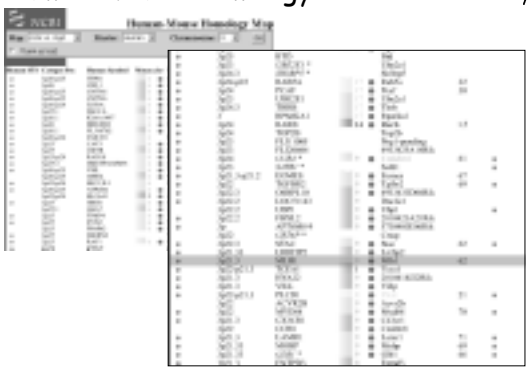
Human Mouse Homology: the mouse assembly



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The Mouse Assembly

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NCBI Training

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Field Guide Content

One day practical training course

- Molecular Databases
  - GenBank
  - RefSeq
- Web Access
  - Entrez
  - BLAST
- Genomic Biology

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Summary Aug 1998 - Dec 2002

- 90 Field Guides
- 3 BLAST courses
- 17 short courses
- 36 States plus Puerto Rico
- 6000 participants

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Field Guide Course

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Service Addresses

•*General Help*	`info@ncbi.nlm.nih.gov`
•*BLAST*	`blast-help@ncbi.nlm.nih.gov`

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