HuGE Navigator

Navigating the knowledge base in human genome epidemiology

GTCGACTGGAGTGTCTGTGAATTGACTTTTGTTGCCAGTTGGCAGCGGCAGAAGCAGCAAAGCCCGGCCAACAGCAACAAGCTCCTGCCAGATCCCAAAAGCAAACACG

Marta Gwinn, MD, MPH
Wei Yu, PhD, MS

National Office of Public Health Genomics
Centers for Disease Control and Prevention

about

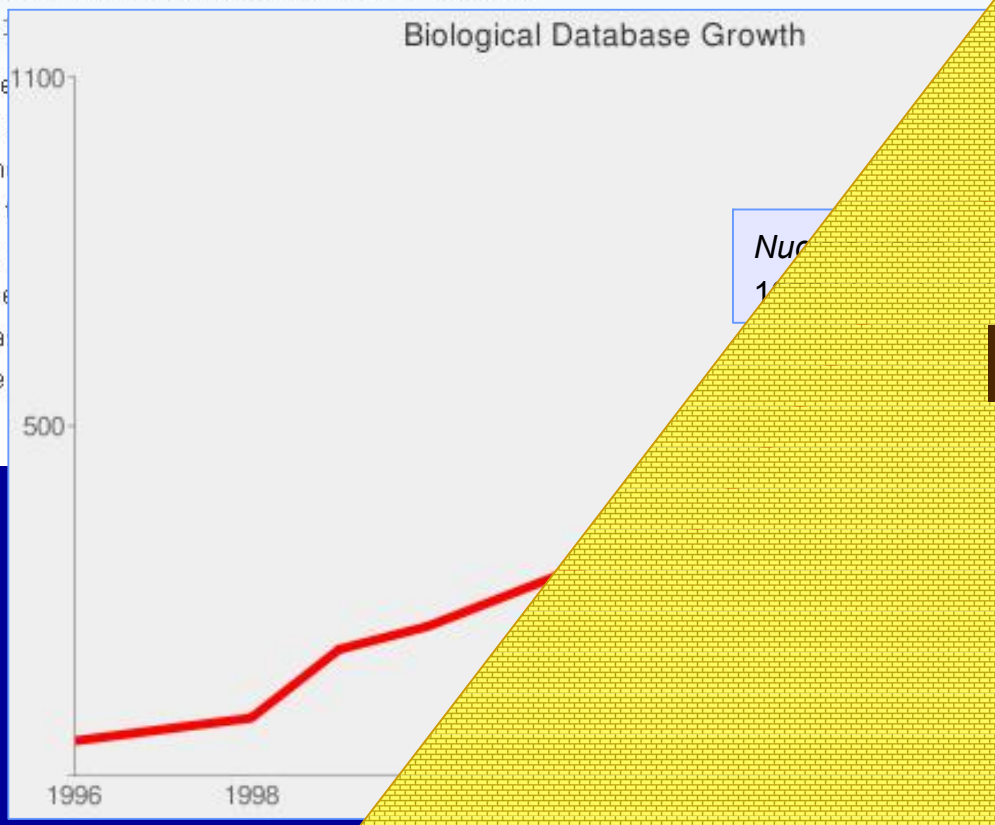
nodalpoint.org

Home › Blogs › Duncan's blog

One Thousand Databases High (and rising)

Fri, 2008-01-18 2

Well it's that time
stamp collecting
also known as th
published earlier
databases listed
previous one (see
thousand databa
proportion of the
be used?



data tombs

HuGE Published Literature, 2001-

GTCGACTGGAGTGTCTGTGAATTGACTTTTGTTGCCAGTTGGCAGCGGCAGAAGCAGCAAAGCCCGGCCAACAGCAACAAGCTCCTGCCAGATCCCAAAAGCAAACACG

- Population-based data
  - Genotype prevalence
  - Genetic association
  - Gene-environment interaction
- Extracted weekly from PubMed
- Curated by epidemiologist
- Searchable, online database

Lin et al., Am J Epidemiol 2006;164(1):1-4.

CDC
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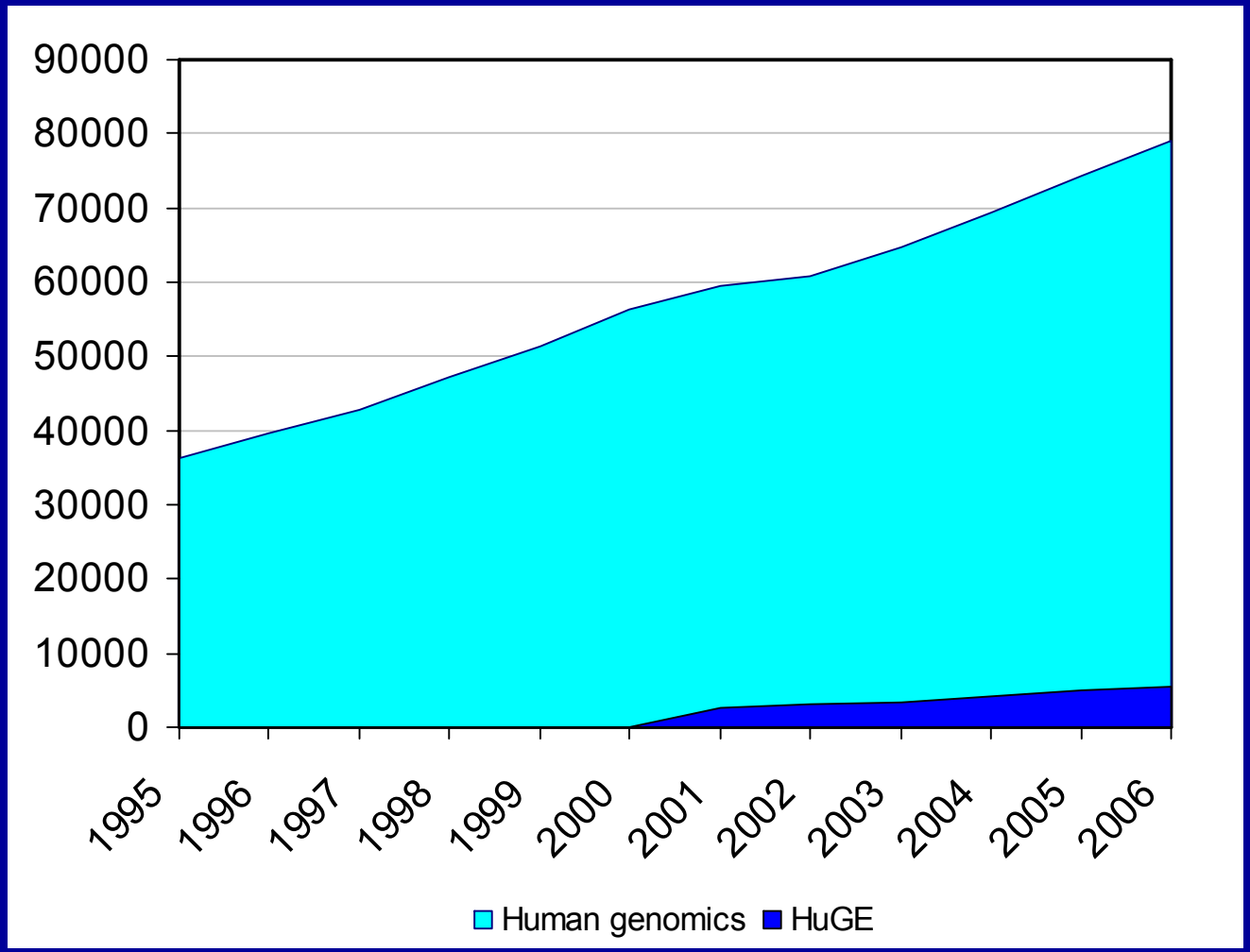
Publications related to human genetics/genomics, PubMed, 2001-2006*

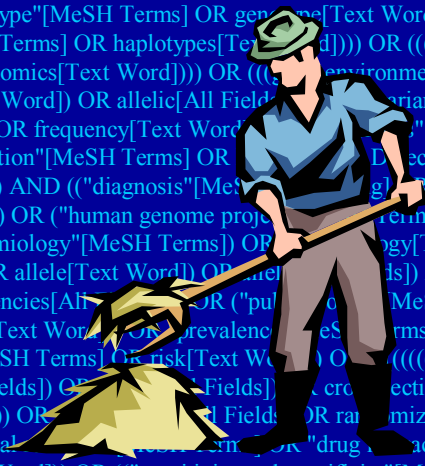


*based on PubMed, HuGE Navigator, Jan 2008

(((((((((((((((((((((((genetic[All Fields] AND (((((("disease"[MeSH Terms] OR ("disease susceptibility"[MeSH Terms] OR predisposition[Text Word])) OR disease[Text Word]) OR defect[Text Word]) OR susceptibility[Text Word]) OR ("counseling"[MeSH Terms] OR counseling[Text Word]))) OR (("disease susceptibility"[MeSH Terms] OR susceptibility[Text Word]) AND (("genes"[MeSH Terms] OR gene[Text Word]) OR ("genes"[MeSH Terms] OR genes[Text

((((((((((((genetic[All Fields] AND ("disease"[MeSH Terms] OR disease[Text Word])) OR ("hereditary diseases"[MeSH Terms] OR genetic disorder[Text Word])) OR (genetic[All Fields] AND ("TEST"[Substance Name] OR test[Text Word]))) OR (("genetic screening"[MeSH Terms] OR genetic screening[Text Word])) OR (genetic[All Fields] AND ("risk"[MeSH Terms] OR risk[Text Word]))) OR ("polymorphism (genetics)"[MeSH Terms] OR genetic polymorphism[Text Word])) OR ("genotype"[MeSH Terms] OR genotype[Text Word])) OR ("genome"[MeSH Terms] OR genome[Text Word])) OR (gene environment interaction[All Fields] OR gene-environment[All Fields])) OR ((genetic[All Fields] OR ("genes"[MeSH Terms] OR gene[Text Word])) AND variant[All Fields])) AND

((((((((("epidemiology"[Subheading] OR "epidemiology"[MeSH Terms]) OR epidemiology[Text Word]) OR ("public health"[MeSH Terms] OR public health[Text Word])) OR (("alleles"[MeSH Terms] OR allele[Text Word]) AND (("epidemiology"[Subheading] OR "epidemiology"[MeSH Terms]) OR frequency[Text Word]))) OR ("public policy"[MeSH Terms] OR policy[Text Word])) OR (("education"[Subheading] OR "education"[MeSH Terms]) OR education[Text Word]))) OR ((((("epidemiology"[Subheading] OR "prevalence"[MeSH Terms]) OR "epidemiology"[MeSH Terms]) OR "Prevalence"[MeSH Terms]) OR prevalence[Text Word])) OR ("prevention and control"[Subheading] OR prevention[Text Word])) OR ("risk"[MeSH Terms] OR risk[Text Word])) OR ("population"[MeSH Terms] OR population[Text Word]) AND study[All Fields]))) NOT ("animals"[MeSH Terms] OR "animal"[MeSH Terms]))



HuGE search query 2001 - 2004

Address http://www.hugenavigator.net/

HuGE Navigator (version 1.0)

An integrated, searchable knowledge base of genetic associations and human genome epidemiology.

Home | HuGENet™ | Open Source Projects | Contact

HuGE Navigator

HuGE Literature Finder

Find published articles in human genome epidemiology.

HuGEpedia

Look up summaries in an online encyclopedia of human genetic variation and health.

HuGE Investigator Browser

Find investigators in a particular field of human genome epidemiology.

GeneSelectAssist

A search engine for finding possible candidate genes based on NCBI Entrez Gene, PubMed and HuGE literature database.

HuGE Watch

Track the evolution of published literature in human genome epidemiology.

HuGE Risk Translator

Calculate the predictive value of genetic markers.

About the Navigator

HuGE Navigator provides access to a continuously updated knowledge base in human genome epidemiology, including information on population prevalence of genetic variants, gene-disease associations, gene-gene and gene-environment interactions, and evaluation of genetic tests.

The Human Genome Epidemiology Network (HuGENet™) is a voluntary, international collaboration focused on assessing the role of human genome variation in health and disease at the population level. Since 2001, HuGENet™ has maintained a database of published, population-based epidemiologic studies of human genes extracted and curated from PubMed. The HuGE Navigator replaces earlier search tools for use with this database and provides additional applications for use by researchers and the public.

Announcements

- A robust automatic screening tool (GAPscreener) for human genetic association study publications from PubMed is available for free downloading. (12/7/2007)

HuGE Navigator: www.hugenavigator.net

GTCGACTGGAGTGTCTGTGAATTGACTTTTGTTGCCAGTTGGCAGCGGCAGAAGCAGCAAAGCCCGGCCAACAGCAACAAGCTCCTGCCAGATCCCAAAAGCAAACACG

- Screen PubMed using machine learning method
- Curate by hand
  - Select abstracts
  - Index with HUGO gene symbol
  - Assign study type, category
- Auto-index using Entrez Gene, MeSH, UMLS
- Search, sort, filter, display data

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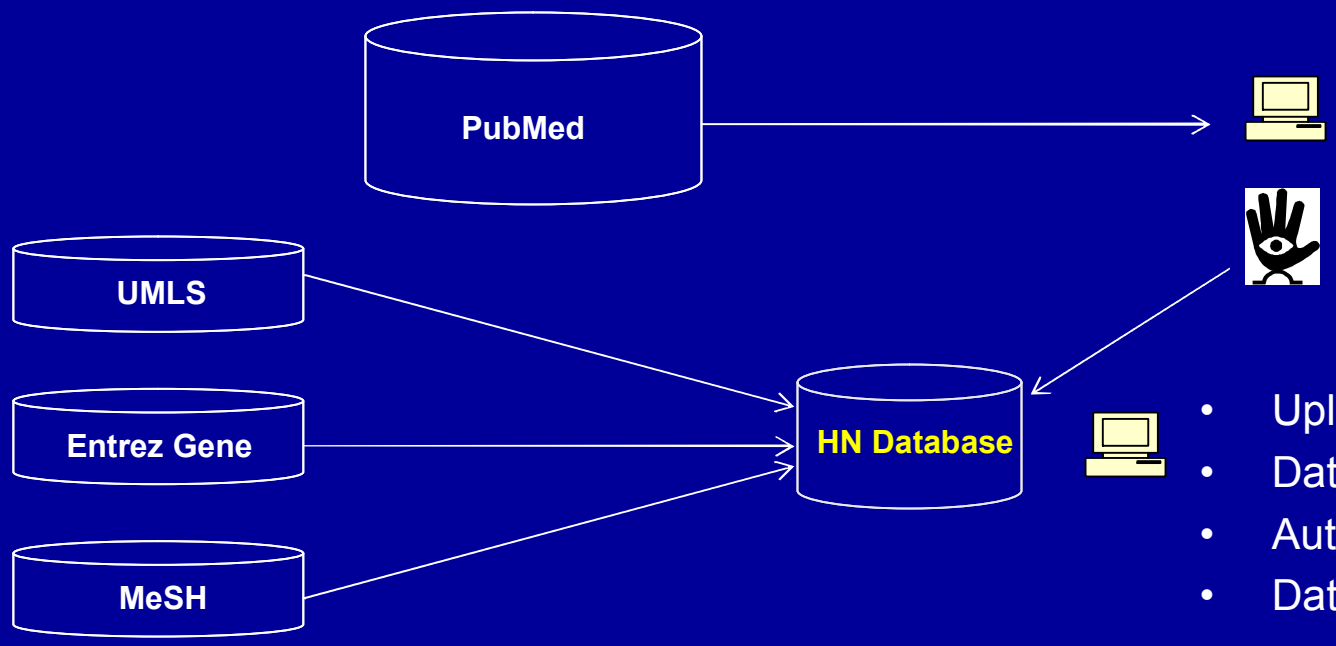
HuGE Navigator Schema



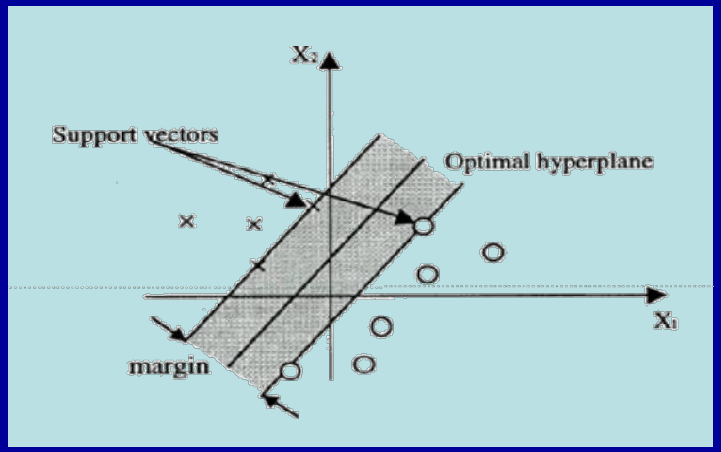
- Screening
- Indexing
- Extracting

- Uploading
- Data preprocessing
- Auto-indexing
- Data mining

GAPscreener: Genetic Association Publication Screener

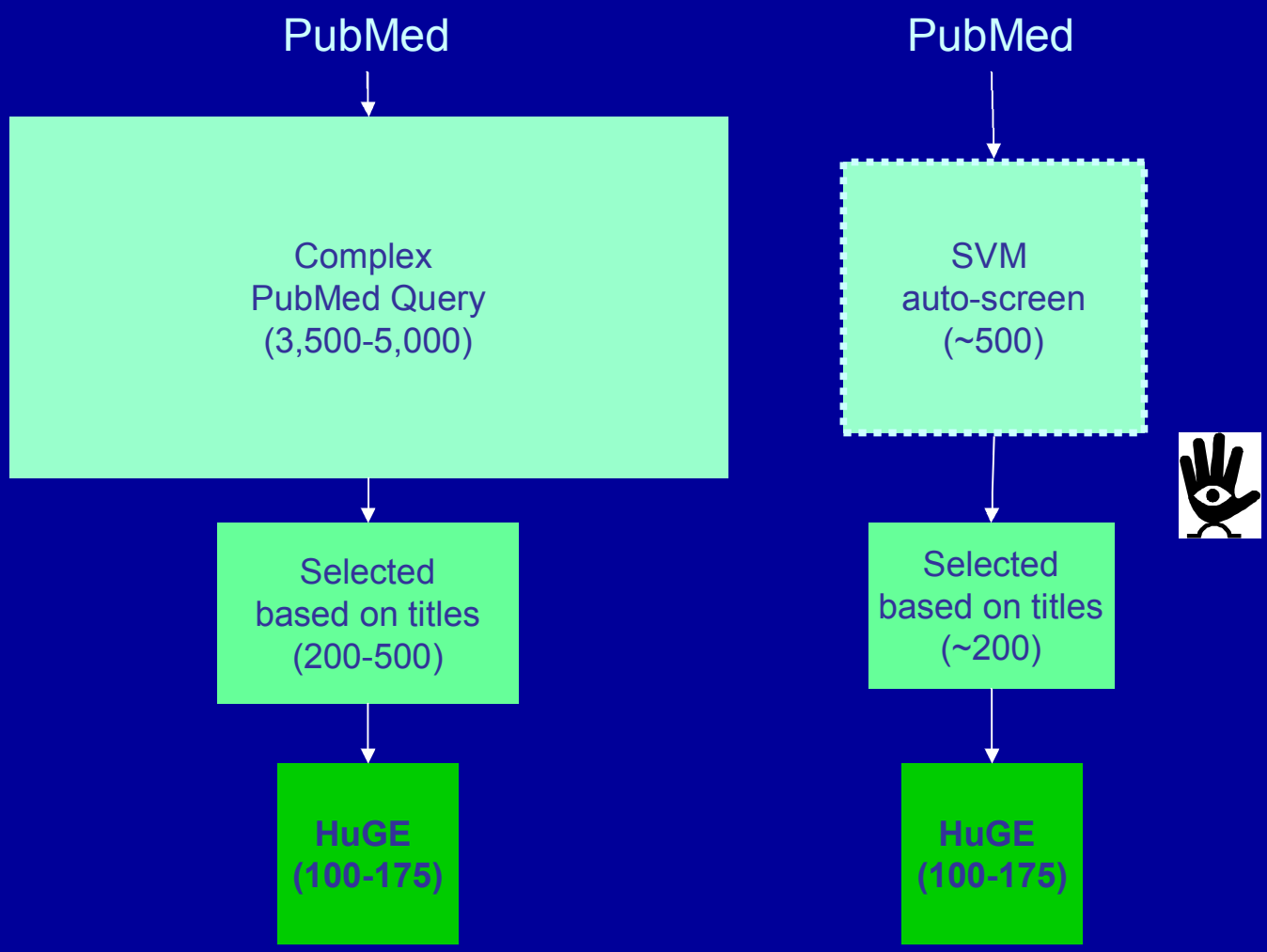
GTCGACTGGAGTGTCTGTGAATTGACTTTTGTTGCCAGTTGGCAGCGGCAGAAGCAGCAAAGCCCGGCCAACAGCAACAAGCTCCTGCCAGATCCCAAAAGCAAACACG

- Support Vector Machine (SVM)



- Stand-alone application
- Can be used for domain-specific search

Weekly HuGE Pub Lit Curation Process



80% sensitivity

97% sensitivity

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HuGE Navigator > Open Source Projects > GAPscreener

Open Source Projects

GAPscreener: An Automatic Tool for Screening Human Genetic Association Literature in PubMed Using Support Vector Machine Technique

Abstract

Motivation: Synthesis of data from published human genetic association studies is a critical step in the translation of human genome discoveries into health application. Although genetic association studies account for a substantial proportion of the abstracts in PubMed, identifying them with standard queries is not always accurate or efficient. Further automating the literature screening process can reduce the burden of a labor-intensive and time-consuming traditional literature search. The Support Vector Machine (SVM), a well-established machine learning technique, has been successful in classifying text, including biomedical literature. The GAPscreener, a free SVM-based software, can be used to assist in screening PubMed abstracts for human genetic association studies. GAPscreener has been used in the screening and curation of HuGE Navigator database (http://www.hugenavigator.net).

Results: Weighted SVM feature selection based on a keyword list obtained by the two-way z-score method demonstrated the best screening performance, achieving 97.5% sensitivity and 98.3% specificity in performance testing. Compared with the

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Address http://www.hugenavigator.net/HuGENavigator/startPagePubLit.do

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HuGE Navigator > HuGE Literature Finder

HuGE Literature Finder

Home | About | Search Instructions | FAQs

Search Literature **for** Go Clear

Database Statistics

Total Documents
31559

Meta-analysis
660

HuGE Review
65

Genome-wide Association
93

Disease Terms Indexed
1946

Genes Indexed
3163

Last Update: 07 Jan 2008

- Enter search terms into the text box.
- Search terms can include disease, exposure, gene, author, journal, etc.
- Simple Boolean operators are allowed, such as AND or OR.
- Use the Search dropdown list to switch to other HuGE Navigator applications.

HuGE Literature Finder is a search engine for finding published literature on genetic associations and other human genome epidemiology. The search query can include disease/outcome, environmental factors, genes, author's name, affiliation, etc. The results can be further refined by the filtering feature. The list of selected articles can be redirected to the PubMed website to take advantage of the functionality it provides, such as uploading to reference software.

Note: Database includes publications since 2001.

Address http://www.hugenavigator.net/HuGENavigator/searchSummary.do;jsessionid=938BCAC85689C1FF63512BF368375353?firstQuery=alzheimer

HuGE Navigator > HuGE Literature Finder

HuGE Literature Finder

Home | About | Search Instructions | FAQs

Search Literature **for** alzheimer Go Clear

Search Criteria: alzheimer[Text+MeSH] **[Query Detail]**

Filtered By Disease Gene Category StudyType Year Author Journal Country

Articles 1 - 25 of 1175

Export **Display** 25 on Page 1 of 48 >>

1. Cholesteryl ester transfer protein polymorphism D442G associated with a potential decreased risk for Alzheimer's disease as a modifier for APOE epsilon4 in Chinese. **[Detail]**
Brain research 2008 Jan 1187 52-7.
Chen DW, Yang JF, Tang Z, Dong XM, Feng XL, Yu S, Chan P

2. Interaction between CD14 and LXRbeta genes modulates Alzheimer's disease risk. **[Detail]**
Journal of the neurological sciences 2008 Jan 264 (1-2): 97-9.
Rodríguez-Rodríguez E, Sánchez-Juan P, Mateo I, Infante J, Sánchez-Quintana C, García-Gorostiaga I, Berciano J, Combarros O

3. The association of the regulatory region of the presenilin-2 gene with Alzheimer's disease in the Northern Han Chinese population. **[Detail]**
Journal of the neurological sciences 2008 Jan 264 (1-2): 38-42.
Liu Z, Jia J

4. Alpha 7 Nicotinic acetylcholine receptor gene and reduced risk of Alzheimer's disease. **[Detail]**
J Med Genet 2007 Dec .
Carson R, Craig D, McGuinness B, Johnston J, O'Neill T, Passmore P, Ritchie C

Address http://www.hugenavigator.net/HuGENavigator/searchSu

HuGE Navigator > HuGE Literature Finder

HuGE Li

Search Literature for alzheimer

Search Criteria: alzheimer[Text+MeSH]

Filtered By Disease Gene Category

Articl

Export Display 25

1. Cholesteryl ester transfer protein polymorphism D442G modifier for APOE epsilon4 in Chinese. [Detail]
Brain research 2008 Jan 1187 52-7.
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http://www.hugenavigator.net - Literature Detail Information - Windows Internet Expl...

Literature Detail Information

Title	Interaction between CD14 and LXRbeta genes modulates Alzheimer's disease risk.
Author	Rodríguez-Rodríguez E, Sánchez-Juan P, Mateo I, Infante J, Sánchez-Quintana C, García-Gorostiaga I, Berciano J, Combarros O,
Journal	Journal of the neurological sciences
PMID	17900622
Publication Date	2008 Jan 264 (1-2): 97-9.

Abstract

A chronic inflammatory process with activation of microglial cells contribute to the neurodegeneration associated with Alzheimer's disease (AD). CD14 and LXRbeta are receptors involved in the regulation of inflammatory responses of microglia in response to bacterial infection or lipopolysaccharide stimulation. In a case-control study in 266 AD patients and 273 healthy controls, we examined whether the combined gene effects between CD14 (-260) polymorphism and LXRbeta (intron 5) polymorphism might be responsible for susceptibility to AD. Subjects carrying both the CD14 (-260) C/C and the LXRbeta (intron 5) G/G genotypes had a six times lower risk of developing AD than subjects without these risk genotypes (OR 0.16, 95% CI 0.04-0.67, p=0.01). These data support a role for innate immune response genes in risk for AD.

Literature Indexing Information

Category Type	Gene-disease associations Gene-gene interactions
Study Type	Observational Study
Gene	CD14 NR1H2
Indexing Term	

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HuGEpedia

Search Encyclopedia for Alzheimer Disease Go Clear Disease Gene All

Alzheimer Disease

Summary

- Total Publications 1164
- Meta-Analyses 43
- MA Summary
- Genes 299
- GWAS Publications 6
- Investigators 1364(F/L) 4688(All)
- Trend/Pattern

Last Update: 07 Jan 2008

Field Synopsis
by Bertram et al.

NCBI Entry
Alzheimer

GWAS Database
NA

299 genes have been studied in association with Alzheimer Disease

[Click to re-sort the table]

Gene	Total Pub	MA Pub (Summary)	Trend/Pattern
APOE	593	20	
ACE	34	5	
PSEN1	32	3	
A2M	29	1	
IL1A	29	1	
IL1B	23	0	
BDNF	23	0	
MTHFR	23	1	
BCHE	22	1	
CYP46A1	21	1	
MAPT	19	1	
SLC6A4	18	0	
TNF	18	1	
CTSD	18	1	
IL6	18	0	
LRP1	15	3	
PON1	14	0	
PSEN2	14	0	
IDE	14	1	
CST3	14	1	

Search Encyclopedia for Alzheimer Disease Go Clear Disease Gene All

Alzheimer Disease

Summary

299 genes have been studied in association with Alzheimer Disease

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- GWAS P 6
- Investig 1364(F/ 4688(Al
- Trend/P

Last Update: C

Field Synop
by Bertram

NCBI Entry
Alzheimer

GWAS Database
NA

Disease Site
AlzGene

[Click to re-sort the table]

Gene	Total Pub	MA Pub (Summary)	Trend/Pattern
APOE	593	20	
APP	13	0	
PRNP	13	5	
IL10	12	0	

Meta Table for Alzheimer Disease and PRNP

Variant: codon 129
Gene(s): (PRNP)

Phenotype	Reference	Analysis Type*	#Studies	#Cases	#Controls	Contrast	Effect size*	Het*
Alzheimer's disease	Qian HR, 2006	A	4	1095	940	(MM + VV) vs. MV	1.100 (0.890-1.350)	none found
Alzheimer's disease	Qian HR, 2006	A	Not Reported	Not Reported	Not Reported	V* vs MM	0.800 (0.650-0.980)	none found
Alzheimer's disease	Qian HR, 2006	A	Not Reported	Not Reported	Not Reported	M* vs VV	1.380 (1.010-1.890)	none found

A: Meta analysis of group level data (and/or HuGE review)
B: Consortium-based analysis with individual level data
Effect Size: OR unless noted otherwise
Het: Heterogeneity

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HuGE Navigator > HuGEPedia

HuGEpedia

Home | About | Search Instructions | FAQs

Search Encyclopedia for APOE Go Clear Disease Gene All

APOE
(apolipoprotein E)

Total Publication	Meta-Analyses	MA Summary	Disease	Investigator	Trend/Pattern
1662	49		350	2269(F/L)/ 7651(All)	

Last Update: 07 Jan 2008

APOE has been studied in association with 350 diseases.

[Click to re-sort the table]

Disease	Total Pub	MA Pub (Summary)	Trend/Pattern
Alzheimer Disease	624	19	
Genetic Predisposition to Disease	442	20	
Neuropsychological Tests	140	2	
Cognition Disorders	127	0	
Dementia	78	3	
Coronary Disease	63	4	
Disease Progression	62	0	
Diabetes Mellitus, Type 2	51	0	
Cardiovascular Diseases	51	1	
Cognition	48	2	
Hyperlipidemias	38	0	

in/hgTracks?position=chr19:50000001-53800000&hgsid=102694247

Blat Tables Gene Sorter PCR DNA Convert Ensembl NCBI PDF

UCSC Genome Browser on Human Mar. 2006 Assembly

move <<< << < > >> >>> zoom in 1.5x 3x 10x base zoom out 1.5x 3x 10x

position/search chr19:50,000,001-53,800,000 jump clear size 3,800,000 bp. configure

chr19 (q13.32) 19p13.3 p13.2 19p12 19q12 13.2

chr19: 50500000 51000000 51500000 52000000 52500000 53000000 53500000

Human Genome Epidemiology Knowledge Base (HuGE Navigator)

PVRL2
APOE
APOC1
APOC4
APOC2
CLPTM1
CKM
ERCC2
PPP1R13L
CD3EAP
ERCC1
GIPR
DMPK
PTGIR
GRLF1
SULT2A1
PLA2G4C
LIG1
CARD8
EMP3
GRIN2D
SULT2B1

move start < 2.0 >

Click on a feature for details. Click on base position to zoom in around cursor. Click gray/blue bars on left for track options and descriptions.

move end < 2.0 >

default tracks hide all manage custom tracks configure refresh

Use drop down controls below and press refresh to alter tracks displayed.
Tracks with lots of items will automatically be displayed in more compact modes.

Custom Tracks

HuGE

full

HuGE Navigator for Networks

GTCGACTGGAGTGTCTGTGAATTGACTTTTGTTGCCAGTTGGCAGCGGCAGAAGCAGCAAAGCCCGGCCAACAGCAACAAGCTCCTGCCAGATCCCAAAAGCAAACACG

- GAPscreener for domain-specific searching

GAPscreener (Genetic Association Publication screener)

Export Help

PubMed Query breast cancer Submit Reset

Screening Result

PMID	Title	Author	Year
17661812	Validation study of the lambda model for predicting the BRCA1 or BRCA2 m...	Apicella C	2007
17661717	Genome-wide association studies of cancer.	Jorgenson E	2007
17661168	BRCA1/BRCA2 rearrangements and CHEK2 common mutations are infrequ...	Falchetti M	2007
17660459	Germline E-Cadherin mutations in familial lobular breast cancer.	Masciari S	2007
17660454	Nonsteroidal Antiinflammatory Drug Use and Breast Cancer Risk: Subgroup...	Kirsh VA	2007
17660348	Human X-Box binding protein-1 confers both estrogen independence and a...	Gomez BP	2007
17659901	Genetic Sensitivity to 6-n-Propylthiouracil Has No Influence on Dietary Patter...	Drewnowski A	2007
17654121	Reduced mitochondrial DNA copy number is correlated with tumor progress...	Yu M	2007
17653899	Mutation analysis of the DBC2 gene in sporadic and familial breast cancer.	Ohadi M	2007
17649682	[Association among lipids, leptin and leptin receptor polymorphisms with ris...	Han CZ	2007
17641362	Cancer yield of mammography, MR, and US in high-risk women: prospective...	Lehman CD	2007
17640379	Origin and distribution of the BRCA2-8765delAG mutation in breast cancer.	Palomba G	2007
17640362	Association of oestrogen receptor beta 2 (ERbeta2/ERbetacx) with outcome ...	Vinayagam R	2007
17639043	Polymorphisms in the Janus kinase 2 (JAK)/signal transducer and activator ...	Vaclavicek A	2007
17636424	Germline mutations in the breast cancer susceptibility gene PTEN are rare i...	Guénard F	2007
17636421	Familial breast cancer: double heterozygosity for BRCA1 and BRCA2 mutati...	Smith M	2007
17636399	HER2 status in hormone receptor positive premenopausal primary breast c...	Rydén L	2007
17636397	Genetic polymorphisms in the vascular endothelial growth factor gene and b...	Langsenlehner...	2007
17635951	Oral Contraceptives and Breast Cancer Risk in the International BRCA1/2 C...	Brohet RM	2007
17634835	Chemoprevention Strategies 2006.	Vogel VG	2007

Date Range Setting

Start Date 07-02-2007

End Date 08-02-2007

Date Type EDAT

Status Monitor

0 hour(s) 0 minute(s) -13 second(s) was estimated to finish the rest.

48 positives were predicted.

Finished at 2007-08-02 11:32:46.941

HuGE Navigator for Networks

GTCGACTGGAGTGTCTGTGAATTGACTTTTGTTGCCAGTTGGCAGCGGCAGAAGCAGCAAAGCCCGGCCAACAGCAACAAGCTCCTGCCAGATCCCAAAAGCAAACACG

- GAPscreener for domain-specific searching
- Investigator Browser

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HuGE Investigator Browser

Search Investigator for bladder cancer Go Clear First & Last Authors All Authors

Search Criteria: bladder cancer[Query]

Filtered By Country Institute

223 investigators with the first or last authorship were found.

Click to re-sort the table.

Investigator Name	Number of Publications (F/L)
Wu X	16
Taylor JA	7
Mittal RD	7
García-Closas M	6
Vineis P	6
Shen JH	5
Sakano S	4
Matullo G	4
Stern MC	4
Rothman N	4
Karagas MR	4
Kelsey KT	4
Zhou JW	4

HuGE Navigator for Networks

GTCGACTGGAGTGTCTGTGAATTGACTTTTGTTGCCAGTTGGCAGCGGCAGAAGCAGCAAAGCCCGGCCAACAGCAACAAGCTCCTGCCAGATCCCAAAAGCAAACACG

- GAPscreener for domain-specific searching
- Investigator Browser
- Encyclopedia
- More…

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HuGE Team

GTCGACTGGAGTGTCTGTGAATTGACTTTTGTTGCCAGTTGGCAGCGGCAGAAGCAGCAAAGCCCGGCCAACAGCAACAAGCTCCTGCCAGATCCCAAAAGCAAACACG

Wei Yu – HuGE Navigator architect

Mindy Clyne – curator-for-life

Ajay Yesupriya – epidemiologist

Anja Wulf
Alex Charles
Lori Durand
} NOPHG web

Rachel Flynt – student

Idris Guessous – student

HuGENet and NOPHG Colleagues

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