



# Desktop Text Mining for Life Sciences

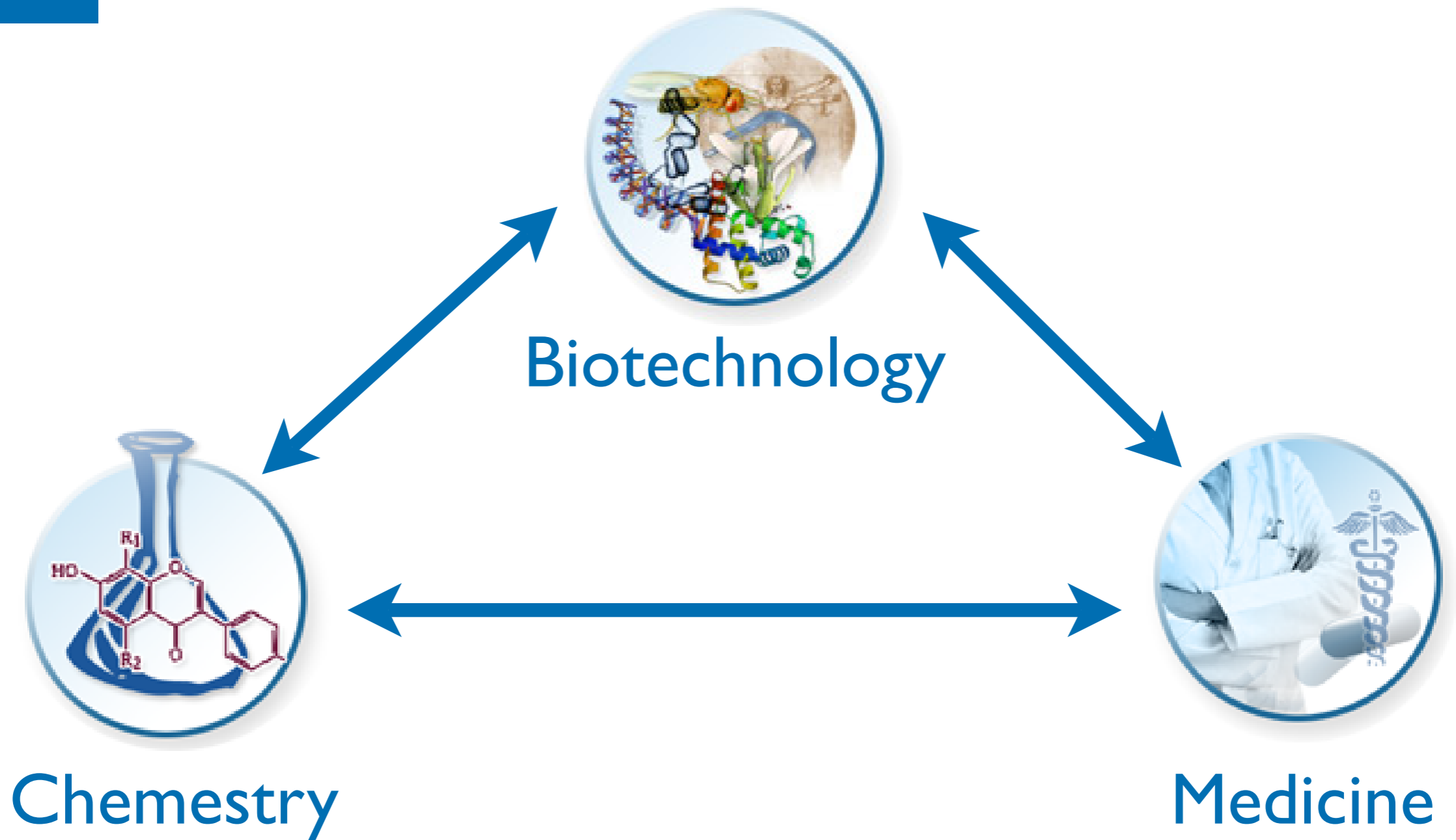
ICIC, Nimes Oct. 2006

*Ramón Alonso-Allende*  
[allende@bioalma.com](mailto:allende@bioalma.com)

# The problem

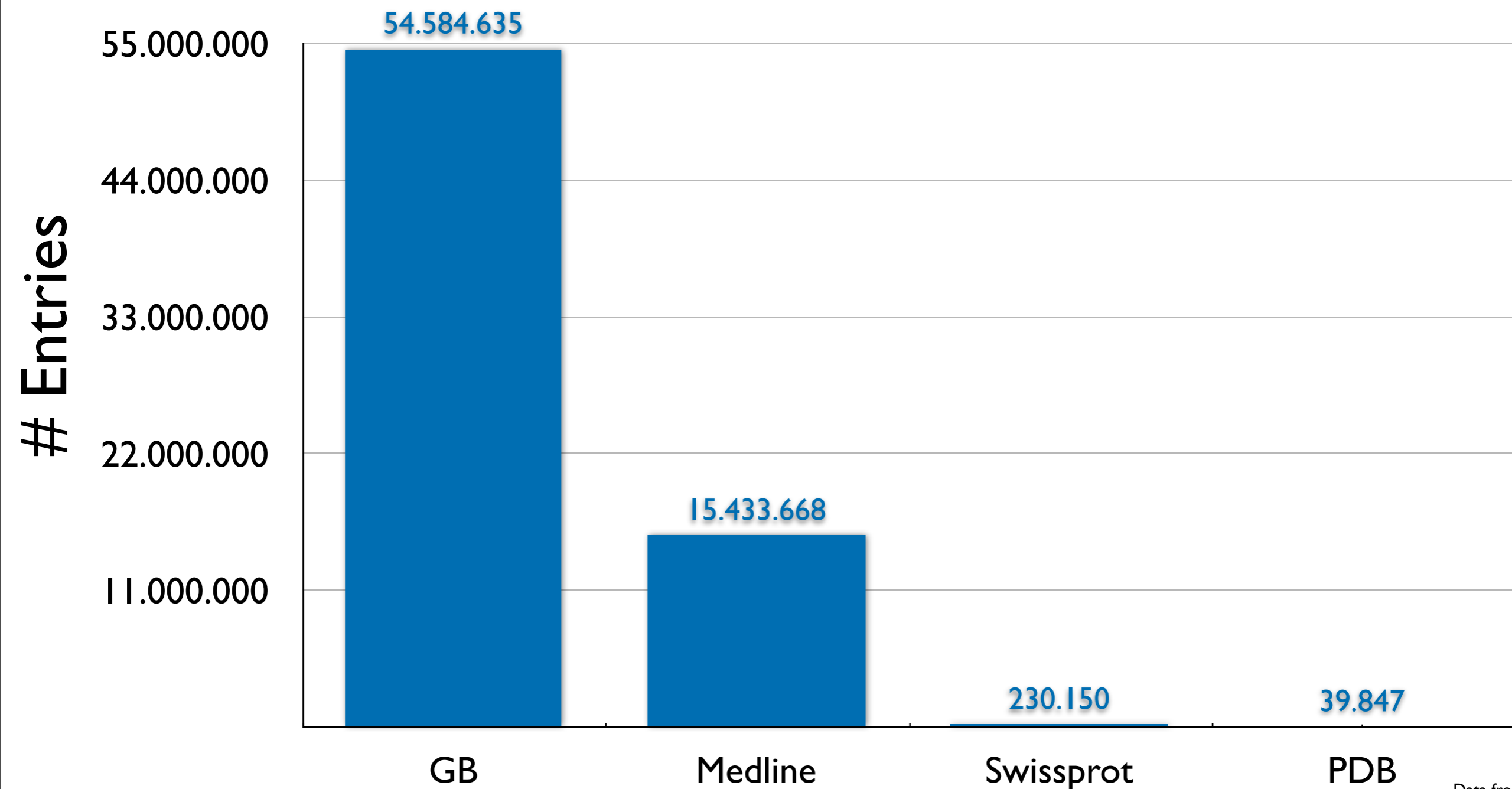
- Knowledge areas
- Amount of data
- Language ambiguity

# I Knowledge areas

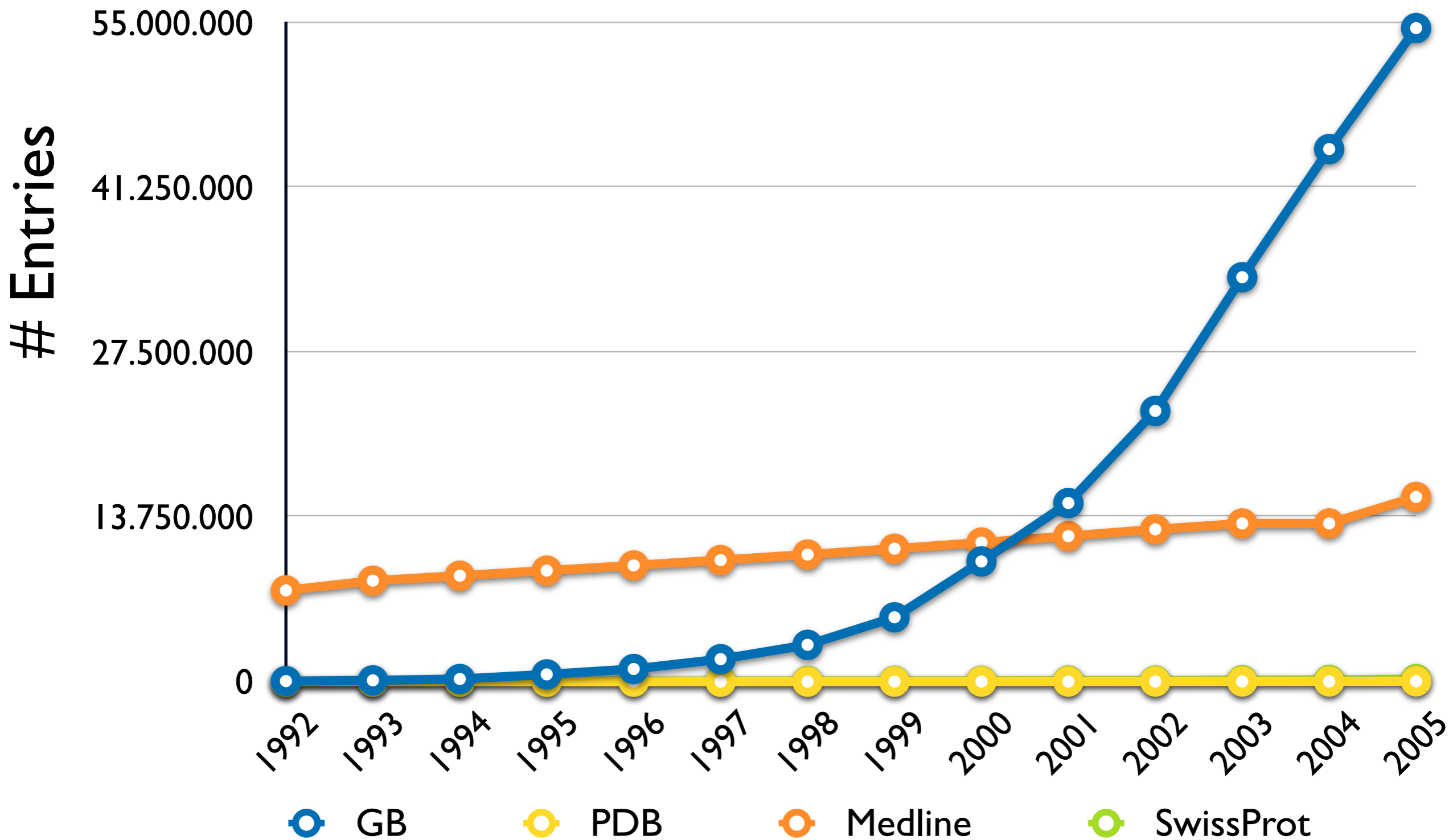


2

## Amount of data



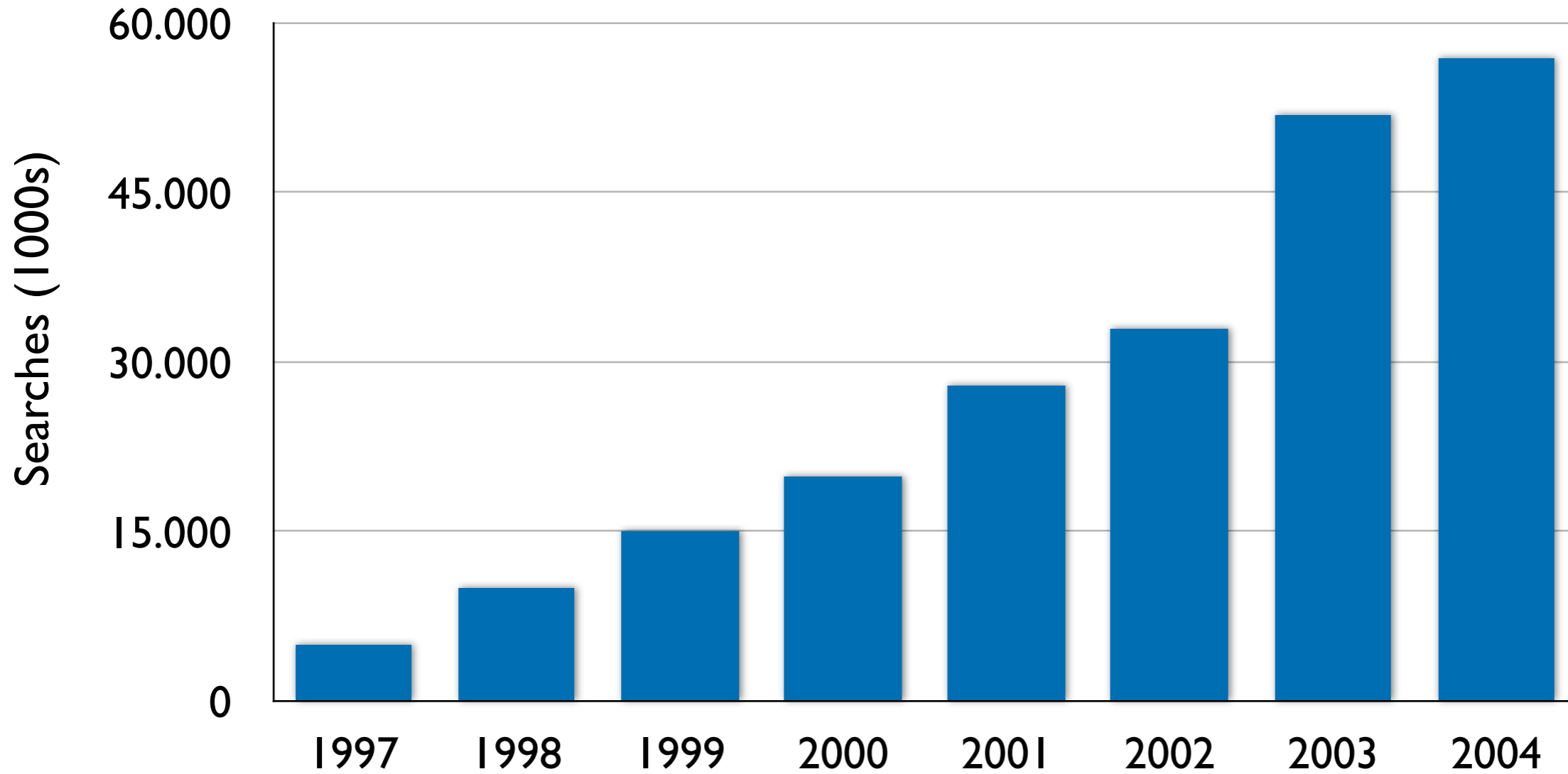
# Database growth



The increasing amount of data and the advance in technology arises an additional challenge:

Information reliability

# PubMed searches



• 2 million searches a day

# Human communication process

Overestimation  
of computer power?

Underestimation  
of human capabilities?



Hal 9000

2001 A space Odyssey  
(1968)



# 3

## Language ambiguity

### Synonyms

Different word for the same biomedical entity

- In Human there are at least 5.418 genes with synonyms (38% of the total genome)
- Drugs have a commercial name and a chemical name

### Homonyms

Same name for different biomedical entities

- Symbol PAP is an alias for:
- PAP (Pancreatitis-associated protein)
  - MRPS30 (Mitochondrial ribosomal prot 30s)
  - PAPOLA (PolyA polymerase alpha)

### Acronym

Reduce word representing a biomedical entity

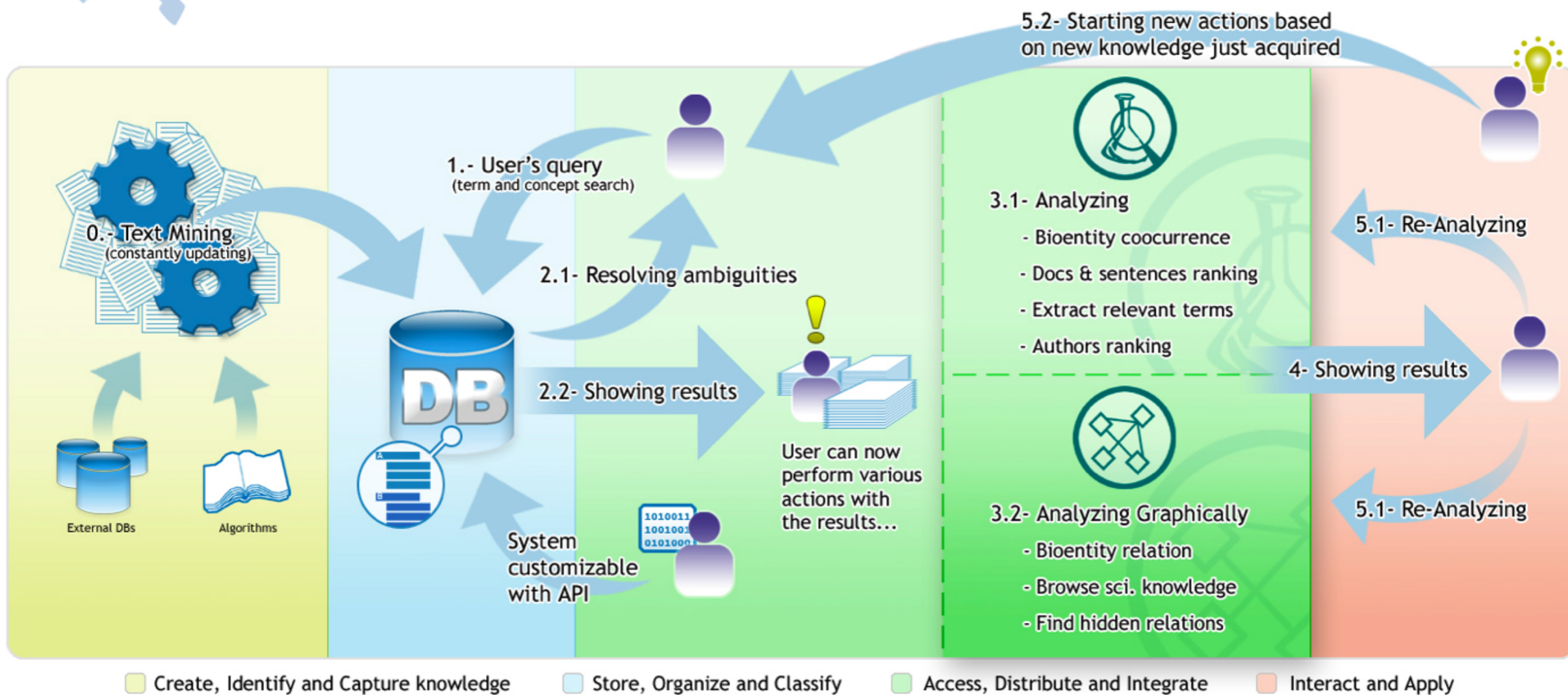
- SCT stands for:
- Stem Cell Transplant
  - Secretin
  - Salmon calcitonin

# The AKS<sup>2</sup> system

AKS<sup>2</sup> is a scientific knowledge system to help the biomedical professional to go fast and further in the analysis of scientific literature

# The Technology

- Create, capture and identify knowledge
- Store, organize and clasify
- Access, distribute and integrate
- Interact and apply



# Create and identify

- Database integration
- Text mining



I

# Database integration

## Sequence DBs

UniProt  
GenBank  
RefSeq  
PIR  
EMBL  
Entrez Protein  
UniSTS

## Gene DBs

GDB  
Ensembl  
Entrez Gene  
UniGene  
H-InvDB  
MGC  
HGNC

## Pathway DBs

KEGG  
EC  
Reactome

## Domain DBs

Pfam  
PROSITE  
SMART  
ProDom  
InterPro

## Other DBs

Affymetrix  
GO  
PDB  
MIM  
CCDS  
HPRD  
HGNC  
PubChem  
UMLS

## 2 Text mining

Gene: GHI  
Growth Hormone I  
GeneID: 2688

Synonym: GHN  
Synonym: GH

adenoma (0.300)  
adipocyte (0.418)  
adipose (0.324)  
age-related (0.442)  
genotropin (19.368)

Gene: GGI  
Gamma Glutamyl Hydrolase  
GeneID: 8836

Synonym: conjugasa  
Synonym: GH

antifolate (2.850)  
carboxypeptidase (12.618)  
folate (0.674)  
gamma-glu-x (15.452)  
antifolypoly-gamma-glutamate (12.054)

Store and organize



- Scalable, robust and fast RDBMS
- Highly redundant data model
- Centralize data distribution  
update

# Access and distribute

- Conceptual search approach
- The document search approach
- The graphical interface
- API



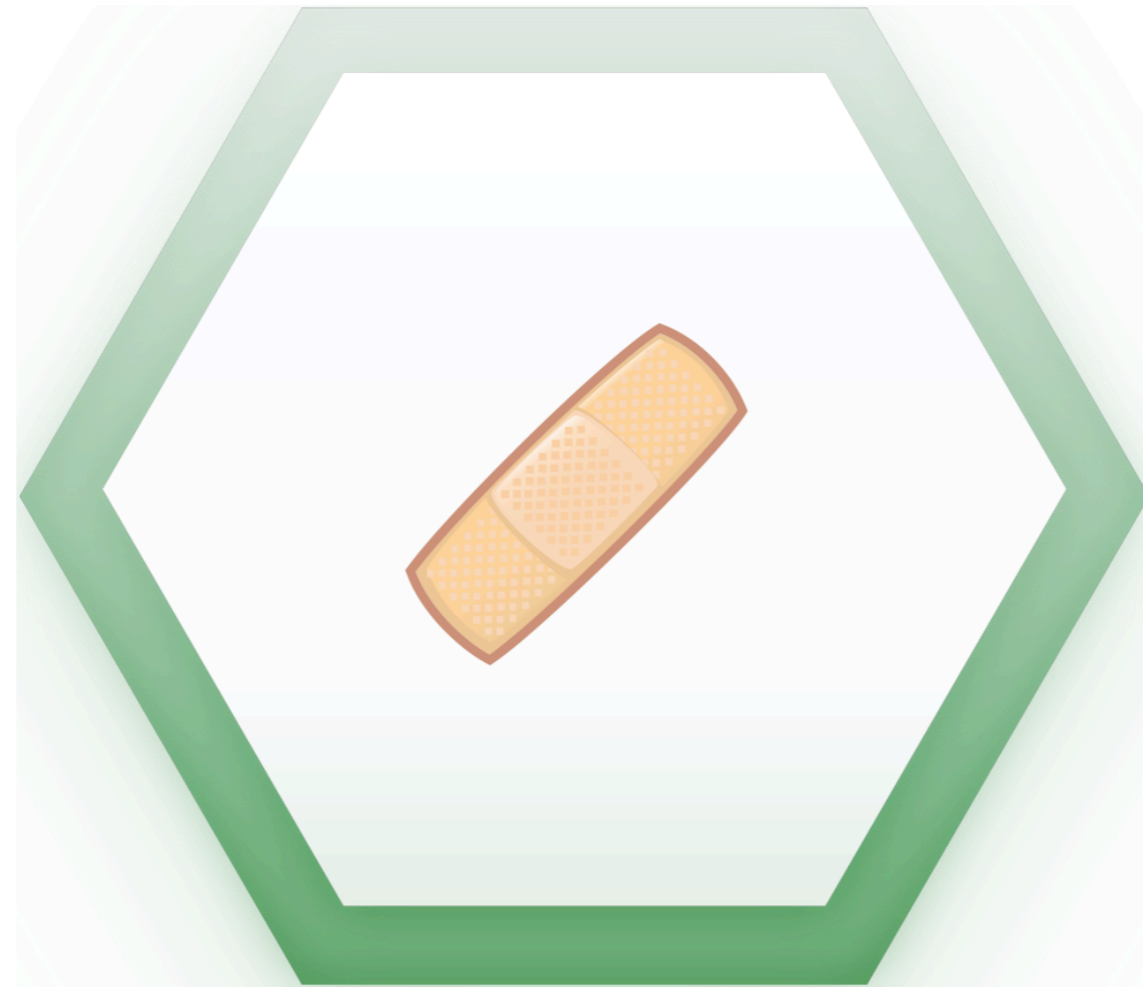
I

## Conceptual search approach: Bioentity

“Term with relevant meaning for the  
biomedical community”



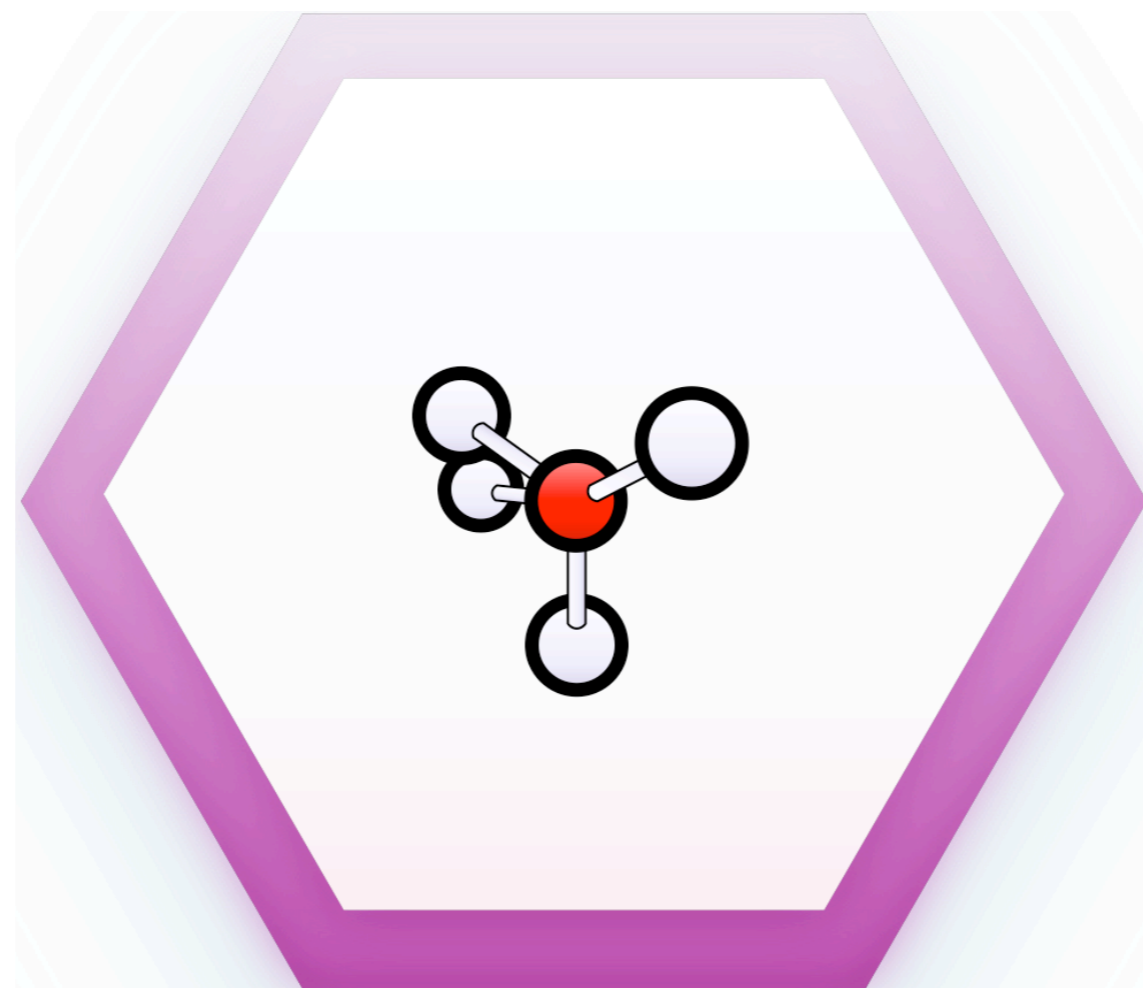
**1,344,331**



29,789



13,784



697,200

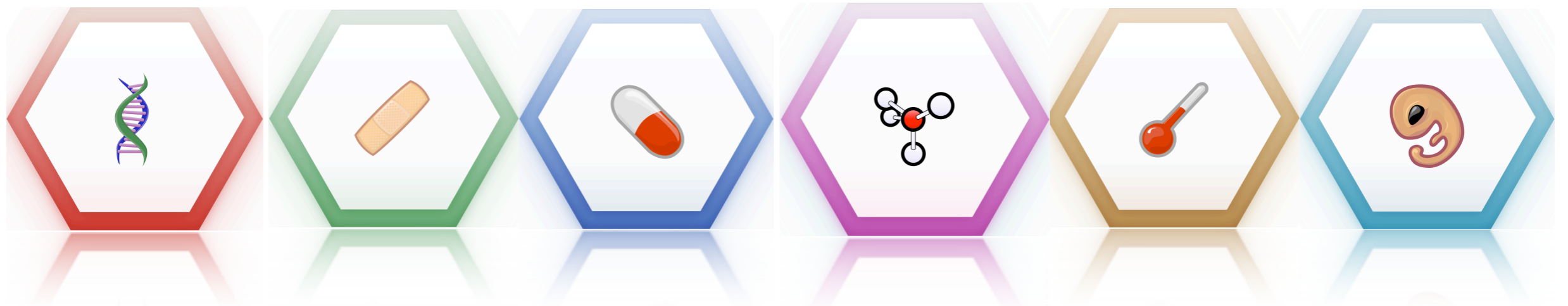


1,937





146,711



1,344,331	29,789	13,784	697,200	1,937	146,711
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Total

2.365.654

**External database information**

**Relevant bioentity cooccurrence**

**Recent documents**

**Authors**

Detail: COX2

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<b>Name:</b>	COX2
<b>Synonyms</b>	PGHS-2 , COX 2 , PTGS2 , HCOX-2 , PGH2 , PHS-2 , PGHS 2 , PHS II , COX-2 , PGG/HS , HCOX 2 , PHS 2
<b>Ext. Database IDs</b>	<a href="#">9605 (HGNC)</a> , <a href="#">Q16876 (UniProt)</a> , <a href="#">5743 (Entrez Gene)</a>
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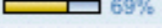
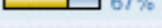
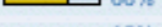




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Profile





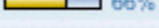
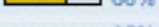


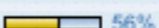

Chemicals

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Name	Relevance
CELECOXIB	 87%
ROFECOXIB	 84%
NIMESULIDE	 73%
MELOXICAM	 69%
PROSTANOID	 67%
ENDOPEROXIDE	 66%
R(+)-METHANANDAMIDE	 65%
CYCLOXYGENASE-2	 60%
ETODOLAC	 54%
ARACHIDONIC ACID	 54%

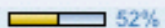


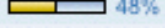
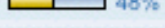
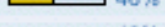




Genes/ proteins

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COX1	 97%
INOS	 79%
COX	 75%
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IL1-BETA	 66%
NF-KAPPA-B	 66%
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Diseases

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Name	Relevance
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INFLAMMATION	 49%
TUMORS	 48%
ADENOMA	 48%
INTESTINAL POLYPS	 46%
FAMILIAL ADENOMATOUS POLY...	 43%
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Authors

## Detail: COX2





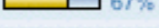
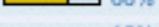
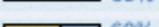



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## Profile





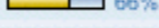
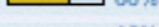
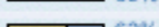
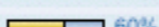
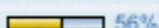
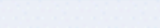
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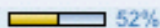


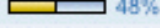
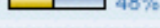


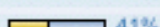
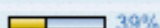

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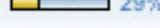
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## Authors

View all

Name	Relevance
Subbaramaiah, K	 41%
Dannenberg, Andrew J	 37%
Subbaramaiah, Kotha	 33%
Dubois, R N	 32%
Dannenberg, A J	 29%



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Detail: COX2





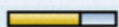





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Authors

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Name	Relevance
Subbaramaiah, K	 41%
Dannenberg, Andrew J	 37%
Subbaramaiah, Kotha	 33%
Dubois, R N	 32%
Dannenberg, A J	 29%



# Conceptual search approach: Relation

aks2 Home p53 ANALYSIS 04 ANALYSIS 05

Summary Detail Profile Documents Authors

### Relation detail [View all](#)

Relation elements: p53, Bcl-2  
Relation documents: 2622  
Relation sentences: 4855

### Relation profile

Drugs [View all](#)

Name	Relevance
VEGF	37%
Paclitaxel	31%
Doxorubicin	20%
Etoposide	17%
Retinoic Acid	12%
bortezomib	8%
5-FU	6%
Vincristine	6%
Adriamycin	6%
Methotrexate	4%

Genes/ proteins [View all](#)

Name	Relevance
BAX	100%
Ki-67	88%
Ki-67	87%
p21	85%
c-Myc	84%
MDM2	82%
MIB-1	81%
bcl-xL	81%
NEU	81%
Ki67	80%

Diseases [View all](#)

Name	Relevance
Tumors	74%
Carcinoma	57%
Carcinoma Squamous Cell	52%
NSCLC	50%
Adenoma	48%
BREAST CARCINOMA	47%
Breast Cancer	47%
Adenocarcinoma	47%
ENDOMETRIAL CARCINOMA	46%
Retinoblastoma	45%

### Recent documents [View all](#)

06/2006	Loss of proapoptotic bcl-2-related multidomain proteins in primary melanomas is associated with poor prognosis.
06/2006	Helicobacter pylori CagA-Dependent Macrophage Migration Inhibitory Factor Produced by Gastric Epithelial Cells Binds to CD74 and Stimulates Procarcinogenic Events.
05/2006	The BH3-only protein, PUMA, is involved in oxaliplatin-induced apoptosis in colon cancer cells.
05/2006	A Short Mitochondrial Form of p19(ARF) Induces Autophagy and Caspase-Independent Cell Death.
05/2006	In vitro folate deficiency induces apoptosis by a p53, Fas (Apo-1, CD95) independent, bcl-2 related mechanism in phytohaemagglutinin-stimulated human peripheral blood lymphocytes.

### Authors [View all](#)

Name	Relevance
Reed J C	100%
McDonnell T J	96%
Krajewski S	95%
Soini Y	89%
Giatromanolaki A	88%

I

# Conceptual search approach: Group

aks2 Home ANALYSIS 01

Summary Detail Profile Documents Authors

### Group profile

Genes/ proteins (735) 2 bioentities selected (1 group element selected)

Name	Rel. with	Tot. Sents.	Relevance
<input checked="" type="checkbox"/> VEGF	3/3	53087	73%
<input checked="" type="checkbox"/> Bcl-2	3/3	36713	66%
<input type="checkbox"/> HIF1-ALPHA	3/3	5419	62%
<input type="checkbox"/> NEU	3/3	20795	59%
<input type="checkbox"/> P-gp	3/3	20431	56%
<input type="checkbox"/> PCNA	3/3	18497	55%
<input type="checkbox"/> EGFR	3/3	29880	53%

Name	Related
<input checked="" type="checkbox"/> p53	2
<input type="checkbox"/> VEGF	2
<input type="checkbox"/> Doxorubicin	2

Documents Sentences ANY ALL

54 Documents	PMID	Date	Relevance
<input type="checkbox"/> Cell proliferation markers and growth factors in ovarian cancer.	<a href="#">7742006</a>	02/1995	100%
<input type="checkbox"/> Biological markers as a predictor for response and prognosis of unresectable gastric cancer patients treated with 5-fluorouracil and cis-platinum.	<a href="#">9626464</a>	06/1998	100%
<input type="checkbox"/> Role of HIF-1alpha in hypoxia-mediated apoptosis, cell proliferation and tumour angiogenesis.	<a href="#">9697772</a>	07/1998	100%
<input type="checkbox"/> Bcl2 and p53 regulate vascular endothelial growth factor (VEGF) mediated angiogenesis in non-small cell lung	<a href="#">9713990</a>	04/2000	100%



## 2

## Document search approach

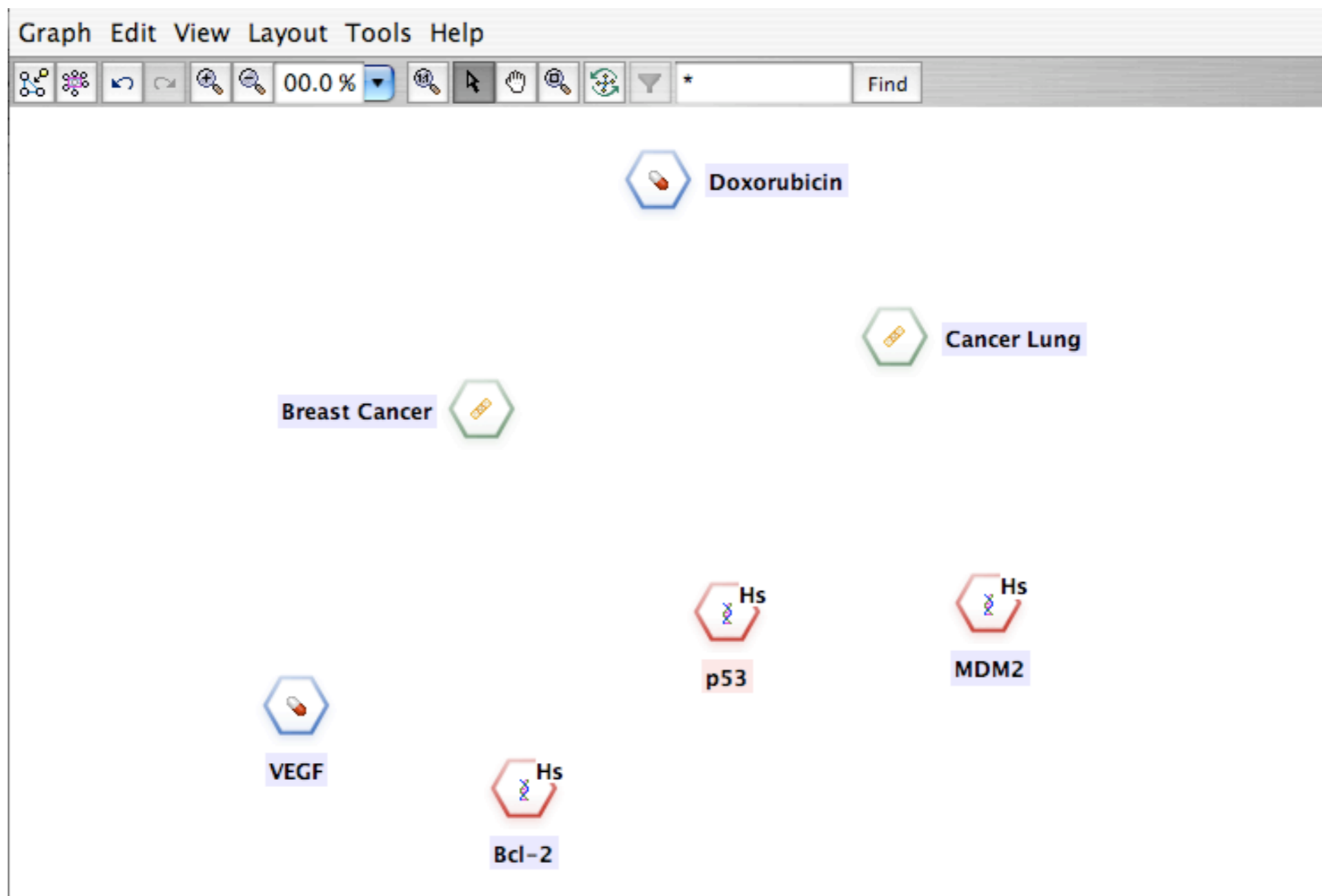
The screenshot shows a web-based search interface with the following elements:

- Navigation tabs: aks2 Home, ANALYSIS 01, ANALYSIS 02.
- Search results header: Search results: ( p53 - MDM2) (Date range: from 12-2003 to 12-2005) returned 4320 documents.
- View options: Documents (selected), Sentences.
- Page controls: Navigation arrows, page numbers 1-5, and a dropdown for 'Show 20 documents per page'.
- Document list: A table of search results with columns for document ID, title, journal information, authors, and date.

		Date ▼
<input type="checkbox"/>	<b>Survivin gene expression is negatively regulated by the p53 tumor suppressor gene in non-small cell lung cancer.</b> <a href="#">16211215</a>   Int J Oncol 2005,Nov,01;27(5):1215-21 Nakano Jun ; Huang Cheng-Long ; Liu Dage ; Ueno Masaki ; Sumitomo Shinichi ; Yokomise Hiroyasu	11/2005
<input type="checkbox"/>	<b>Cell-cycle regulators, bcl-2 and NF-kappaB in Epstein-Barr virus-positive gastric carcinomas.</b> <a href="#">16211221</a>   Int J Oncol 2005,Nov,01;27(5):1265-72 Chang Mee Soo ; Lee Hye Seung ; Jung Eun Ji ; Kim Chul Woo ; Lee Byung Lan ; Kim Woo Ho	11/2005
<input type="checkbox"/>	<b>OGG1 Cys326 variant, allelic imbalance of chromosome band 3p25.3 and TP53 mutations in ovarian cancer.</b> <a href="#">16211227</a>   Int J Oncol 2005,Nov,01;27(5):1315-20 Arcand Suzanna L ; Provencher Diane ; Mes-Masson Anne-Marie ; Tonin Patricia N	11/2005
<input type="checkbox"/>	<b>Activation of p53 and the pro-apoptotic p53 target gene PUMA during depolarization-induced apoptosis of chromaffin cells.</b> <a href="#">16112113</a>   Exp Neurol 2005,Nov,01;196(1):96-103 Gomez-Lazaro M ; Galindo M F ; Fernandez-Gomez F J ; Prehn J H M ; Jordán J	11/2005
<input type="checkbox"/>	<b>Gender-dependent hepatic alterations in H-ras12V transgenic mice.</b> <a href="#">16087271</a>   J Hepatol 2005,Nov,01;43(5):836-44 Wang Ai-Guo ; Moon Hyung-Bae ; Lee Mi-Ran ; Hwang Chae Young ; Kwon Ki-Sun ; Yu Seong-Lan ; Kim Yong-Sung ; Kim Mirang , et al.	11/2005
<input type="checkbox"/>	<b>Pifithrin-alpha induced p53 inhibition does not affect liver regeneration after partial hepatectomy in mice.</b> <a href="#">16087272</a>   J Hepatol 2005,Nov,01;43(5):829-35 Eipel Christian ; Schuett Harald ; Glawe Claudia ; Bordel Reingart ; Menger Michael D ; Vollmar Brigitte	11/2005

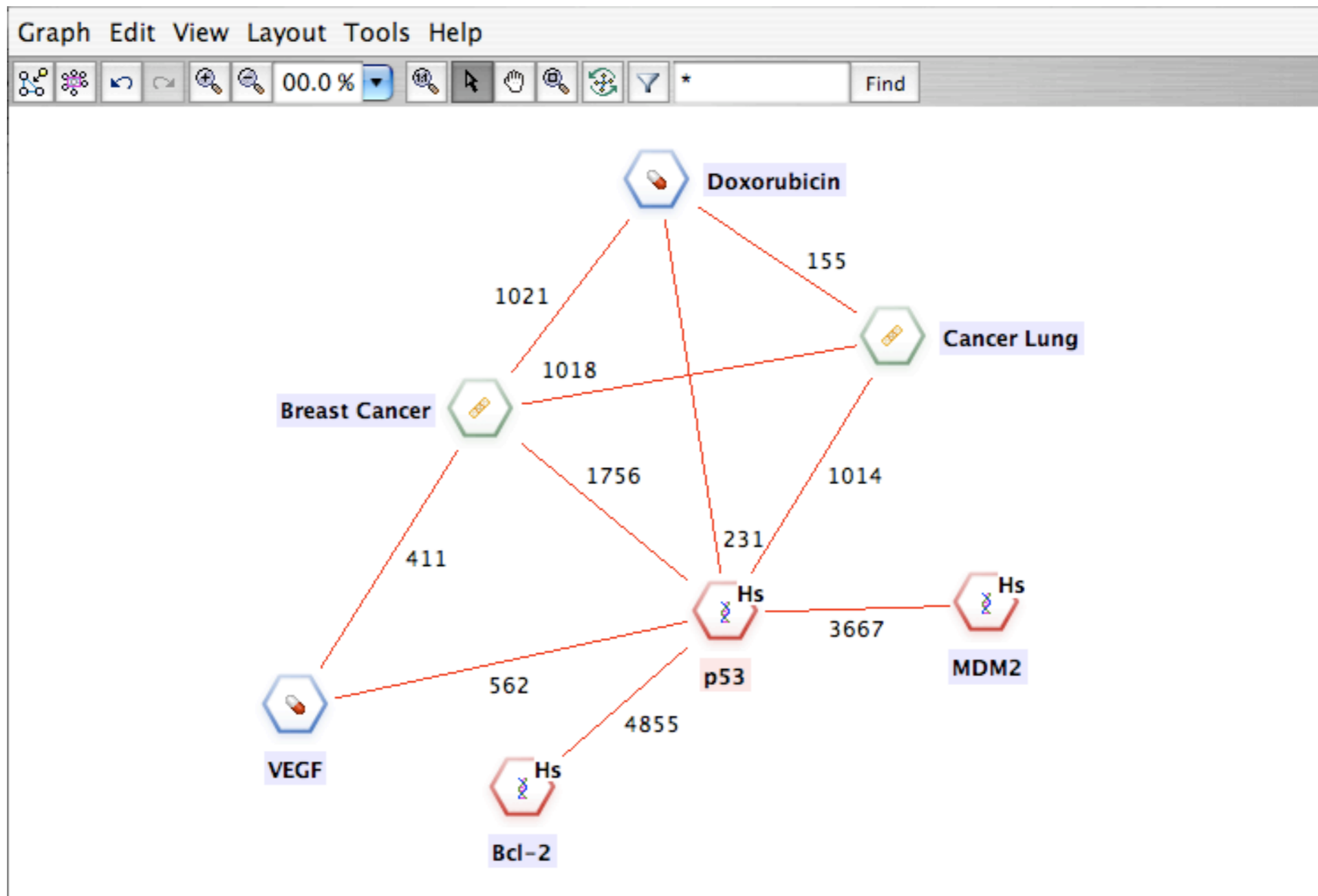
# 3

## The graphical interface



# 3

## The graphical interface



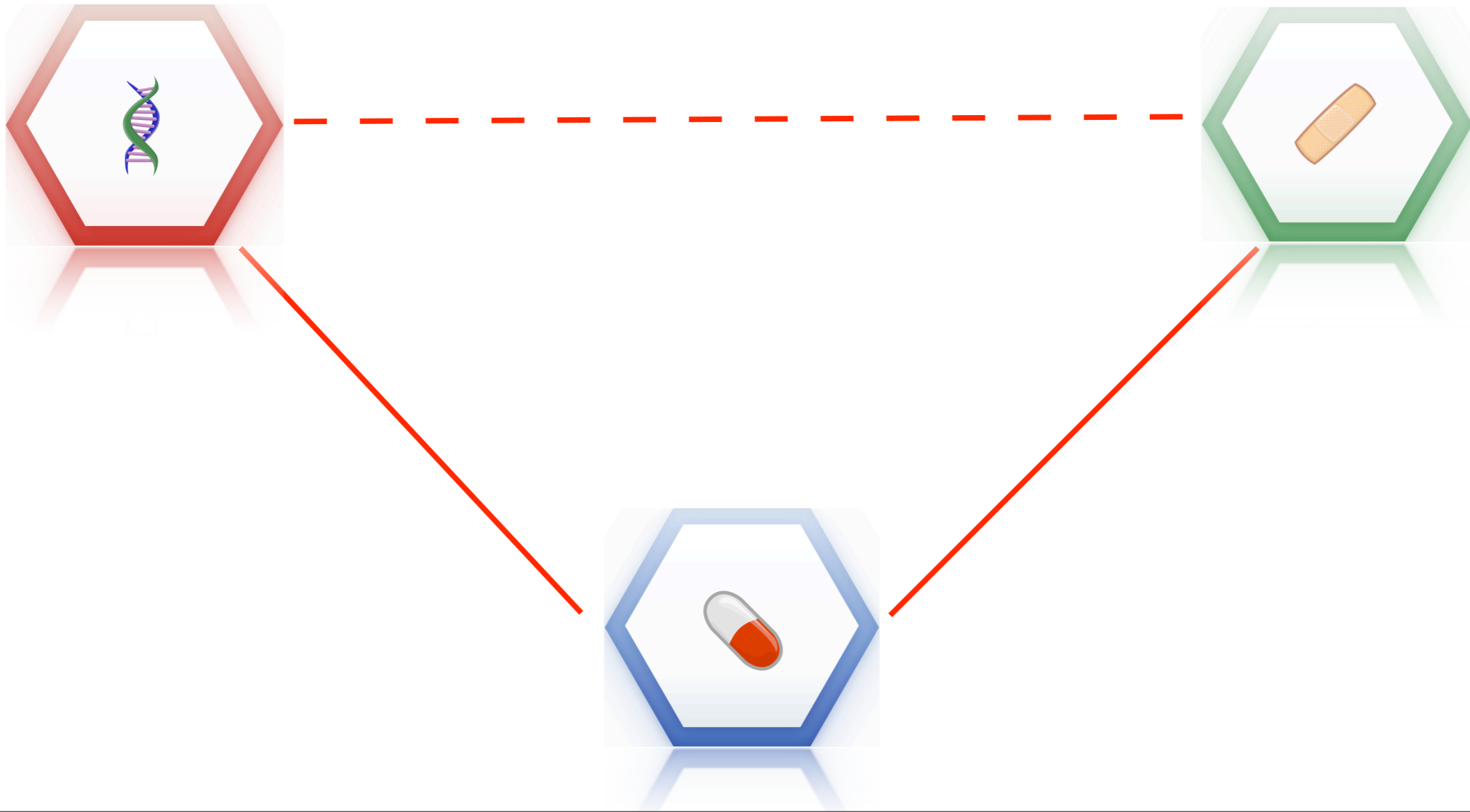
3

# The graphical interface: Knowledge discovery

3

## The graphical interface: Knowledge discovery

Is this gene related to this disease?

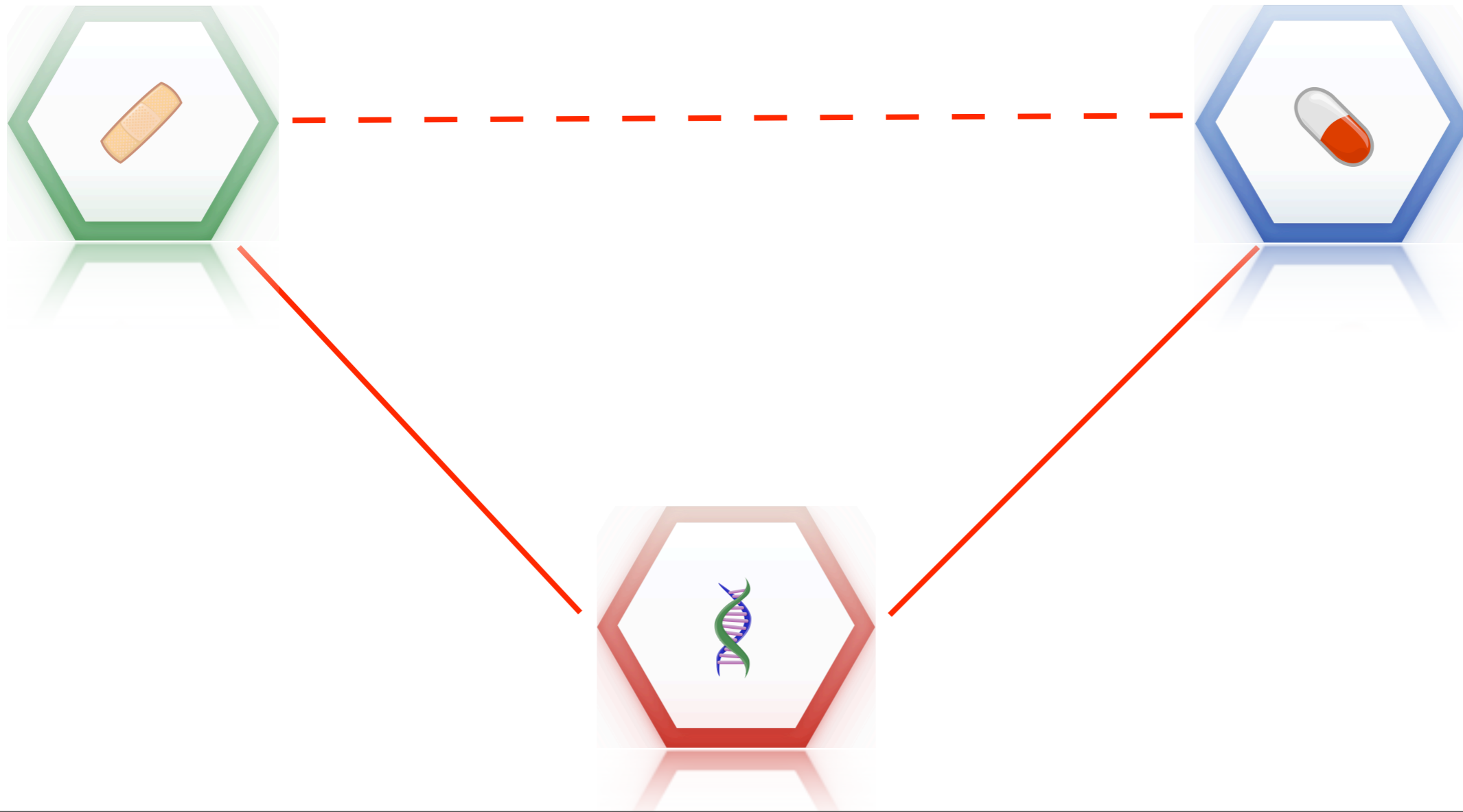




3

## The graphical interface: Knowledge discovery

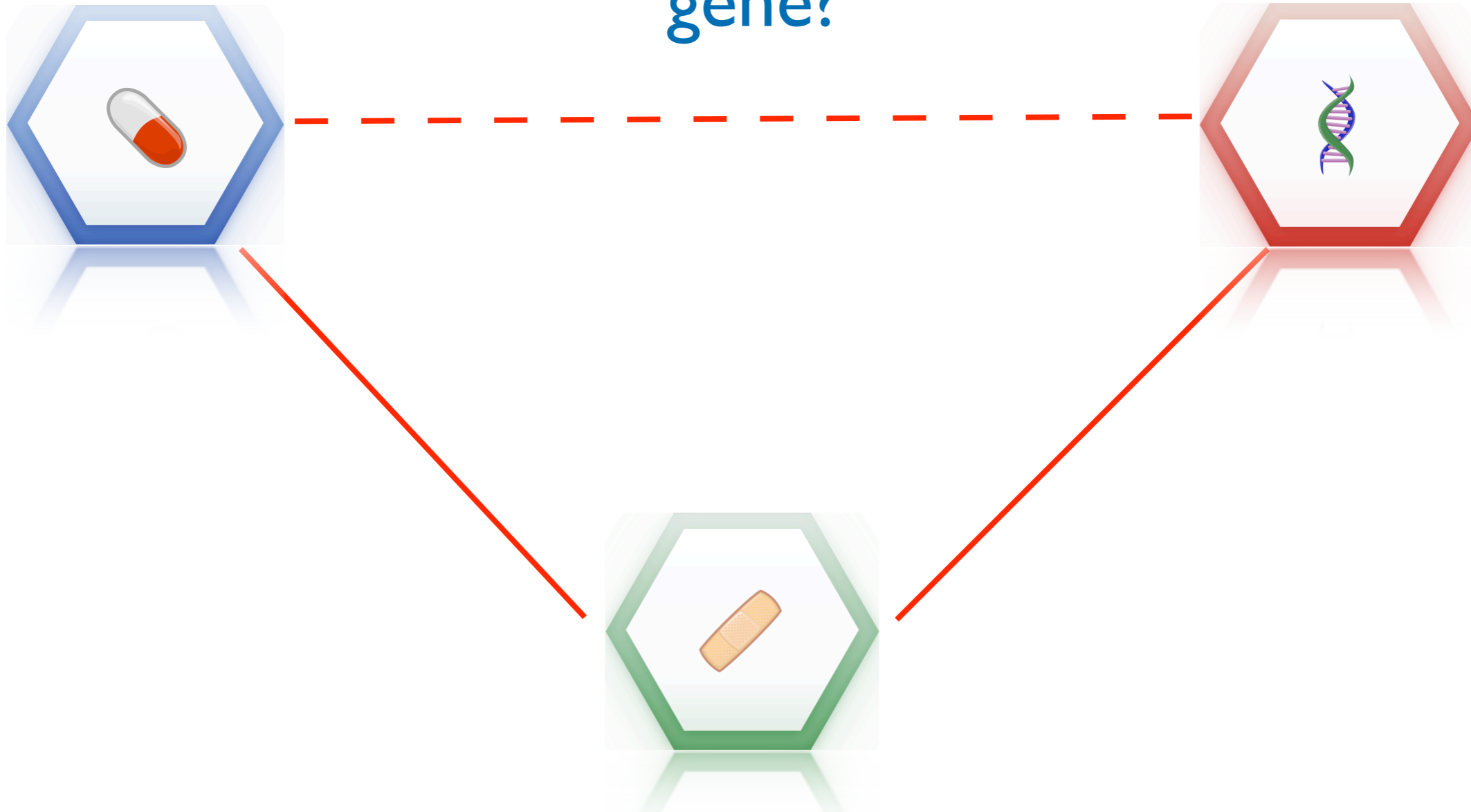
Can this disease be treated with this drug?



3

## The graphical interface: Knowledge discovery

Would the mechanisms of this drug be through this gene?





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alzheimer's

Search

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## Web

Results 1 - 10 of about 25,600,000 for alzheimer's. (0.07 seconds)

Refine results for **alzheimer's**:

[Treatment](#)   [Tests/diagnosis](#)   [For patients](#)   [From medical authorities](#)  
[Symptoms](#)   [Causes/risk factors](#)   [For health professionals](#)   [Alternative medicine](#)

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**Alzheimer's** disease, information for caregivers, research.

[www.alz.org/](http://www.alz.org/) - 51k - [Cached](#) - [Similar pages](#)

### [Alzheimer's Society website - the leading UK care and research ...](#)

The **Alzheimer's** Society is the leading UK care and research charity for people with dementia, their families and carers. This site is frequently updated ...

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### [Default Error Page](#)

Government site with information on research and practical resources for the aging population.

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### [Alzheimer's Disease Fact Sheet](#)

AD is named after Dr. Alois **Alzheimer**, a German doctor. ... For more information on ADNI, call the NIA's **Alzheimer's** Disease Education and Referral (ADEAR) ...

[www.nia.nih.gov/Alzheimers/Publications/adfact.htm](http://www.nia.nih.gov/Alzheimers/Publications/adfact.htm) - 32k - [Cached](#) - [Similar pages](#)

### [MedlinePlus: Alzheimer's Disease](#)

Search MEDLINE/PubMed for recent research articles on **Alzheimer's** Disease: ... Select services and providers for **Alzheimer's** Disease in your area. ...

[www.nlm.nih.gov/medlineplus/alzheimersdisease.html](http://www.nlm.nih.gov/medlineplus/alzheimersdisease.html) - 59k - [Cached](#) - [Similar pages](#)

### [Alzheimer's disease - Wikipedia, the free encyclopedia](#)

**Alzheimer's** disease (AD) is a neurodegenerative disease characterized by ... **Alzheimer's** disease is the most frequent type of dementia in the elderly and ...

[en.wikipedia.org/wiki/Alzheimer's\\_disease](http://en.wikipedia.org/wiki/Alzheimer's_disease) - 82k - [Cached](#) - [Similar pages](#)

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Display Summary Show 20 Sort by Send to

All: 51329 Review: 10138

Items 1 - 20 of 51329

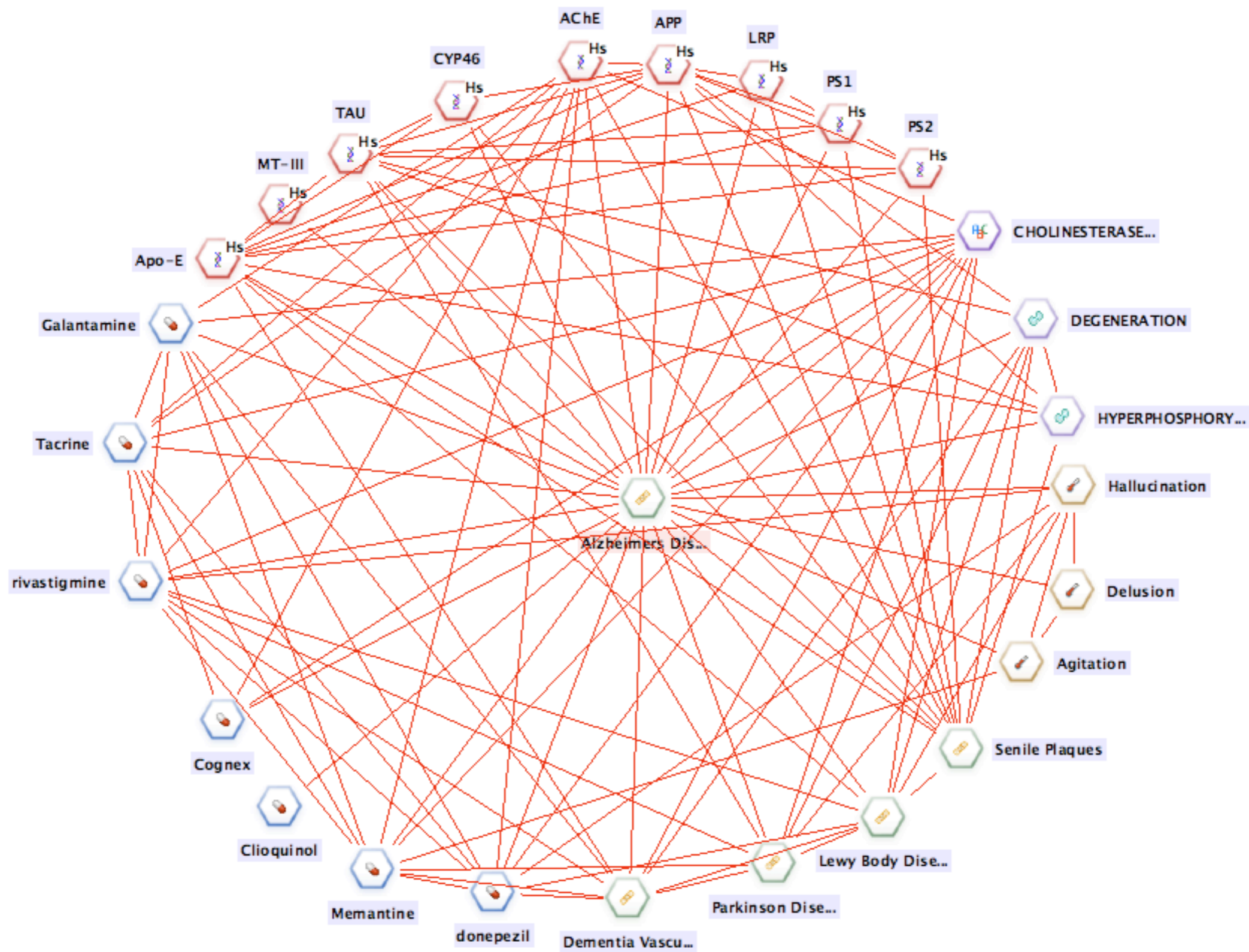
Page 1 of 2567 Next

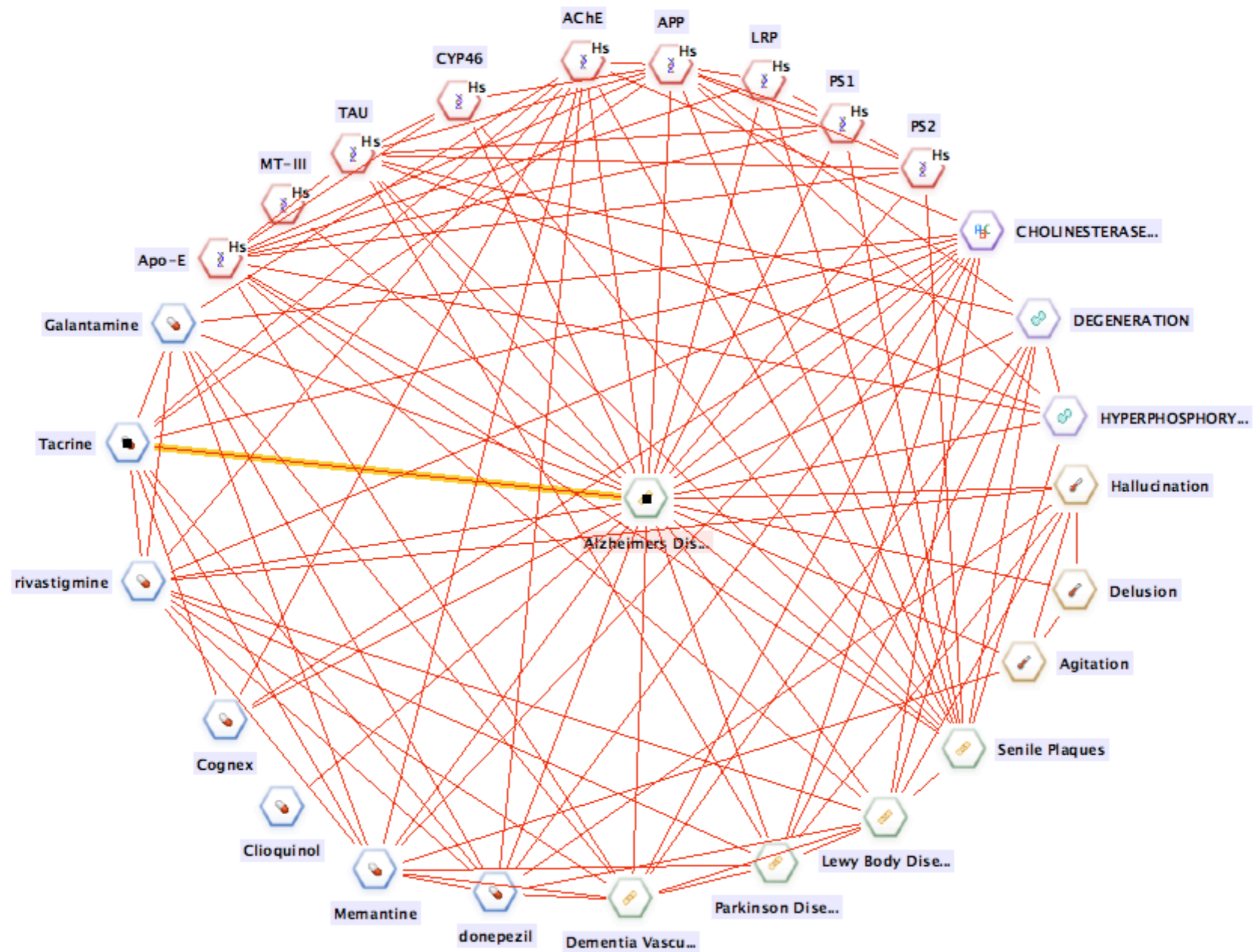
- 1:** [Rockwood K, Black S, Bedard MA, Tran T, Lussier I.](#) Links  
 Specific symptomatic changes following donepezil treatment of Alzheimer's disease: a multi-centre, primary care, open-label study.  
 Int J Geriatr Psychiatry. 2006 Sep 27; [Epub ahead of print]  
 PMID: 17006874 [PubMed - as supplied by publisher]
- 2:** [Sultana R, Butterfield DA.](#) Links  
 Regional Expression of Key Cell Cycle Proteins in Brain from Subjects with Amnesic Mild Cognitive Impairment.  
 Neurochem Res. 2006 Sep 28; [Epub ahead of print]  
 PMID: 17006763 [PubMed - as supplied by publisher]
- 3:** [Previll LA, Crosby ME, Castellani RJ, Bowser R, Perry G, Smith MA, Zhu X.](#) Links  
 Increased Expression of p130 in Alzheimer Disease.  
 Neurochem Res. 2006 Sep 28; [Epub ahead of print]  
 PMID: 17006760 [PubMed - as supplied by publisher]
- 4:** [von Arnim CA, Spoelgen R, Peltan ID, Deng M, Courchesne S, Koker M, Matsui T, Kowa H, Lichtenthaler SF, Irizarry MC, Hyman BT.](#) Links  
 GGA1 acts as a spatial switch altering amyloid precursor protein trafficking and processing.  
 J Neurosci. 2006 Sep 27;26(39):9913-22.  
 PMID: 17005855 [PubMed - in process]
- 5:** [Vitvitsky V, Thomas M, Ghorpade A, Gendelman HE, Banerjee R.](#) Links  
 A functional transsulfuration pathway in brain links to glutathione homeostasis.  
 J Biol Chem. 2006 Sep 27; [Epub ahead of print]

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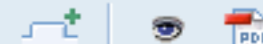




## Relation Documents

Documents

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521 Documents

	Date	Relevance ▼
<input type="checkbox"/> <b>Tacrine</b> in relation to amino acid transmitters in <b>Alzheimer's disease</b> . <a href="#">1967197</a>   Adv Neurol 1990,Jan,01;51:91-6 Bowen D M ; Steele J E ; Lowe S L ; Palmer A M	01/1990	100%
<input type="checkbox"/> <b>Treatment of Alzheimer's disease</b> with short- and long-term oral THA and lecithin: a double-blind study. <a href="#">2405720</a>   Am J Psychiatry 1990,Feb,01;147(2):239-42 Fitten L J ; Perryman K M ; Gross P L ; Fine H ; Cummins J ; Marshall C	03/1990	100%
<input type="checkbox"/> <b>Influence of tetrahydro-9-aminoacridine</b> on excitatory amino acid release. <a href="#">2306748</a>   Clin Neuropharmacol 1990,Feb,01;13(1):58-66 Palmer A M ; Steele J E ; Lowe S L ; Bowen D M	03/1990	100%
<input type="checkbox"/> <b>Tacrine (tetrahydroaminoacridine; THA)</b> and lecithin in senile dementia of the Alzheimer type: a multicentre trial. Groupe Français d'Etude de la <b>Tetrahydroaminoacridine</b> . <a href="#">2107926</a>   BMJ 1990,Feb,24;300(6723):495-9 Chatellier G ; Lacomblez L	03/1990	100%
<input type="checkbox"/> <b>Tetrahydroaminoacridine-lecithin</b> combination treatment in patients with intermediate-stage <b>Alzheimer's disease</b> . Results of a Canadian double-blind, crossover, multicenter study. <a href="#">2183056</a>   N Engl J Med 1990,May,03;322(18):1272-6 Gauthier S ; Bouchard R ; Lamontagne A ; Bailey P ; Bergman H ; Ratner J ; Tesfaye Y ; Saint-Martin M , et al.	05/1990	100%
<input type="checkbox"/> <b>Tacrine</b> and lecithin in <b>Alzheimer's disease</b> . <a href="#">2337722</a>   BMJ 1990,Apr,07;300(6729):939-40	04/1990	100%
<input type="checkbox"/> <b>Heterogeneity of adverse hepatic reactions</b> to <b>tetrahydroaminoacridine</b> .	04/1990	100%



Summary

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## Relation Documents

Documents

Sentences


 Filter

&lt;&lt; &lt; 1 2 3 4 5 6 7 8 9 10 &gt; &gt;&gt;

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 401 Sentences

	PMID	Date	Relevance ▼
<input type="checkbox"/> The authors support that penetration of <b>tacrine</b> into CSF is highly variable in patients with <b>Alzheimer's disease</b> and that disparity in <b>tacrine</b> concentrations at the site of action may be one reason for conflicting results from studies of the efficacy of <b>tacrine</b> in <b>Alzheimer's disease</b> .	<a href="#">9472847</a>	03/1998	<div style="width: 100%;"><div style="width: 100%;"></div></div> 100%
<input type="checkbox"/> OBJECTIVE--To see whether combined treatment with oral <b>tacrine</b> ( <b>tetrahydroaminoacridine</b> ; THA) and lecithin improves the symptoms of patients with <b>Alzheimer's disease</b> .	<a href="#">2107926</a>	03/1990	<div style="width: 60%;"><div style="width: 60%;"></div></div> 60%
<input type="checkbox"/> Because orthostatic blood pressure response is regulated, in part, by central cholinergic and noradrenergic systems, and both are implicated in <b>Alzheimer's disease</b> , PSOP was assessed as a predictor of initial response in <b>Alzheimer's disease</b> outpatients in a treatment protocol with <b>tacrine</b> , a cholinesterase inhibitor.	<a href="#">1775604</a>	01/1991	<div style="width: 60%;"><div style="width: 60%;"></div></div> 60%
<input type="checkbox"/> CONCLUSIONS. In this short-term study in patients with <b>Alzheimer's disease</b> who were selected for apparent responsiveness to <b>tacrine</b> , treatment with <b>tacrine</b> resulted in a statistically significant reduction in the decline of cognitive function, although this reduction was not large enough to be detected by the study physicians' global assessments of the patients.	<a href="#">1406817</a>	10/1992	<div style="width: 60%;"><div style="width: 60%;"></div></div> 60%
<input type="checkbox"/> Three patients with <b>Alzheimer's disease</b> , a 68-year-old woman with mild dementia and 2 men (aged 64 and 72 years) with moderate dementia were treated orally with the cholinesterase inhibitor <b>tacrine</b> ( <b>tetrahydroaminoacridine</b> ), 80 mg daily, for several months.	<a href="#">1491741</a>	11/1992	<div style="width: 60%;"><div style="width: 60%;"></div></div> 60%
<input type="checkbox"/> Seventy-nine patients with probable <b>Alzheimer's disease</b> were enrolled into a double-blind, placebo-controlled cross-over study to assess the therapeutic effect and safety of THA ( <b>tetrahydroaminoacridine</b> ; <b>tacrine</b> ) without concomitant lecithin administration.	<a href="#">8237620</a>	09/1993	<div style="width: 60%;"><div style="width: 60%;"></div></div> 60%
<input type="checkbox"/> The potential efficacy of oral l-deprenyl (5 mg b.i.d.) added to the regimen of 10 patients with <b>Alzheimer's disease</b> receiving either <b>tacrine</b> or physostigmine was assessed in a double-blind, placebo-controlled, 4-week, two-period crossover pilot study. l-Deprenyl was associated with significant improvement in scores on the cognitive subscale of the <b>Alzheimer's Disease</b> Assessment Scale, suggesting possible additive effects of l-deprenyl to the effects of cholinesterase inhibitors.	<a href="#">8422085</a>	03/1993	<div style="width: 60%;"><div style="width: 60%;"></div></div> 60%
<input type="checkbox"/> Previously used in <b>Alzheimer disease Tacrine</b> (THA): <b>tetrahydroaminoacridine</b> has shown a rise of hepatic transaminase enzyme	<a href="#">1295125</a>	05/1992	<div style="width: 60%;"><div style="width: 60%;"></div></div> 60%



## 8 Documents

Date ▼

- 
- Penetration of tacrine into cerebrospinal fluid in patients with Alzheimer's disease.**

03/1998

[9472847](#) | J Clin Psychopharmacol 1998, Feb, 01; 18(1): 78-81

Grothe D R ; Piscitelli S C ; Dukoff R ; Fullerton T ; Sunderland T ; Molchan S E

**Abstract:**

**Tacrine** is widely used for the treatment of **Alzheimer's disease**, but data are limited regarding cerebrospinal fluid (CSF) concentrations at steady state. To evaluate CSF penetration, seven patients with **Alzheimer's disease** who were receiving **tacrine** at doses of 40 to 140 mg/day as a part of a double-blind trial were studied. After 6 weeks of **tacrine** therapy, concomitant plasma and CSF samples were collected 30 minutes after the morning dose of **tacrine**. Although this time point is before the peak oral absorption in most patients, the critical issue for this study is that the plasma and CSF samples were collected concomitantly so that a percentage of **tacrine** penetration could be derived. The morning dose of **tacrine** ranged from 10 to 40 mg, which was given in the fasting state. Mean (+/-SD) plasma levels of **tacrine** were 8.01 +/- 7.07 ng/mL, whereas mean (+/-SD) CSF levels of **tacrine** were 5.21 +/- 6.00 ng/mL. The mean (+/-SD) ratio of CSF to plasma **tacrine** concentration was 0.50 +/- 0.45, with wide interindividual variability. No relationship between dose and percentage of penetration was observed. Plasma concentrations ranged from 0.99 to 22.6 ng/mL and were unrelated to dose, suggesting erratic oral absorption and/or rapid metabolism. CSF concentrations ranged from not detectable to 15.92 ng/mL. **The authors support that penetration of tacrine into CSF is highly variable in patients with Alzheimer's disease and that disparity in tacrine concentrations at the site of action may be one reason for conflicting results from studies of the efficacy of tacrine in Alzheimer's disease.**

- 
- An evaluation of the efficacy and safety of tetrahydroaminoacridine (THA) without lecithin in the treatment of Alzheimer's disease.**

09/1993

[8237620](#) | Age Ageing 1993, Sep, 01; 22(5): 316-24

Wilcock G K ; Surmon D J ; Scott M ; Boyle M ; Mulligan K ; Neubauer K A ; O'Neill D ; Royston V H

**Abstract:**

**Seventy-nine patients with probable Alzheimer's disease were enrolled into a double-blind, placebo-controlled cross-over study to assess the therapeutic effect and safety of THA (tetrahydroaminoacridine; tacrine) without concomitant lecithin administration.** Forty-one patients completed the trial which consisted of two 12-week treatment phases separated by a 4-week wash-out period. Twenty-six subjects were withdrawn during the active treatment phase, mostly because of elevated transaminases or cholinergic side-effects, and ten during treatment with placebo. Statistical analyses were conducted on two groups of patients; those completing the cross-over and those with at least one evaluation in the first treatment period. This latter analysis, using the last observation carried forward was used to approximate an intention-to-treat analysis. THA was favoured over placebo in all three primary outcome measures (MMSE, ADAS Non-cognitive Scale, and the Functional Life Scale), but the results did not reach statistical significance. THA was favoured over placebo in five of the seven secondary outcome measures, but for only two of these was statistical significance attained. In terms of a three-point or greater increase in MMSE score, three to four times as many subjects improved on THA as on placebo.

- 
- A double-blind crossover pilot study of l-deprenyl (selegiline) combined with cholinesterase inhibitor in Alzheimer's disease.**

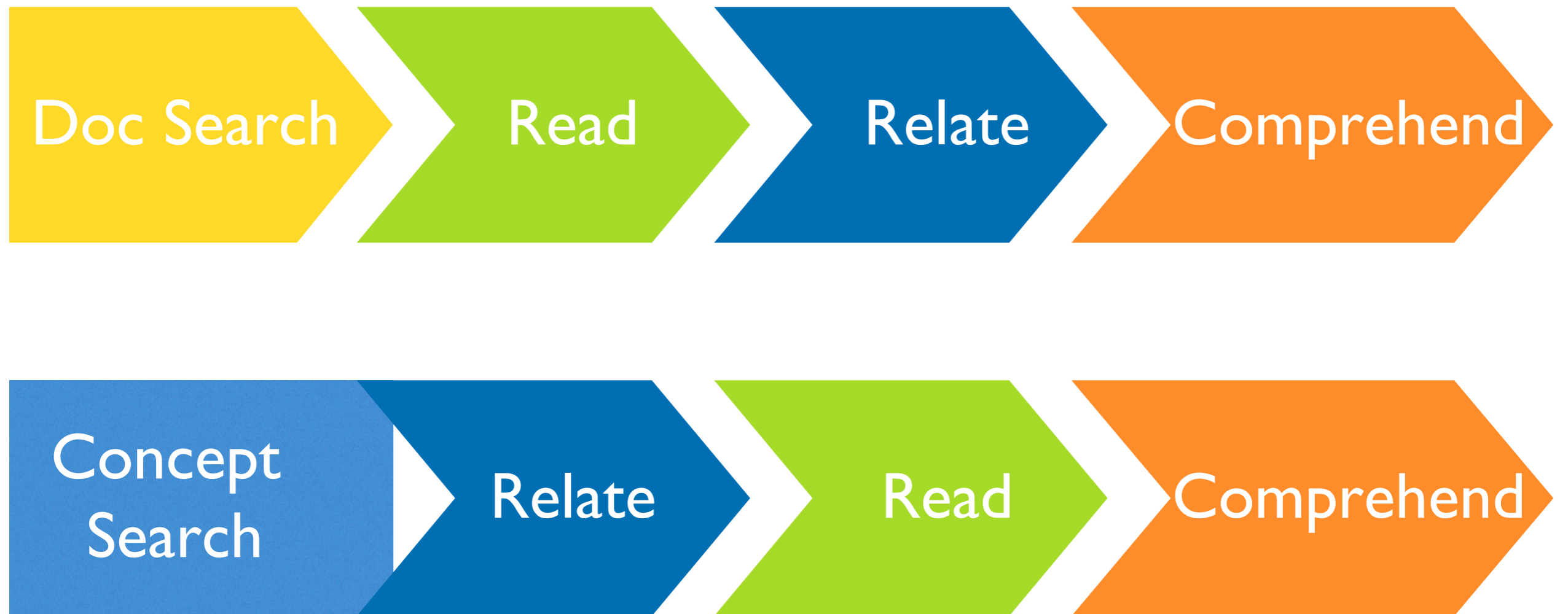
03/1993

[8422085](#) | Am J Psychiatry 1993, Feb, 01; 150(2): 321-3

Schneider L S ; Olin J T ; Pawluczyk S

3

## The graphical interface



# Abstract detail

# Document list

Document list

8 Documents

Penetration of tacrine into cerebrospinal fluid in patients with Alzheimer's disease. [Abstract](#) | J Clin Psychopharmacol 1988;8(2):118-21  
 Gratha D R.; Pappalà S C.; Duloff R.; Fullerton T.; Sunderland T.; Mohr J S E

**Abstract:**  
 Tacrine is widely used for the treatment of Alzheimer's disease, but data are limited regarding cerebrospinal fluid (CSF) concentrations at steady state. To evaluate CSF penetration, seven patients with Alzheimer's disease who were receiving tacrine at doses of 40 to 140 mg/day as a part of a double-blind trial were studied. After 6 weeks of tacrine therapy, concurrent plasma and CSF samples were collected 30 minutes after the morning dose of tacrine. Although the time point is before the peak oral absorption in most patients, the critical issue for this study is that the plasma and CSF samples were collected concomitantly so that a percentage of tacrine penetration could be derived. The morning dose of tacrine ranged from 10 to 40 mg, which was given in the fasting state. Mean (±SD) plasma levels of tacrine were 8.01±7.07 ng/mL, whereas mean (±SD) CSF levels of tacrine were 0.21±0.09 ng/mL. The mean (±SD) ratio of CSF to plasma tacrine concentration was 0.04±0.45, with wide interindividual variability. No relationship between dose and percentage of penetration was observed. Plasma concentrations ranged from 0.99 to 22.6 ng/mL, and were unrelated to dose, suggesting erratic oral absorption and/or rapid metabolism. CSF concentrations ranged from not detectable to 15.53 ng/mL. The authors support that penetration of tacrine into CSF is highly variable in patients with Alzheimer's disease and that disparity in tacrine concentrations at the site of action may be one reason for conflicting results from studies of the efficacy of tacrine in Alzheimer's disease.

An evaluation of the efficacy and safety of tetrahydroaminoacridine (THA) without lecithin in the treatment of Alzheimer's disease. [Abstract](#)  
 Wilcock G K.; Samson D J.; Scott M.; Boyle M.; Mulligan K.; Naubauer K A.; O'Neill D.; Royston V H

**Abstract:**  
 Seventy-nine patients with probable Alzheimer's disease were enrolled into a double-blind, placebo-controlled cross-over study to assess the therapeutic effect and safety of THA (tetrahydroaminoacridine; tacrine) without concomitant lecithin administration. Forty-one patients completed the trial which consisted of two 12-week treatment phases separated by a 4-week wash-out period. Twenty-six subjects were withdrawn during the active treatment phases, mostly because of elevated transaminases or cholinergic side-effects, and ten during treatment with placebo. Statistical analyses were conducted on two groups of patients: those completing the cross-over and those with at least one evaluation in the first treatment period. The latter analysis, using the last observation carried forward to approximate an intention-to-treat analysis, THA was favoured over placebo in all three primary outcome measures (MMSE, ADAS Non-cognitive Scale, and the Functional Life Scale), but the results did not reach statistical significance. THA was favoured over placebo in five of the seven secondary outcome measures, but for only two of these was statistical significance attained. In terms of a three-point or greater increase in MMSE score, three to four times as many subjects improved on THA as on placebo.

A double-blind crossover pilot study of donepezyl (belingyl) combined with cholinesterase inhibitor in Alzheimer's disease. [Abstract](#)  
 Schroeder L S.; Oh J T.; Pawluczak S

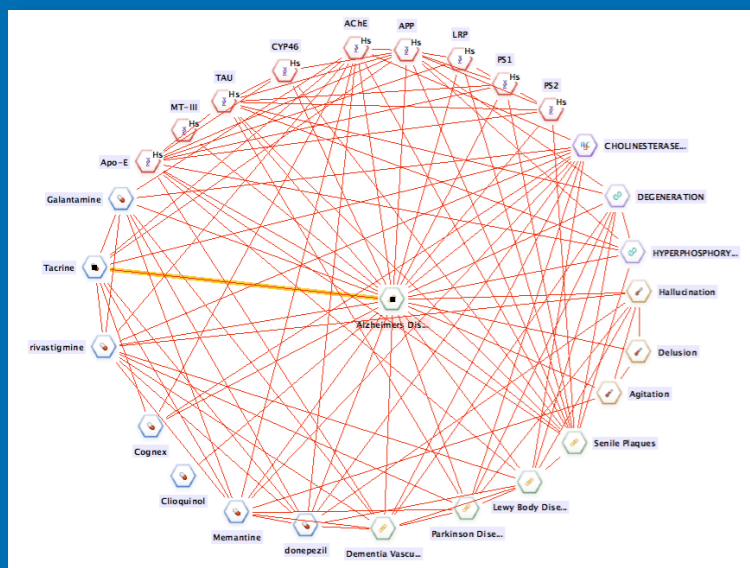
Relation Documents

Documents Sentences

521 Documents

Documents	Date	Relevance
Tacrine in relation to amino acid transmitters in Alzheimer's disease. <a href="#">Abstract</a> 1967197   Adv Neuro 1990;Jan;01:51-9:6 Bowen D M.; Steele J E.; Lowe S L.; Palmer A M	01/1990	100%
Treatment of Alzheimer's disease with short- and long-term oral THA and lecithin: a double-blind study. <a href="#">Abstract</a> 2453722   Am J Psychiatry 1990;146:01:147(2):239-42 Folan L J.; Phenyman N M.; Gross P L.; Fife W.; Cameron J.; Marshall C	03/1990	100%
Influence of tetrahydro-9-aminoacridine on excitatory amino acid release. <a href="#">Abstract</a> 2362759   Can Neuropharmacol 1990;Feb;01:13(1):59-66 Palmer A M.; Steele J E.; Lowe S L.; Bowen D M	03/1990	100%
Tacrine (tetrahydroaminoacridine, THA) and lecithin in senile dementia of the Alzheimer type: a multicentre trial. Groupe Français d'Etude de la Tetrahydroaminoacridine. <a href="#">Abstract</a> 2107928   BMJ 1990;Feb;24:300(5723):495-9 Chastellier G.; Lacomblez L	03/1990	100%
Tetrahydroaminoacridine-lecthin combination treatment in patients with intermediate-stage Alzheimer's disease. Results of a Canadian double-blind, crossover, multicenter study. <a href="#">Abstract</a> 2183098   N Engl J Med 1990;May;03:322(18):1272-6 Gauthier S.; Bouchard R.; Lamontagne A.; Billey P.; Bergman H.; Rotzer J.; Teasdale Y.; Saint-Martin M.; et al.	05/1990	100%
Tacrine and lecithin in Alzheimer's disease. <a href="#">Abstract</a> 2451722   BMJ 1990;Apr;07:300(6729):939-40	04/1990	100%
Heterogeneity of adverse hepatic reactions to tetrahydroaminoacridine.	04/1990	100%

# Graph view



Relation Documents

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401 Sentences

Documents	PMID	Date	Relevance
The authors support that penetration of tacrine into CSF is highly variable in patients with Alzheimer's disease and that disparity in tacrine concentrations at the site of action may be one reason for conflicting results from studies of the efficacy of tacrine in Alzheimer's disease. <a href="#">Abstract</a>	9472847	03/1998	100%
OBJECTIVE.—To see whether combined treatment with oral tacrine (tetrahydroaminoacridine, THA) and lecithin improves the symptoms of patients with Alzheimer's disease. <a href="#">Abstract</a>	2107928	03/1990	90%
Because orthostatic blood pressure response is regulated, in part, by central cholinergic and noradrenergic systems, and both are implicated in Alzheimer's disease, PSOP was assessed as a predictor of initial response in Alzheimer's disease outpatients in a treatment protocol with tacrine, a cholinesterase inhibitor. <a href="#">Abstract</a>	1773604	01/1991	90%
CONCLUSIONS. In this short-term study in patients with Alzheimer's disease who were selected for apparent responsiveness to tacrine, treatment with tacrine resulted in a statistically significant reduction in the decline of cognitive function, although this reduction was not large enough to be detected by the study physicians' global assessments of the patients. <a href="#">Abstract</a>	1408817	10/1992	90%
Three patients with Alzheimer's disease, a 68-year-old woman with mild dementia and 2 men (aged 64 and 72 years) with moderate dementia were treated orally with the cholinesterase inhibitor tacrine (tetrahydroaminoacridine), 80 mg daily, for several months. <a href="#">Abstract</a>	1491741	11/1992	90%
Seventy-nine patients with probable Alzheimer's disease were enrolled into a double-blind, placebo-controlled cross-over study to assess the therapeutic effect and safety of THA (tetrahydroaminoacridine, tacrine) without concomitant lecithin administration. <a href="#">Abstract</a>	8237620	09/1993	90%
The potential efficacy of oral l-deprenyl (5 mg b.i.d.) added to the regimen of 10 patients with Alzheimer's disease receiving either tacrine or physostigmine was assessed in a double-blind, placebo-controlled, 4-week, two-period crossover pilot study. l-Deprenyl was associated with significant improvement in scores on the cognitive subscale of the Alzheimer's Disease Assessment Scale, suggesting possible additive effects of l-deprenyl to the effects of cholinesterase inhibitors. <a href="#">Abstract</a>	8420965	03/1993	90%
Previously used in Alzheimer disease Tacrine (THA); tetrahydroaminoacridine has shown a rise of hepatic transaminase enzyme. <a href="#">Abstract</a>	1295125	05/1992	90%

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