MICB 405 Bioinformatics
Mini-Lab #1 – NCBI's Entrez

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Objectives

- By the end of today's tutorial:
  - You will practice searching the Entrez database retrieval system.
  - You will learn to recognize links between the different Entrez databases, and differentiate hard and neighbor links.
  - You will search PubMed using advanced techniques and tips.

What is Entrez?

- “The life sciences search engine”
- text-based search and retrieval system at NCBI
- Covers all major databases of NCBI

Entrez, The Life Sciences Search Engine

Search across databases [ ] GO CLEAR Help

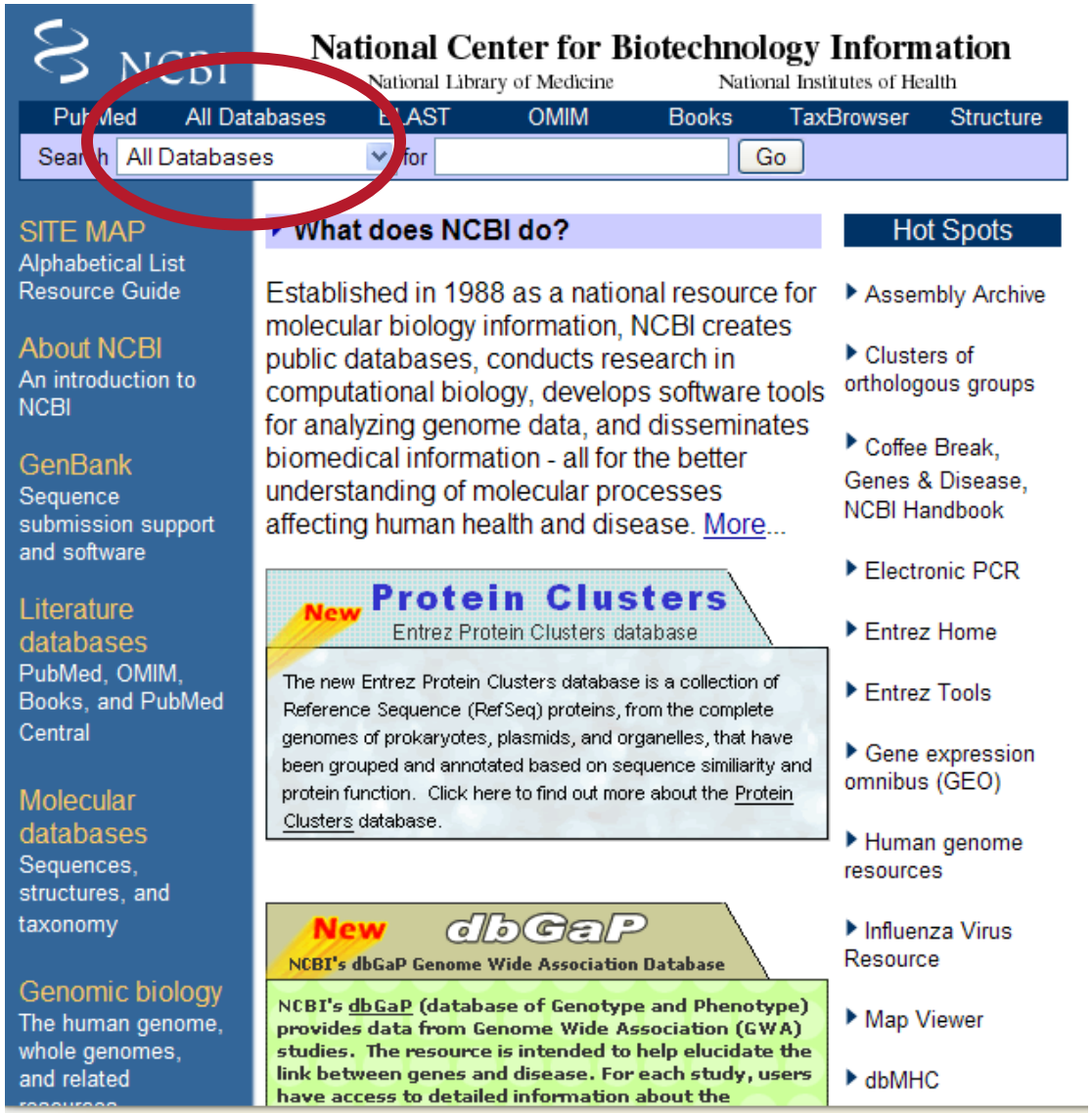
Welcome to the Entrez cross-database search page

- **PubMed:** biomedical literature citations and abstracts
- **PubMed Central:** free, full text journal articles
- **Site Search:** NCBI web and FTP sites
- **Books:** online books
- **OMIM:** online Mendelian Inheritance in Man
- **OMIA:** online Mendelian Inheritance in Animals

- **Nucleotide:** sequence database (GenBank)
- **Protein:** sequence database
- **Genome:** whole genome sequences
- **Structure**: three-dimensional macromolecular structures
- **Taxonomy:** organisms in GenBank
- **SNP:** single nucleotide polymorphism
- **Gene:** gene-centered information
- **HomoloGene:** eukaryotic homology groups
- **PubChem Compound:** unique small molecule chemical structures
- **PubChem Substance:** deposited chemical substance records
- **Genome Project:** genome project information
- **UniGene:** gene-oriented clusters of transcript sequences
- **CDD:** conserved protein domain database
- **3D Domains:** domains from Entrez Structure
- **UniSTS:** markers and mapping data
- **PopSet:** population study data sets
- **GEO Profiles:** expression and molecular abundance profiles
- **GEO DataSets:** experimental sets of GEO data
- **Cancer Chromosomes:** cytogenetic databases
- **PubChem BioAssay:** bioactivity screens of chemical substances
- **GENSAT:** gene expression atlas of mouse central nervous system

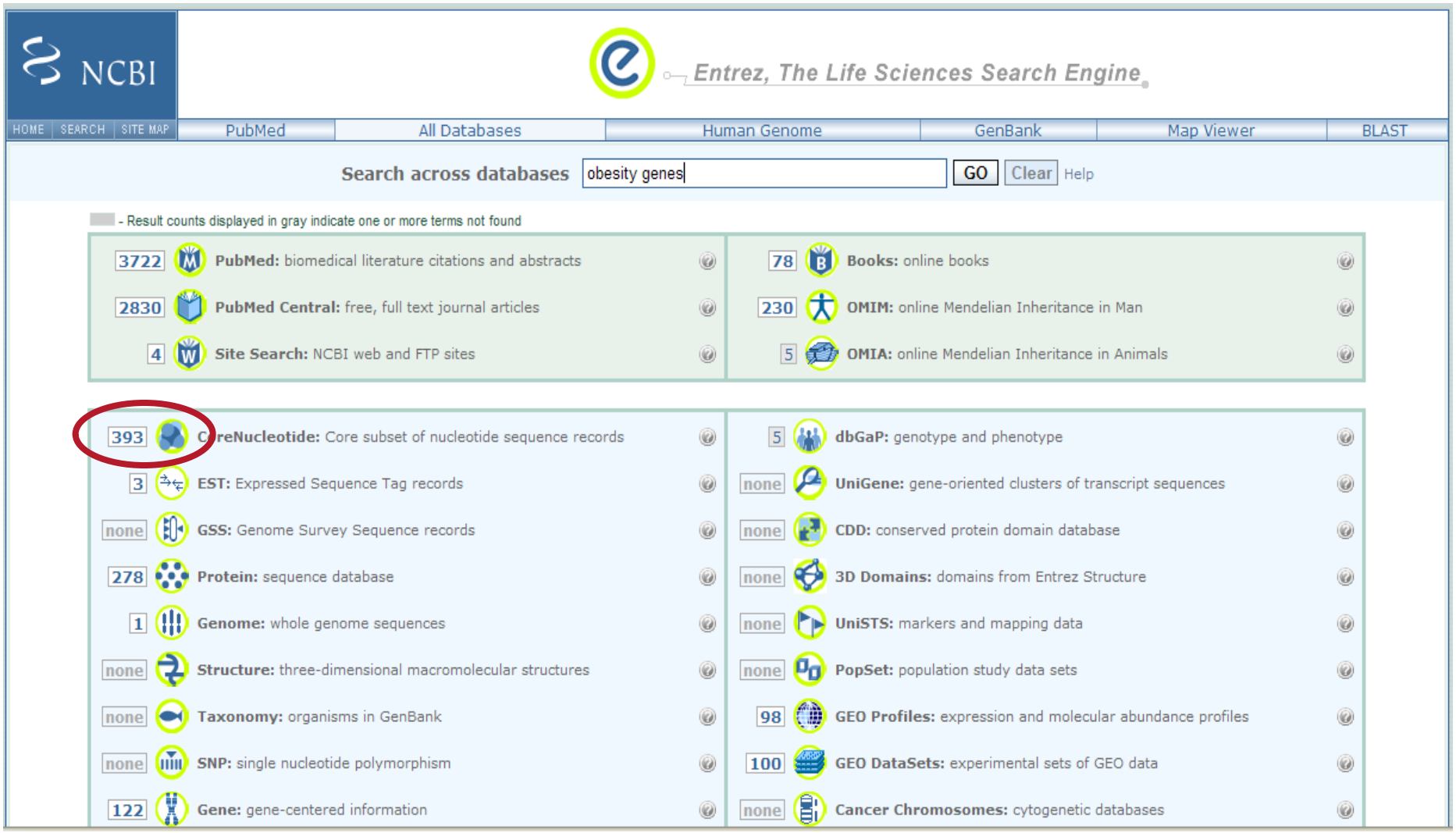
- **Journals:** detailed information *about* the journals indexed in PubMed and other Entrez databases
- **NLM Catalog:** catalog of books, journals, and audiovisuals in the NLM collections
- **MeSH:** detailed information about NLM's controlled vocabulary

Accessing Entrez



Example #1 – Searching for Sequences, Hard and Neighbor links

- We will:
  - go to Entrez
  - do a search for “obesity genes”
  - view the GenBank flat file for the first nucleotide entry in your search results
  - investigate the hard links available from this nucleotide sequence record to PubMed
  - investigate the related articles (neighbor links) available for this PubMed record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2830 PubMed Central: free, full text journal articles
4 Site Search: NCBI web and FTP sites
78 Books: online books
230 OMIM: online Mendelian Inheritance in Man
5 OMIA: online Mendelian Inheritance in Animals
393 CoreNucleotide: Core subset of nucleotide sequence records
3 EST: Expressed Sequence Tag records
none GSS: Genome Survey Sequence records
278 Protein: sequence database
1 Genome: whole genome sequences
none Structure: three-dimensional macromolecular structures
none Taxonomy: organisms in GenBank
none SNP: single nucleotide polymorphism
122 Gene: gene-centered information
5 dbGaP: genotype and phenotype
none UniGene: gene-oriented clusters of transcript sequences
none CDD: conserved protein domain database
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98 GEO Profiles: expression and molecular abundance profiles
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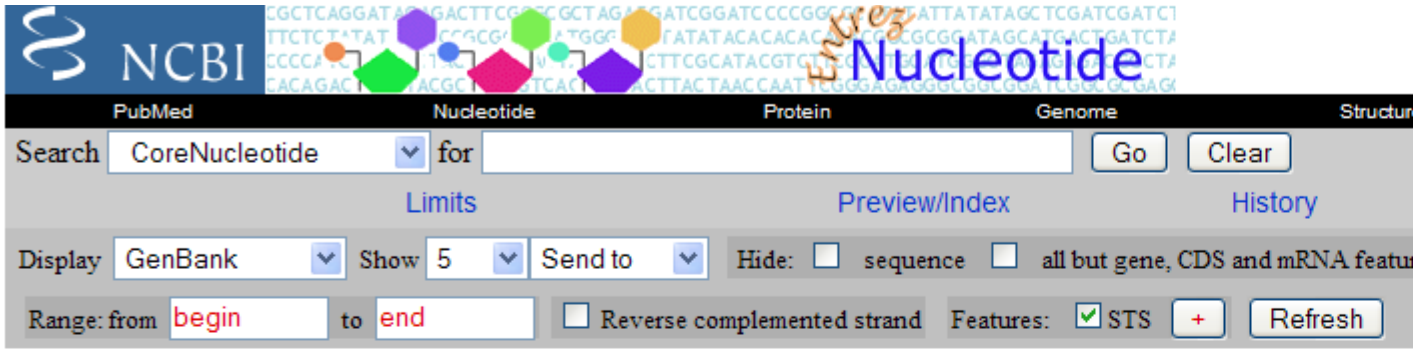
Search for full length cDNAs
Found 396 nucleotide sequences CoreNucleotide [393] EST [3]
Display Summary Show 20 Sort by Send to
All: 393 Bacteria: 0 RefSeq: 195 mRNA: 188
Items 1 - 20 of 393
Page 1 of 20 Next
1: NM_008919 Reports Links
Mus musculus pancreatic polypeptide receptor 1 (Ppyr1), mRNA
gi|157057096|ref|NM_008919.4|[157057096]
2: NM_016708 Reports Links
Mus musculus neuropeptide Y receptor Y5 (Npy5r), mRNA
gi|157057094|ref|NM_016708.3|[157057094]
3: NM_133904 Reports Links
Mus musculus acetyl-Coenzyme A carboxylase beta (Acacb), mRNA
gi|157042797|ref|NM_133904.2|[157042797]
4: NM_012079 Reports Links
Homo sapiens diacylglycerol O-acyltransferase homolog 1 (mouse) (DGAT1), mRNA
gi|145864458|ref|NM_012079.3|[145864458]
5: NM_009766 Reports Links
Mus musculus bombesin-like receptor 3 (Brs3), mRNA

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DEFINITION  Mus musculus pancreatic polypeptide receptor 1 (Ppyr1), mRNA.
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VERSION     NM_008919.4  GI:157057096
KEYWORDS    .
SOURCE      Mus musculus (house mouse)
  ORGANISM  Mus musculus
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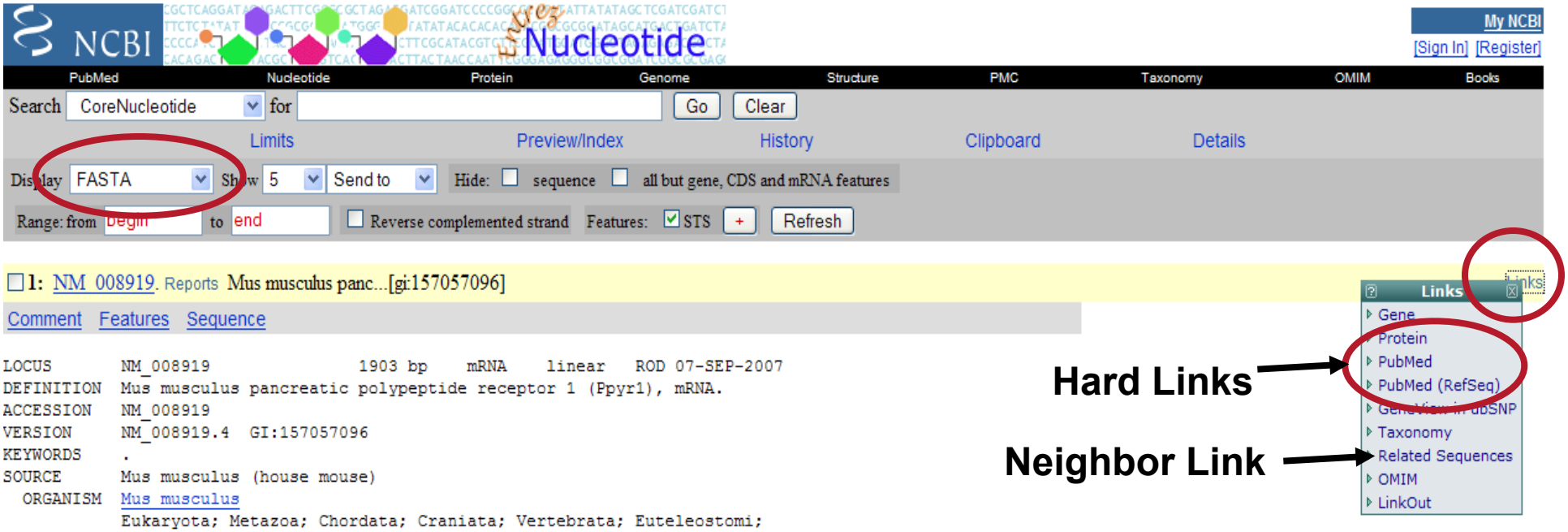
            Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia;
            Sciurognathi; Muroidea; Muridae; Murinae; Mus.
```

http://www.ncbi.nlm.nih.gov/Sitemap/samplerecord.html

Search Google for: “genbank sample record”

```
    PUBMED  17272395
  REMARK    GeneRIF: fasting inhibits the somatotropic axis via direct action
            on Y2 receptors in the Arcuate nucleus and indirectly inhibits the
            gonadotropic axis via Y4 receptors
REFERENCE   2  (bases 1 to 1903)
  AUTHORS   Lin,E.J., Sainsbury,A., Lee,N.J., Boey,D., Couzens,M., Enriquez,R.,
            Slack,K., Bland,R., During,M.J. and Herzog,H.
```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Display FASTA Show 5 Send to Hide: sequence all but gene, CDS and mRNA features
Range: from begin to end Reverse complemented strand Features: STS + Refresh
1: NM_008919. Reports Mus musculus panc...[gi:157057096]
Comment Features Sequence
LOCUS NM_008919 1903 bp mRNA linear ROD 07-SEP-2007
DEFINITION Mus musculus pancreatic polypeptide receptor 1 (Ppyr1), mRNA.
ACCESSION NM_008919
VERSION NM_008919.4 GI:157057096
KEYWORDS .
SOURCE Mus musculus (house mouse)
ORGANISM Mus musculus
Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia;
Sciurognathi; Muroidea; Muridae; Murinae; Mus.
REFERENCE 1 (bases 1 to 1903)
AUTHORS Lin,S., Lin,E.J., Boey,D., Lee,N.J., Slack,K., During,M.J.,
Sainsbury,A. and Herzog,H.
TITLE Fasting inhibits the growth and reproductive axes via distinct Y2
and Y4 receptor-mediated pathways
JOURNAL Endocrinology 148 (5), 2056-2065 (2007)
PUBMED 17272395
REMARK GeneRIF: fasting inhibits the somatotropic axis via direct action
on Y2 receptors in the Arcuate nucleus and indirectly inhibits the
gonadotropic axis via Y4 receptors
REFERENCE 2 (bases 1 to 1903)
AUTHORS Lin,E.J., Sainsbury,A., Lee,N.J., Boey,D., Couzens,M., Enriquez,R.,
Slack,K., Bland,R., During,M.J. and Herzog,H.
Links
Gene
Protein
PubMed
PubMed (RefSeq)
Taxonomy
Related Sequences
OMIM
LinkOut
Hard Links
Neighbor Link

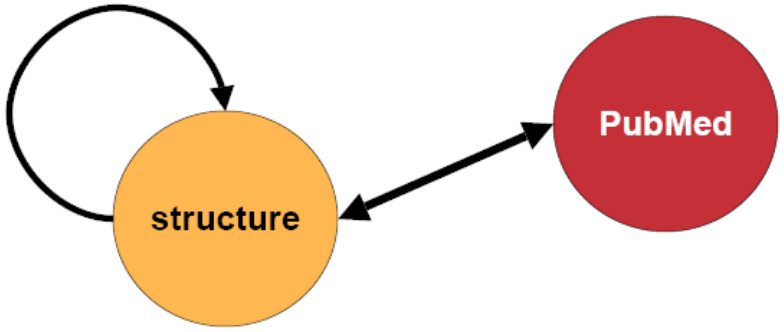
Hard Links and Neighbor Links

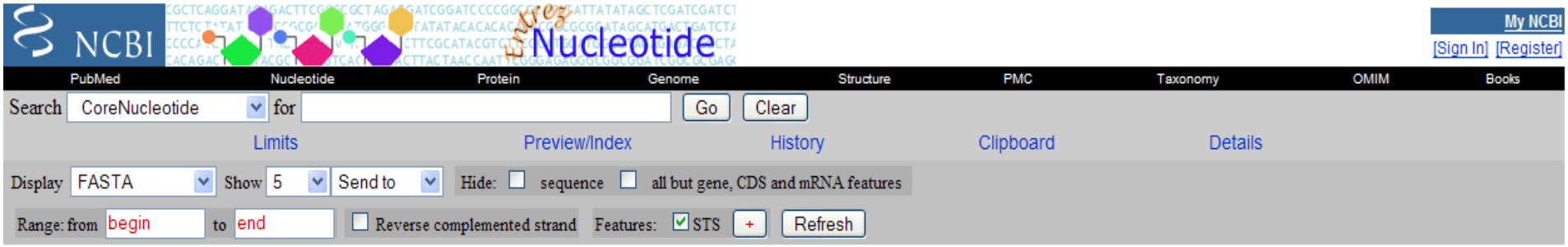
Hard Links are:

- direct connections between entries in different databases.
- Example: a link between nucleotide and protein records at NCBI.

Neighbor Links are:

- connections between entries in the same database.
- based on criteria that can change between databases.
- Examples: similar papers, related sequences, or similar 3D structures.





1: NM_008919. Reports Mus musculus panc...[gi:157057096]

Comment Features Sequence

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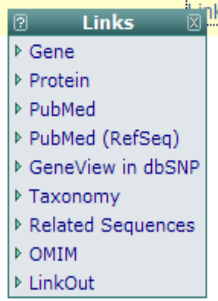

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Items 1 - 10 of 10 — One page.

1: Lin S, Lin EJ, Boey D, Lee NJ, Slack K, During MJ, Sainsbury A, Herzog H. — Related Articles, Links

Fasting inhibits the growth and reproductive axes via distinct Y2 and Y4 receptor mediated pathways.
Endocrinology. 2007 May;148(5):2056-65. Epub 2007 Feb 1.
PMID: 17272395 [PubMed - indexed for MEDLINE]

2: Lin EJ, Sainsbury A, Lee NJ, Boey D, Couzens M, Enriquez R, Slack K, Bland R, During MJ, Herzog H. — Related Articles, Links

Combined deletion of Y1, Y2, and Y4 receptors prevents hypothalamic neuropeptide Y overexpression-induced hyperinsulinemia despite persistence of hyperphagia and obesity.
Endocrinology. 2006 Nov;147(11):5094-101. Epub 2006 Jul 27.
PMID: 16873543 [PubMed - indexed for MEDLINE]

3: Sainsbury A, Bergen HT, Boey D, Bamming D, Cooney GJ, Lin S, Couzens M, Stroth N, Lee NJ, Lindner D, Singewald N, Karl T, Duffy L, Enriquez R, Slack K, Sperk G, Herzog H. — Related Articles, Links

Y2Y4 receptor double knockout protects against obesity due to a high-fat diet or Y1 receptor deficiency in mice.
Diabetes. 2006 Jan;55(1):19-26.
PMID: 16380472 [PubMed - indexed for MEDLINE]

4: Wultsch T, Painsipp E, Donner S, Sperk G, Herzog H, Peskar BA, Holzer P. — Related Articles, Links

Selective increase of dark phase water intake in neuropeptide-Y Y2 and Y4 receptor knockout mice.
Behav Brain Res. 2006 Apr 3;168(2):255-60. Epub 2005 Dec 20.
PMID: 16364461 [PubMed - indexed for MEDLINE]

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1: Endocrinology. 2007 May;148(5):2056-65. Epub 2007 Feb 1.

Final Version Endocrinology

links

Fasting inhibits the growth and reproductive axes via distinct Y2 and Y4 receptor-mediated pathways.

Lin S, Lin EJ, Boey D, Lee NJ, Slack K, During MJ, Sainsbury A, Herzog H.

Neuroscience Research Program, The Garvan Institute of Medical Research, Darlinghurst, New South Wales 2010, Sydney, Australia.

Neuropeptide Y, a neuropeptide abundantly expressed in the brain, has been implicated in the regulation of the hypothalamo-pituitary-somatotropic axis and the hypothalamo-pituitary-gonadotropic axis. Elevated hypothalamic neuropeptide Y expression, such as that occurs during fasting, is known to inhibit both of these axes. However, it is not known which Y receptor(s) mediate these effects. Here we demonstrate, using Y receptor knockout mice, that Y2 and Y4 receptors are separately involved in the regulation of these axes. Fasting-induced inhibition of hypothalamic GHRH mRNA expression and reduction of circulating IGF-I levels were observed in wild-type and Y4(-/-) mice but not Y2(-/-) or Y2(-/-)Y4(-/-) mice. In contrast, fasting-induced reduction of GnRH expression in the medial preoptic area and testis testosterone content were abolished in the absence of Y4 receptors. Colocalization of Y2 receptors and GHRH in the arcuate nucleus (Arc) suggests that GHRH mRNA expression in this region might be directly regulated by Y2 receptors. Indeed, hypothalamic-specific deletion of Y2 receptors in conditional knockout mice prevented the fasting-induced reduction in Arc GHRH mRNA expression. On the other hand, fasting-induced decrease in GnRH mRNA expression in the medial preoptic area is more likely indirectly influenced by Y4 receptors because no Y4 receptors could be detected on GnRH neurons in this region. Together these data show that fasting inhibits the somatotropic axis via direct action on Y2 receptors in the Arc and indirectly inhibits the gonadotropic axis via Y4 receptors.

Related Links

- Expression analysis of hypothalamic and pituitary components of the growth hormone axis in fasted and streptozoto [Neuroendocrinology. 2005]
- Hypothalamic/pituitary-axis of the spontaneous dwarf rat: autofeedback regulation of growth hormone (GH) in [Endocrinology. 1998]
- Y2 receptor deletion attenuates the type 2 diabetic syndrome of ob/ob mice. [Diabetes. 2002]
- Endogenous neuropeptide Y depresses the afferent signaling of gastric acid challenge to the mouse brainstem via neuropep [Neuroscience. 2005]
- Fasting-induced changes in the hypothalamic-pituitary-GH axis in the absence of GH expression: lessons from the spontane [J Endocrinol. 2004]

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1: Endocrinology. 2007 May;148(5):2056-65. Epub 2007 Feb 1.
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GENSAT
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Substance (MeSH Keyword)
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Neuroscience Research Program, The Garvan Institute of Medical Research, Darlinghurst, New South Wales 2010, Sydney, Australia.
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Related Links
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Endogenous neuropeptide Y depresses acid challenge to the mouse brainsten
Fasting-induced changes in the hypoth absence of GH expression: lessons fro
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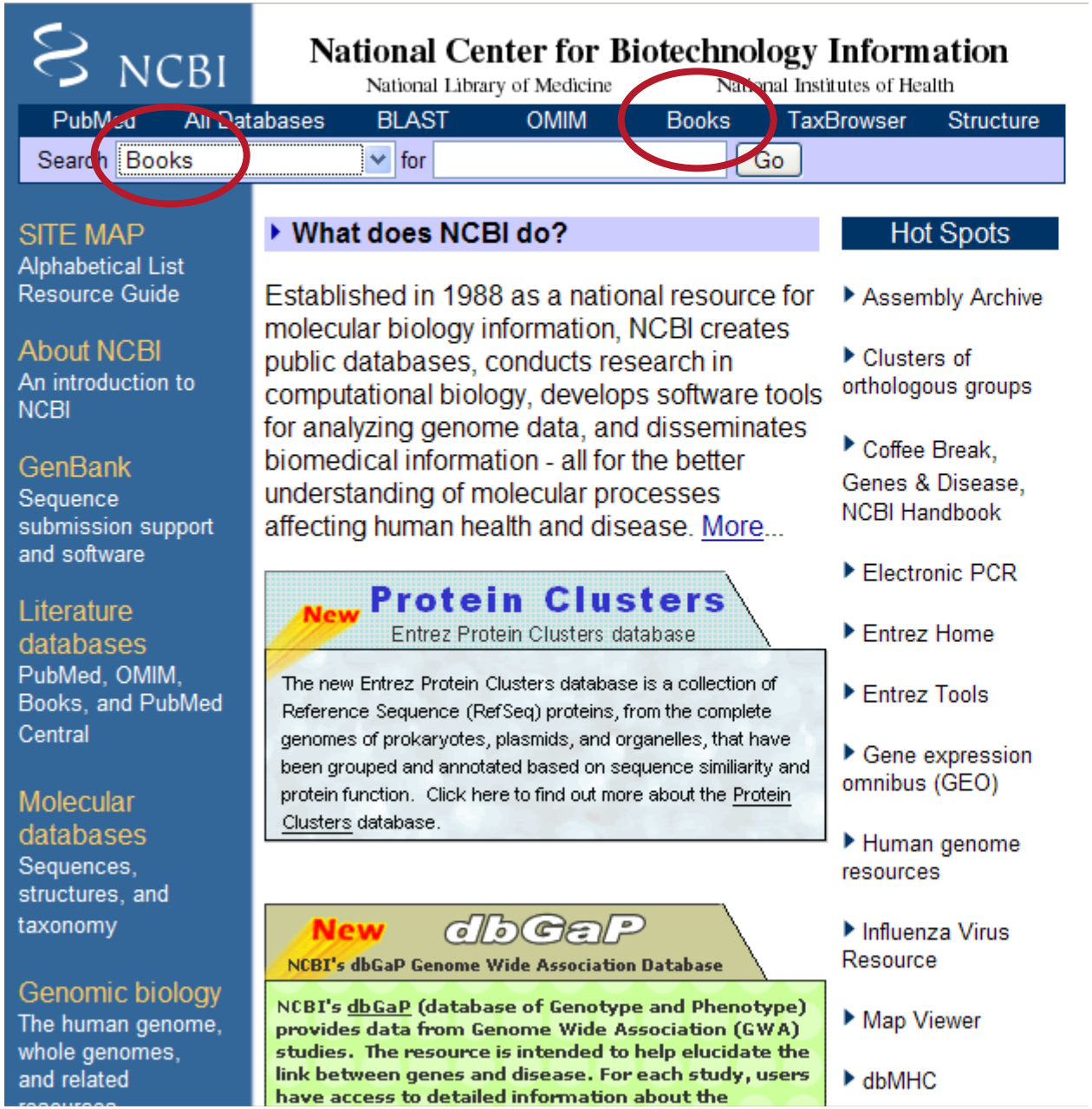

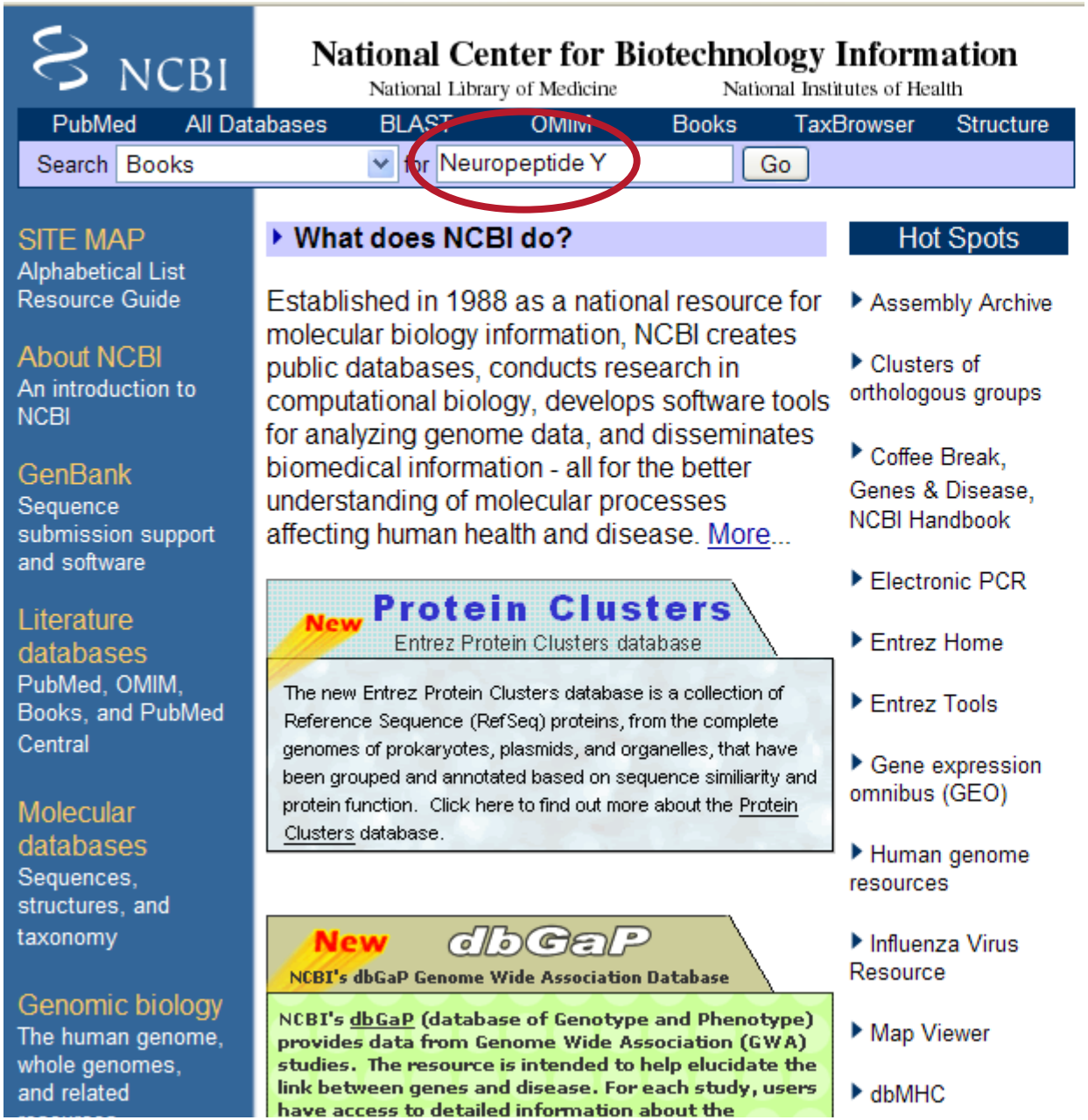
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dbGaP
NCBI's dbGaP Genome Wide Association Database
NCBI's dbGaP (database of Genotype and Phenotype) provides data from Genome Wide Association (GWA) studies. The resource is intended to help elucidate the link between genes and disease. For each study, users have access to detailed information about the
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Clusters of orthologous groups
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Human genome resources
Influenza Virus Resource
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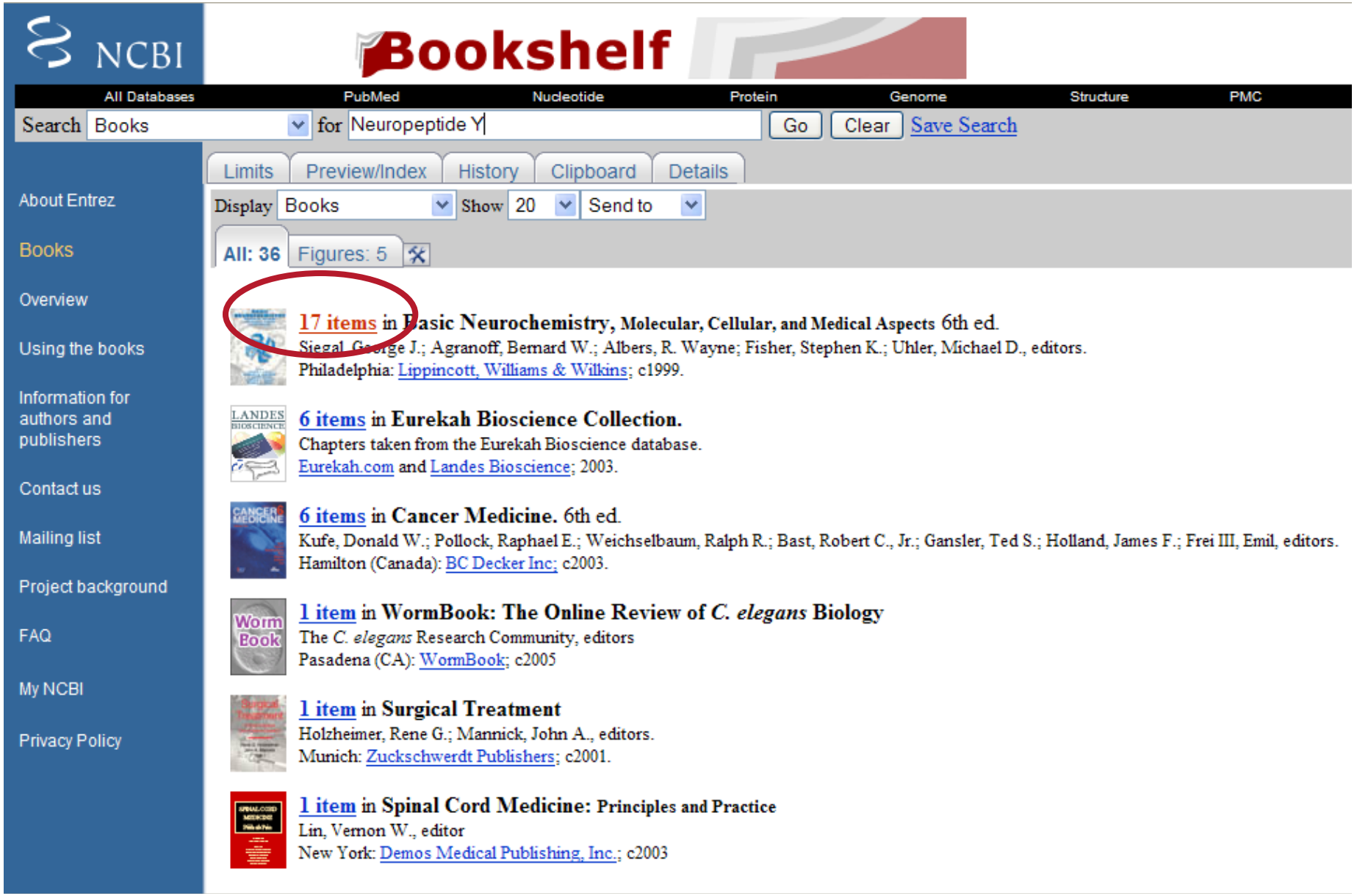
dbMHC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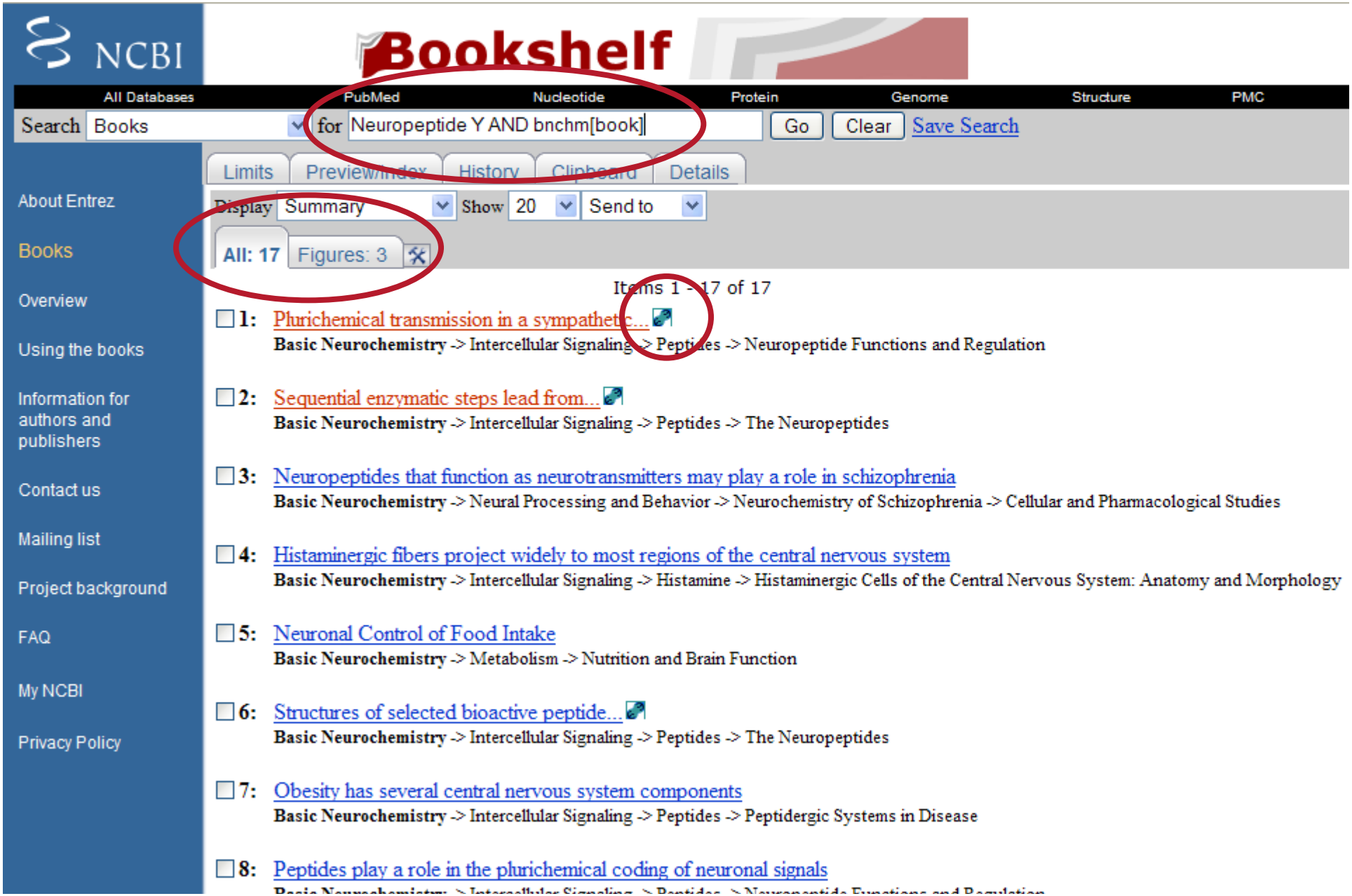
17 items in Basic Neurochemistry, Molecular, Cellular, and Medical Aspects 6th ed.
Siegal, George J.; Agranoff, Bernard W.; Albers, R. Wayne; Fisher, Stephen K.; Uhler, Michael D., editors.
Philadelphia: Lippincott, Williams & Wilkins; c1999.
6 items in Eurekah Bioscience Collection.
Chapters taken from the Eurekah Bioscience database.
Eurekah.com and Landes Bioscience; 2003.
6 items in Cancer Medicine. 6th ed.
Kufe, Donald W.; Pollock, Raphael E.; Weichselbaum, Ralph R.; Bast, Robert C., Jr.; Gansler, Ted S.; Holland, James F.; Frei III, Emil, editors.
Hamilton (Canada): BC Decker Inc; c2003.
1 item in WormBook: The Online Review of C. elegans Biology
The C. elegans Research Community, editors
Pasadena (CA): WormBook; c2005
1 item in Surgical Treatment
Holzheimer, Rene G.; Mannick, John A., editors.
Munich: Zuckschwerdt Publishers; c2001.
1 item in Spinal Cord Medicine: Principles and Practice
Lin, Vernon W., editor
New York: Demos Medical Publishing, Inc.; c2003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1: Plurichemical transmission in a sympathetic...
Basic Neurochemistry -> Intercellular Signaling -> Peptides -> Neuropeptide Functions and Regulation
2: Sequential enzymatic steps lead from...
Basic Neurochemistry -> Intercellular Signaling -> Peptides -> The Neuropeptides
3: Neuropeptides that function as neurotransmitters may play a role in schizophrenia
Basic Neurochemistry -> Neural Processing and Behavior -> Neurochemistry of Schizophrenia -> Cellular and Pharmacological Studies
4: Histaminergic fibers project widely to most regions of the central nervous system
Basic Neurochemistry -> Intercellular Signaling -> Histamine -> Histaminergic Cells of the Central Nervous System: Anatomy and Morphology
5: Neuronal Control of Food Intake
Basic Neurochemistry -> Metabolism -> Nutrition and Brain Function
6: Structures of selected bioactive peptide...
Basic Neurochemistry -> Intercellular Signaling -> Peptides -> The Neuropeptides
7: Obesity has several central nervous system components
Basic Neurochemistry -> Intercellular Signaling -> Peptides -> Peptidergic Systems in Disease
8: Peptides play a role in the plurichemical coding of neuronal signals

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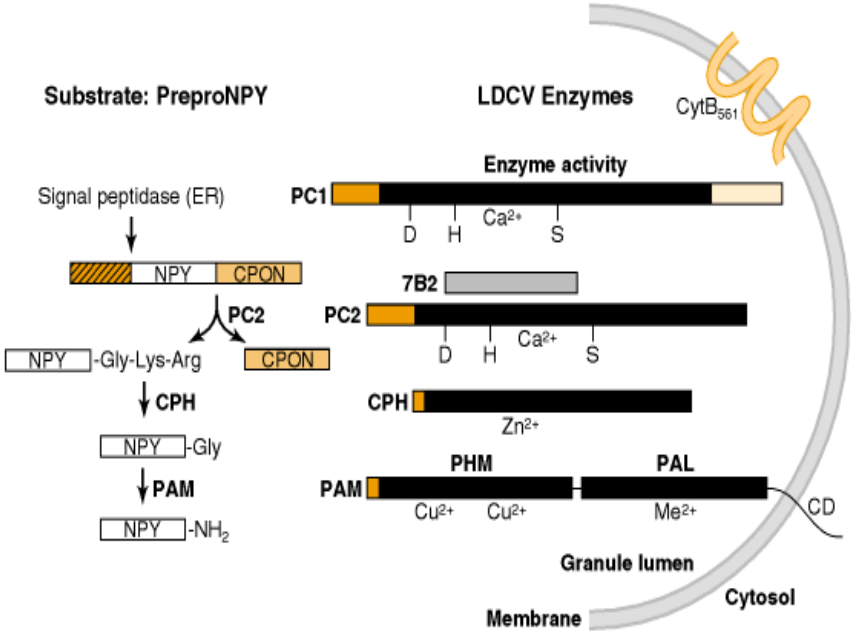

Figure 18-5. Sequential enzymatic steps lead from the peptide precursor to bioactive peptides. The neuropeptide Y *(NPY)* precursor shown at the **left** is processed sequentially by the enzymes of the large dense-core vesicles *(LDCV)* shown at right. *ER*, endoplasmic reticulum; *PC*, prohormone convertase; *CPON*, C-terminal flanking peptide of NPY; *CPH*, carboxypeptidase E; *PAM*, peptidylglycine α-amidating mono-oxygenase; *PHM*, peptidylglycine α-hydroxylating mono-oxygenase; *PAL*, peptidyl-α-hydroxyglycine α-amidating lyase; *CD*, cytoplasmic domain.

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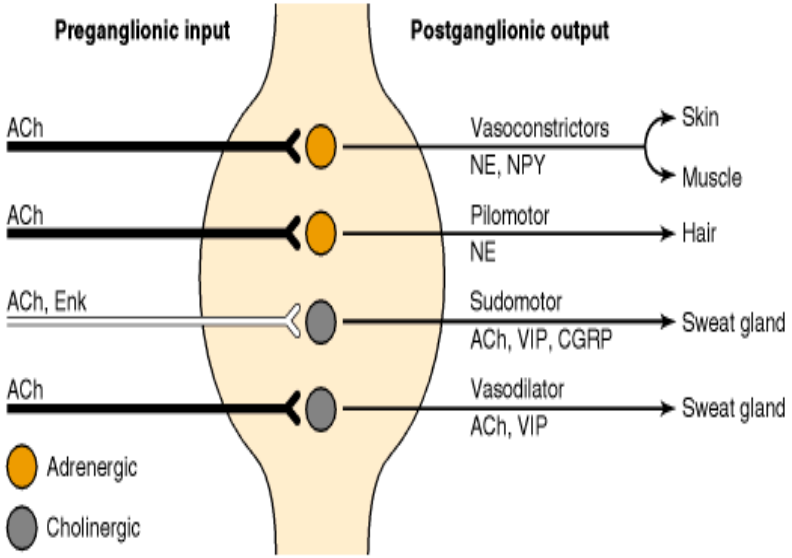
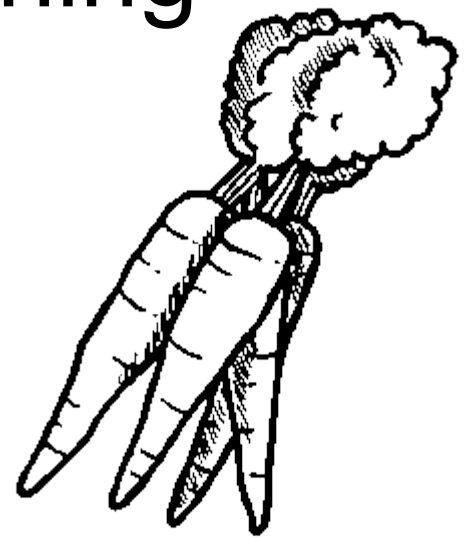


Figure 18-10. Plurichemical transmission in a sympathetic ganglion (adapted from [21]). Cholinergic stimulation of distinct ganglionic neurons leads to distinct neurotransmitter release and physiological actions. *ACh*, acetylcholine; *Enk*, enkephalin; *NE*, norepinephrine; *NPY*, neuropeptide Y; *VIP*, vasoactive intestinal peptide; *CGRP*, calcitonin gene-related peptide.

Example #2 – Searching PubMed



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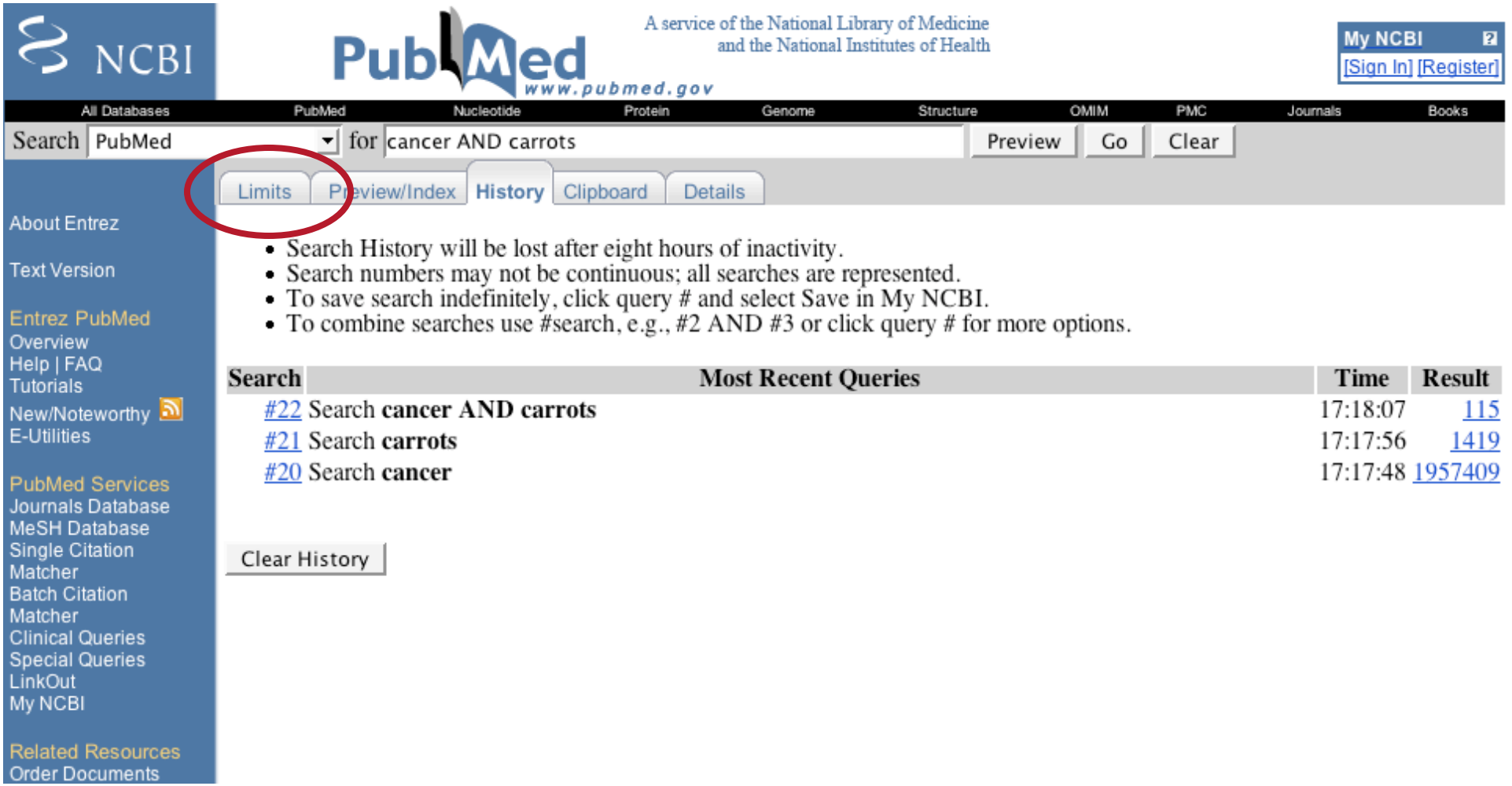
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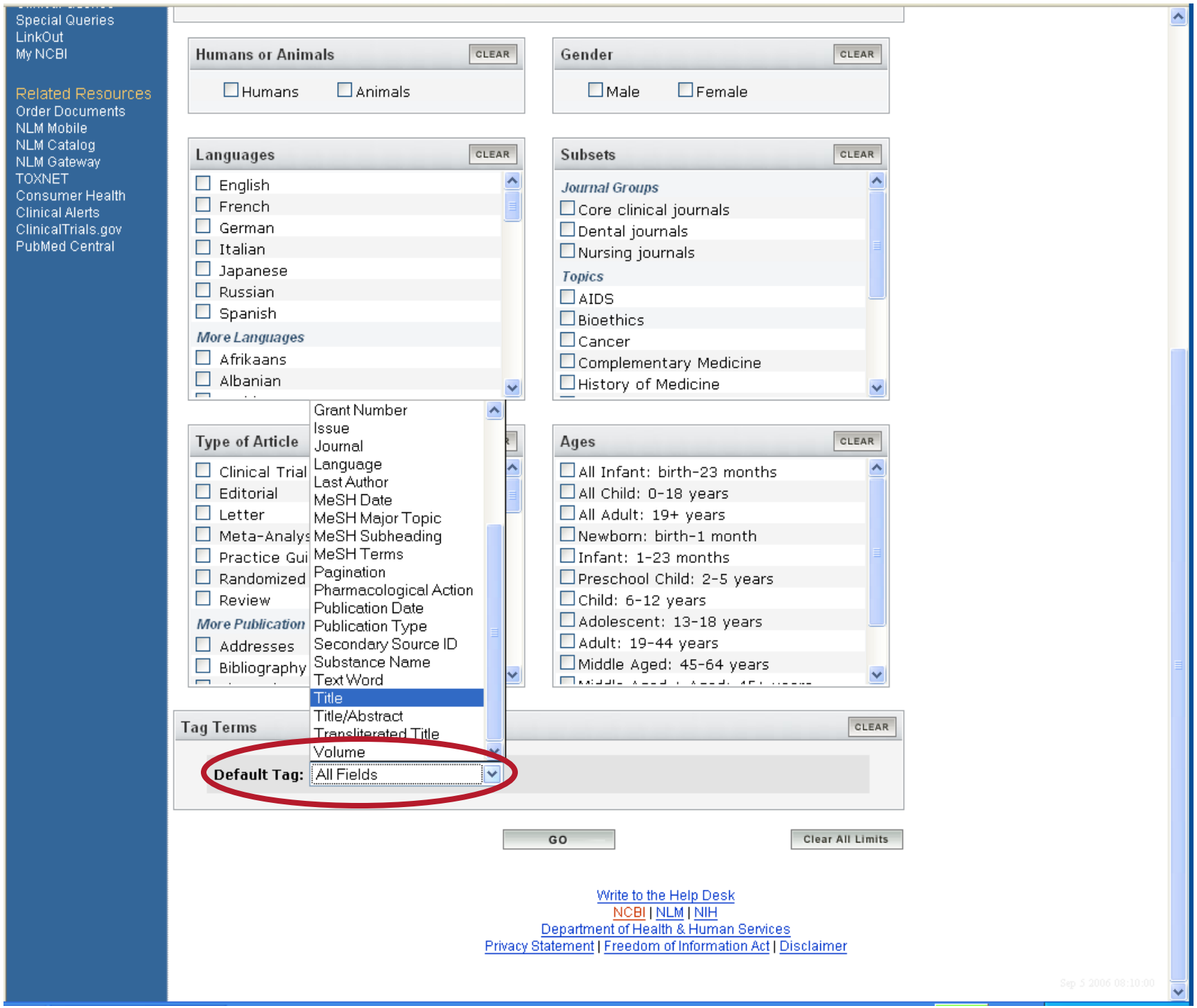
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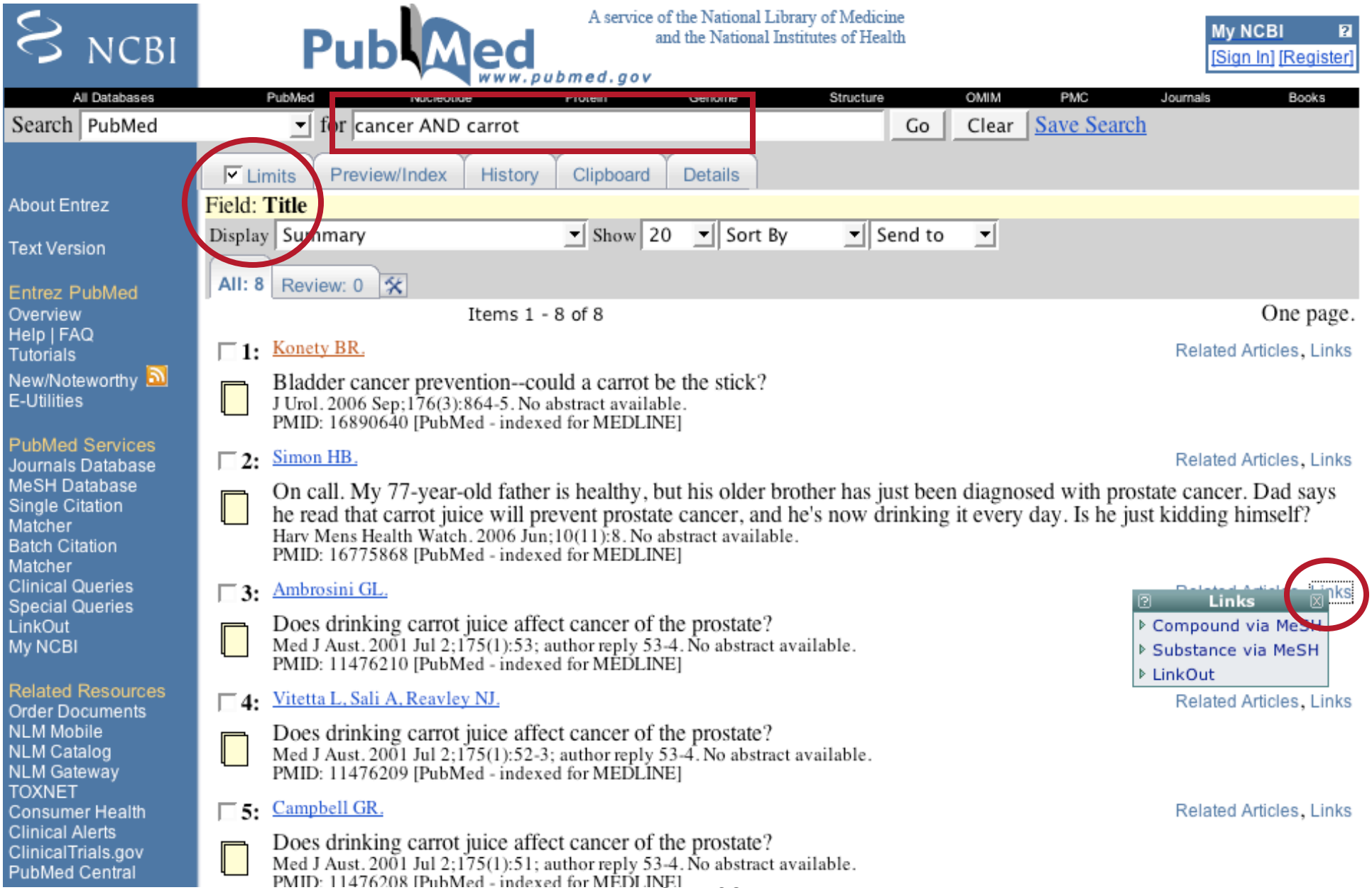
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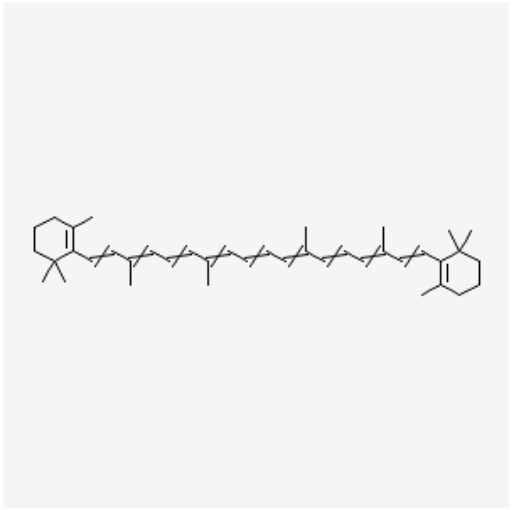

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