Disease-specific databases: AlzGene, PDGene, SzGene

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Overview

1. **Examples of online database structure**
   - ⇨ Example: SzGene (Schizophrenia)
2. **Inclusion and analysis of GWA studies**
   - ⇨ Example: PDGene (Parkinson's disease)
3. **Testing "Top Results" in family-based samples**
   - ⇨ Example: AlzGene (Alzheimer's disease)

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SchizophreniaGene (SZGene)
Published Candidate Genes for Schizophrenia

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SZGene *Updated 15 January 2008*

Chromosome: 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y

Gene: -- Select -- Go

Protein: -- Select -- Go

Polymorphism: -- Select -- Go

Study: -- Select -- Go

Keyword: Go

* New * View large scale studies (including GWA analyses)

Display, print, and download the SchizophreniaGene database index

www.szgene.org

www.pdgene.org

www.alzgene.org

The SchizophreniaGene database aims to provide a comprehensive, unbiased and regularly updated collection of genetic association studies performed on schizophrenia phenotypes. Eligible publications are identified following systematic searches of scientific literature databases, as well as the table of contents of journals in genetics and psychiatry.

The database can be searched either by a variety of dropdown menus or by specific keywords. For each gene, summary overviews are provided displaying key characteristics for each publication, including links to genotype distributions of the polymorphisms studied, random-effects allelic meta-analyses, and funnel plots for an assessment of publication bias.

For more details on the background and methods, see Methods, Disclaimer, and Credits. We encourage authors and readers to contact us to report errors in the presentation of study details, or to notify us of studies that have mistakenly been left out.

How to Cite Content on SchizophreniaGene:
Allen NC, Bagade S, Tanzi R, Bertram L. The SchizophreniaGene Database. Schizophrenia Research Forum. Available at: http://www.schizophreniaforum.org/res/sczgene/default.asp. Accessed [date of access].

SchizophreniaGene Recent Updates
GRIN3A Go

SchizophreniaGene Top Results
View Top Results Methods

1. DRD2
2. GRIN2B
3. GABRB2
4. PLXNA2
5. DTNBP1
6. TPH1
7. DRD4
8. IL1B
9. [illegible]
10. DRD1 [illegible]
11. APOE
12. MTHFR
13. SLC6A4
14. HP
15. DAO
16. [illegible]
17. [illegible]
18. COMT
19. PPP3CC

DESPERATELY SEEKING
- Antibodies
- Collaborators

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SchizophreniaGene (SZGene)
Published Candidate Genes for Schizophrenia

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SZGene

Updated 15 January 2008

Chromosome: 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y

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Mental Health, National Institutes of Health, Department of Health and Human Services

Allen NC, Bagade S, Tanzi R, Bertram L. The SchizophreniaGene Database. Schizophrenia Research Forum. Available at: http://www.schizophreniaforum.org/res/sczgene/default.asp. Accessed [date of access].

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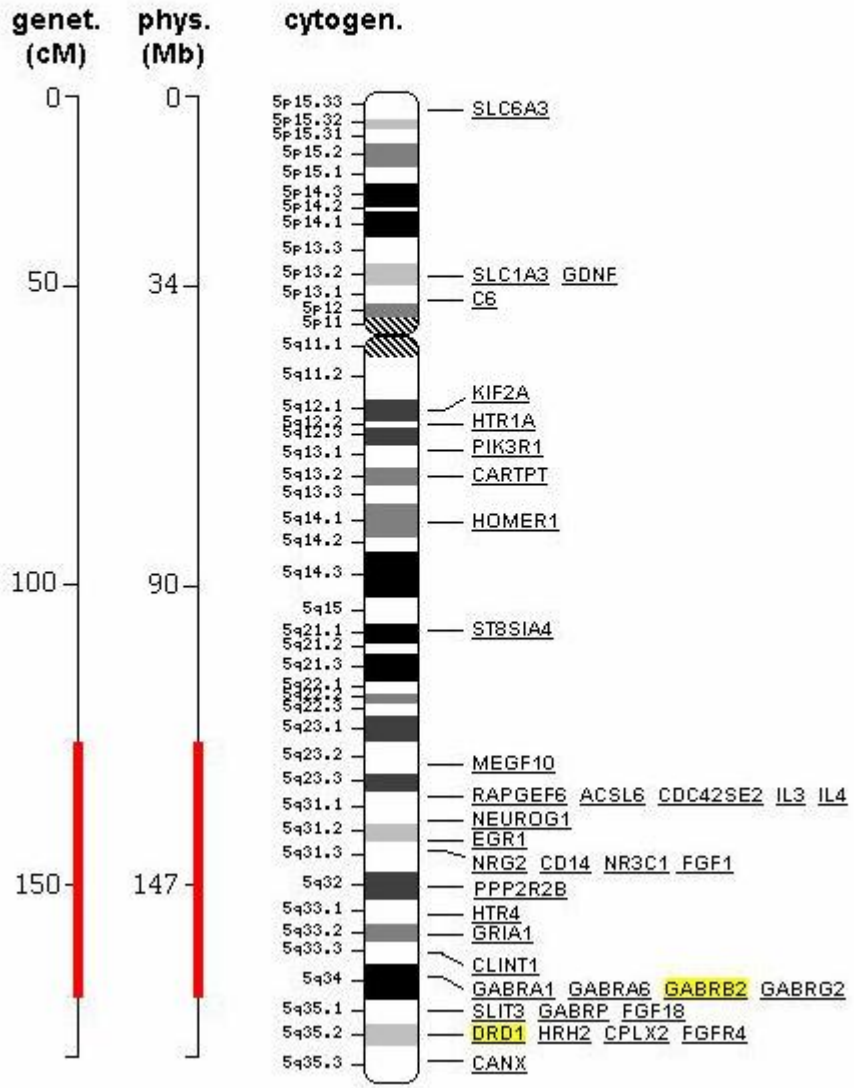
Chromosome: 5

(View: 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y)

Implied SZ Linkage Region (Summary of Linkage Studies)

Top Results Gene (View Top Results Methods)



Gene Overview of All Published Schizophrenia-Association Studies for DRD1

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Gene: DRD1 (DADR, DRD1A) Entrez Gene View on PDGene

Protein: dopamine receptor D1 Protein

Chromosome: 5 (View: 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y)

Status: Updated 4 April 2007

VIEW META-ANALYSIS

1. CASE-CONTROL STUDIES (BY ETHNIC GROUP)

				SZ Cases				Normal Controls			
Study	Population	Source	# Polys	# Subjects (% women)	DX	Onset Age (range)	Age (range)	# Subjects (% women)	Age (range)	Result	Comment
CAUCASIAN											
Campion, 1994	France	PO	1 (detail)	80 (-)	IIIR	-	-	80 (-)	-	Negative	SUBMIT COMMENT
Cichon, 1994	Germany	CL	4 (detail)	36 (36%)	IIIR	-	-	45 (-)	-	Negative	SUBMIT COMMENT
Cichon, 1996	Germany	CL	3 (detail)	36 (-)	IIIR	-	-	45 (-)	28.2 + 5.2 (23-52)	Negative	SUBMIT COMMENT
Dmitrzak-Weglarz, 2006	Poland	CL	1 (detail)	407 (46%)	M	-	31 + 11.5 (-)	399 (62%)	40.6 + 11.8 (-)	Negative	VIEW COMMENTS
Dollfus, 1996	France	PO	1 (detail)	62 (-)	M	-	-	161 (-)	-	Negative	SUBMIT COMMENT
Hoogendoorn, 2005	Netherlands	CL	2 (detail)	208 (-)	IV	-	-	288 (-)	-	Negative	SUBMIT COMMENT
Liu, 1995	USA	CL	1 (detail)	86 (-)	IIIR	-	-	338 (-)	-	Negative	SUBMIT COMMENT
* Initial Study * Nothen, 1993	Germany	CL	1 (detail)	60 (33%)	IIIR	25.2 + 8 (14-46)	34.8 + 11 (-)	60 (47%)	28.2 + 5.2 (-)	Negative	
ASIAN											
Iwata, 2003	Japan	CL	1 (detail)	51 (57%)	IV	13.5 + 1.7 (9-16)	20 + 7 (-)	148 (56%)	21 + 7 (-)	Negative	SUBMIT COMMENT
Kojima, 1999	Japan	CL	1 (detail)	148 (56%)	IV	27.5 + 8.1 (-)	54.3 + 11.5 (16-74)	148 (51%)	55.4 + 6.8 (45-74)	Negative	VIEW COMMENTS

Use our Contact Form to alert us of discrepancies, errors in the representation of study details, or to notify us of your association study regarding this gene.

2. FAMILY-BASED STUDIES (BY ETHNIC GROUP)

				Affecteds				Unaffecteds			
Study	Population	# Polys	# Families	# Subjects (% women)	DX	Onset Age (range)	Age (range)	# Subjects (% women)	Age (range)	Result	Comment
CAUCASIAN											
Fallin, 2005	USA	2 (detail)	263	274 (26%)	IV	19.5 + 4.5 (-)	-	548 (50%)	-	Negative	VIEW COMMENTS

Use our Contact Form to alert us of discrepancies, errors in the representation of study details, or to notify us of your association study regarding this gene.

Meta-Analysis of All Published Schizophrenia-Association Studies (Case-Control Only) rs4532

BACK | SEARCH | METHODS | DISCLAIMER | CREDITS

Polymorphism: rs4532 (DRD1_48A/G)

Gene: DRD1 (DADR, DRD1A) Entrez Gene View on PDGene

Protein: dopamine receptor D1 Protein

Chromosome: 5 (View: 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y)

Status: Updated 4 April 2007

VIEW GENE OVERVIEW

Polymorphism: rs4532 (DRD1_48A/G) Go

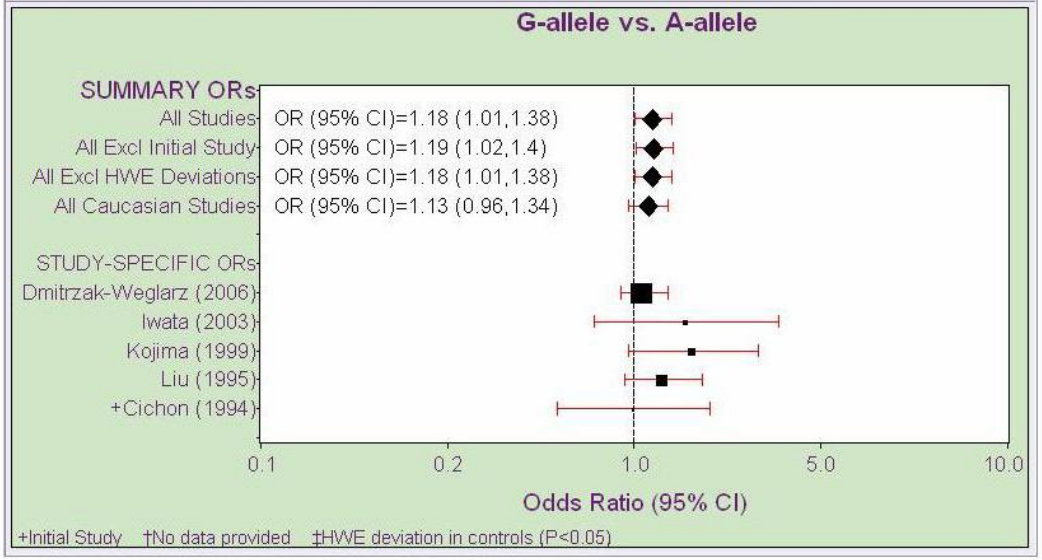
rs4532 (DRD1_48A/G)

1) SUMMARY OF AL[illegible]N OF ALL PUBLISHED ASSOCIATION STUDIES (BY ETHNIC GROUP)

			Alleles		Genotypes		
	# Case-Control Samples		G-Allele (frequency)	A-Allele (frequency)	G/G (frequency)	G/A (frequency)	A/A (frequency)
Caucasian	3	SZ	0.39	0.61	88 (0.166)	240 (0.454)	201 (0.380)
		CTR	0.38	0.63	108 (0.138)	370 (0.473)	304 (0.389)
Asian	2	SZ	0.12	0.89	2 (0.010)	41 (0.209)	153 (0.781)
		CTR	0.07	0.93	1 (0.003)	40 (0.137)	252 (0.860)
TOTAL	5	SZ	0.32	0.68	90 (0.124)	281 (0.388)	354 (0.488)
		CTR	0.29	0.71	109 (0.101)	410 (0.381)	556 (0.517)

Meta-Analysis Methods Funnel Plot

2) POOLED ODDS RATIO ESTIMATES OF ALL PUBLISHED ASSOCIATION STUDIES FOR POLYMORPHISM rs4532 (DRD1_48A/G)



Please also see disclaimer for more information on these meta-analyses.

Funnel Plot for Polymorphism rs4532

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Polymorphism: rs4532 (DRD1_48A/G)

Gene: DRD1 (DADR, DRD1A) Entrez Gene View on PDGene

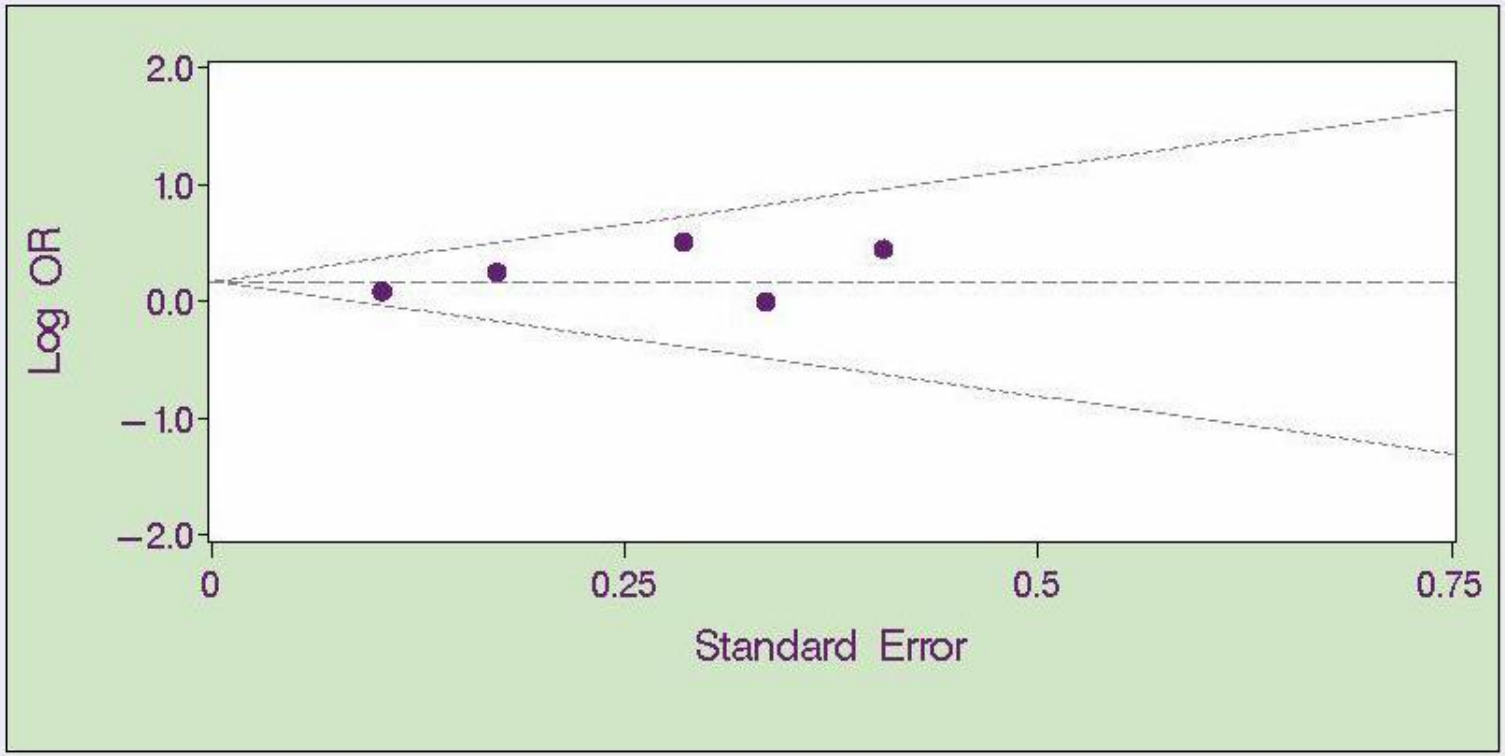
Protein: dopamine receptor D1 Protein

Chromosome: 5 (View: 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y)

Status: Updated 4 April 2007

VIEW META-ANALYSIS | VIEW GENE OVERVIEW

FUNNEL PLOT FOR POLYMORPHISM rs4532 (DRD1_48A/G) Display



Overview

1. **Examples of online database structure**
   - ⇨ Example: SzGene (Schizophrenia)
2. **Inclusion and analysis of GWA studies**
   - ⇨ Example: PDGene (Parkinson's disease)
3. **Testing "Top Results" in family-based samples**
   - ⇨ Example: AlzGene (Alzheimer's disease)

Stepwise inclusion of GWA studies

1. Treat “featured” GWA genes like any other locus:

⇨ Focuses on most interesting data (“featured gene” = “real gene”??)

⇨ Straightforward, because genotypes are usually supplied in paper

✓ *Implemented in current versions of AlzGene, SzGene, PDGene*

PDGene

A database for Parkinson's disease genetic association studies developed by Massachusetts General Hospital/Harvard Medical School, The Michael J. Fox Foundation and the Alzheimer Research Forum

The Michael J. Fox Foundation for Parkinson's Research

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- News & Events
- Funding Programs
- About

Alzheimer Research Forum

- Current Papers
- ARF Recommends
- Research News

PDGENE - PUBLISHED PD CANDIDATE GENES

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Updated 11 January 2008

Chromosome: 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y

Gene: -- Select -- Go

Protein: -- Select -- Go

Polymorphism: -- Select -- Go

Study: -- Select -- Go

Keyword: Go

* New * View large scale studies (including GWA analyses)

Display, print, and download the PDGene database index

The PDGene database aims to provide a comprehensive, unbiased and regularly updated collection of genetic association studies performed on Parkinson's disease (PD) phenotypes. Eligible publications are identified following systematic searches of scientific literature databases, as well as the table of contents of journals in genetics, neurology, and psychiatry.

The database can be searched either by a variety of dropdown menus or by specific keywords. For each gene, summary overviews are provided displaying key characteristics for each publication, including links to genotype distributions of the polymorphisms studied, random-effects allelic meta-analyses, and funnel plots for an assessment of publication bias.

For more details on the background and methods, see Methods, Disclaimer, and Credits. We encourage authors and readers to contact us to report errors in the presentation of study details, or to notify us of studies that have mistakenly been left out.

Please note that this database will not sample and catalogue reports of causal mutations leading to PD or parkinsonism of classic Mendelian inheritance (for a summary of these genes the please consult the Parkinson's disease Mutation Databases curated by the Parkinson's Institute, or Indiana University).

How to Cite Content on PDGene:

Bagade S, Allen NC, Tanzi R, Bertram L. The PDGene Database. Alzheimer Research Forum. Available at: http://www.pdgene.org/. Accessed [date of access].

PDGene Recent Updates

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Top PDGene Results

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1. LRRK2
2. SNCA
3. MAPT/STH
4. PINK1
5. APOE
6. CYP2D6
7. ELAVL4
8. GWA 2q36.3
9. UCHL1
10. GWA 7p14.2 [see more]

THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH

The PDGene database is supported by a grant from The Michael J. Fox Foundation in partnership with the Alzheimer Research Forum.

ALZHEIMER RESEARCH FORUM

PDGene Related Links

- Parkinson's disease Mutation Database Curated by Indiana University
- Parkinson's disease Mutation Database Curated by the Parkinson's Institute

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Summary of GWA studies and display of “featured genes”

OVERVIEW OF ALL PUBLISHED LARGE-SCALE AND GENOME-WIDE ASSOCIATION STUDIES IN PD

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Status: Updated 8 October 2007; ** See Large Scale Study Methods **

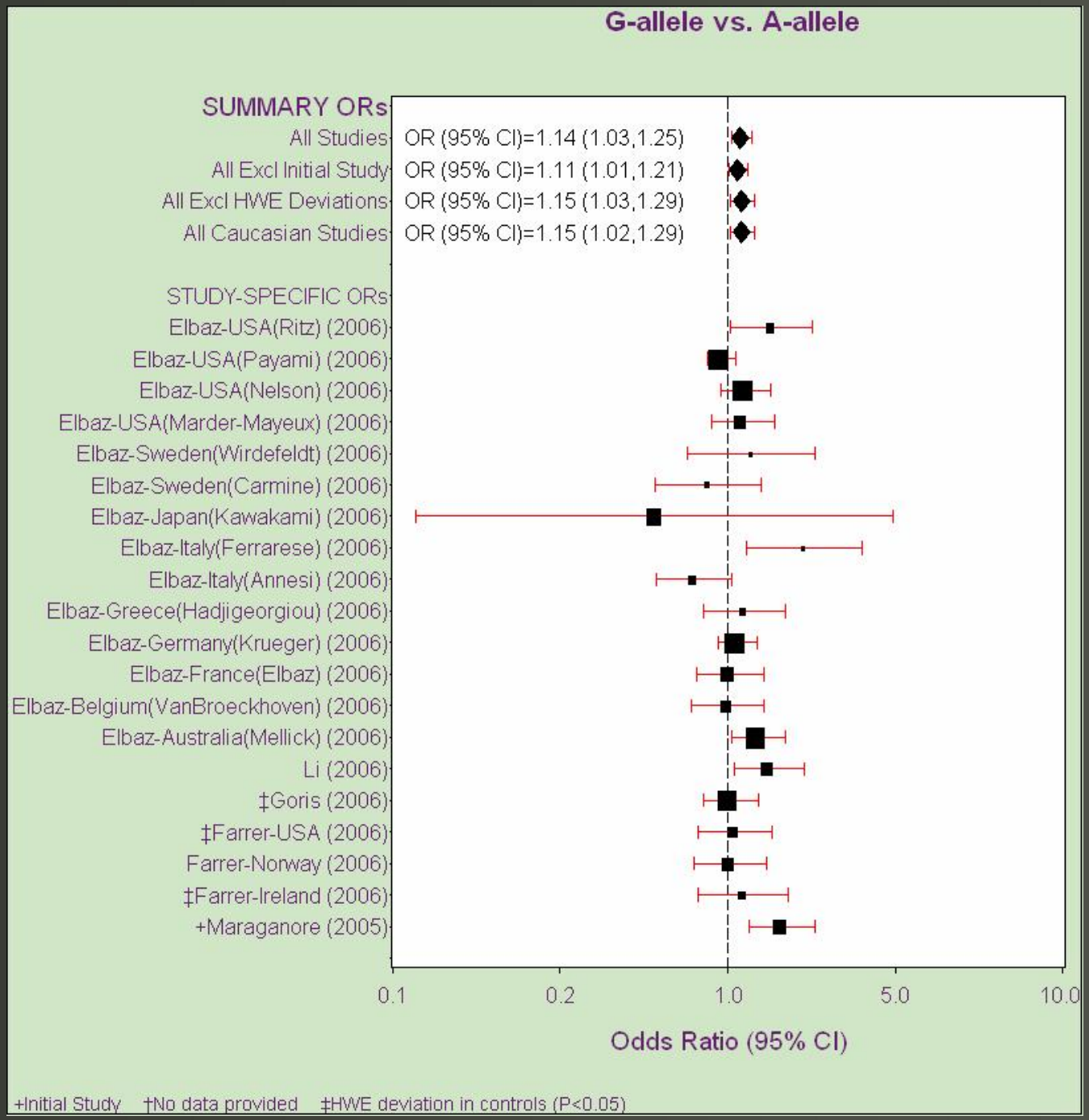
OVERVIEW OF ALL PUBLISHED LARGE-SCALE AND GENOME-WIDE ASSOCIATION STUDIES IN PD

								PD Cases				Normal Controls			
Study	Design	Type	Population	Source	Platform	# of SNPs	Genotype Data Publicly Available	# Subjects (% women)	DX	Onset Age (range)	Age (range)	# Subjects (% women)	Age (range)	Featured Genes	Comment
CAUCASIAN															
Fung, 2006	CC	GWA	USA (NINDS)	CL	Illumina (Infinium I & HumanHap300)	408,000	Yes	267 (-)	C	-	-	270 (-)	68 (55-88)	BRDG1 Go	SUBMIT COMMENT TO ALZFORUM
Maraganore, 2005	CC, FBAT	GWA	USA	CL	Perlegen (250K hap-tag)	198,345	Yes	775 (40%)	C	62 (31-94)	68 (33-96)	775 (47%)	66.5 (29-91)	CDCP2 Go	VIEW COMMENT ON ALZFORUM

CDCP2
GALNT3
GWA_10q21.1
GWA_2q36.3
GWA_4q28.1
GWA_4q28.3
GWA_5p15.32
GWA_7p14.2
PASD1
PRDM2
SEMA5A

Contact us if you are an author of an association study regarding this gene, and don't find your study in this table, or find errors in the representation of your study details.

Design: "CC" (case-control), "FBAT" (family-based)
Type: "GWA" (genome-wide association study); "CWA" (chromosome-wide association study); "LSA" (other large-scale association study); "cSNP" (coding-region SNP)
Source: Source of case population -> "CL" (clinic-based), "PO" (population-based), or "CO" (community-based).
Platform: Please refer to orignal publication for exact description.
 # SNPs: Approximate number of polymorphisms covered.
Onset Age and Age: Mean or median age at onset or examination, respectively.
DX: Criteria used to determine PD diagnosis -> "C" (clinical PD diagnosis), "N" (neuropathological PD diagnosis), "M" (mixed, i.e. PD sample contains both clinical and neuropathological cases), "U" (unl
Featured Genes: Dropdown menu of genes highlighted ("featured") in original publication as potential PD susceptibility genes/loci after completion of all analyses, e.g. replication in multiple samples
(-) : No information provided.


G-allele vs. A-allele
SUMMARY ORs
All Studies
OR (95% CI)=1.14 (1.03,1.25)
All Excl Initial Study
OR (95% CI)=1.11 (1.01,1.21)
All Excl HWE Deviations
OR (95% CI)=1.15 (1.03,1.29)
All Caucasian Studies
OR (95% CI)=1.15 (1.02,1.29)
STUDY-SPECIFIC ORs
Elbaz-USA(Ritz) (2006)
Elbaz-USA(Payami) (2006)
Elbaz-USA(Nelson) (2006)
Elbaz-USA(Marder-Mayeux) (2006)
Elbaz-Sweden(Wirdefeldt) (2006)
Elbaz-Sweden(Carmine) (2006)
Elbaz-Japan(Kawakami) (2006)
Elbaz-Italy(Ferrarese) (2006)
Elbaz-Italy(Annesi) (2006)
Elbaz-Greece(Hadjigeorgiou) (2006)
Elbaz-Germany(Krueger) (2006)
Elbaz-France(Elbaz) (2006)
Elbaz-Belgium(VanBroeckhoven) (2006)
Elbaz-Australia(Mellick) (2006)
Li (2006)
‡Goris (2006)
‡Farrer-USA (2006)
Farrer-Norway (2006)
‡Farrer-Ireland (2006)
+Maraganore (2005)
0.1
0.2
1.0
5.0
10.0
Odds Ratio (95% CI)
+Initial Study †No data provided ‡HWE deviation in controls (P<0.05)

Stepwise inclusion of GWA studies

1. Treat “featured” GWA genes like any other locus:

⇨ Focuses on most interesting data (“featured gene” = “real gene”??)

⇨ Straightforward, because genotypes are usually supplied in paper

✓ *Implemented in current versions of AlzGene, SzGene, PDGene*

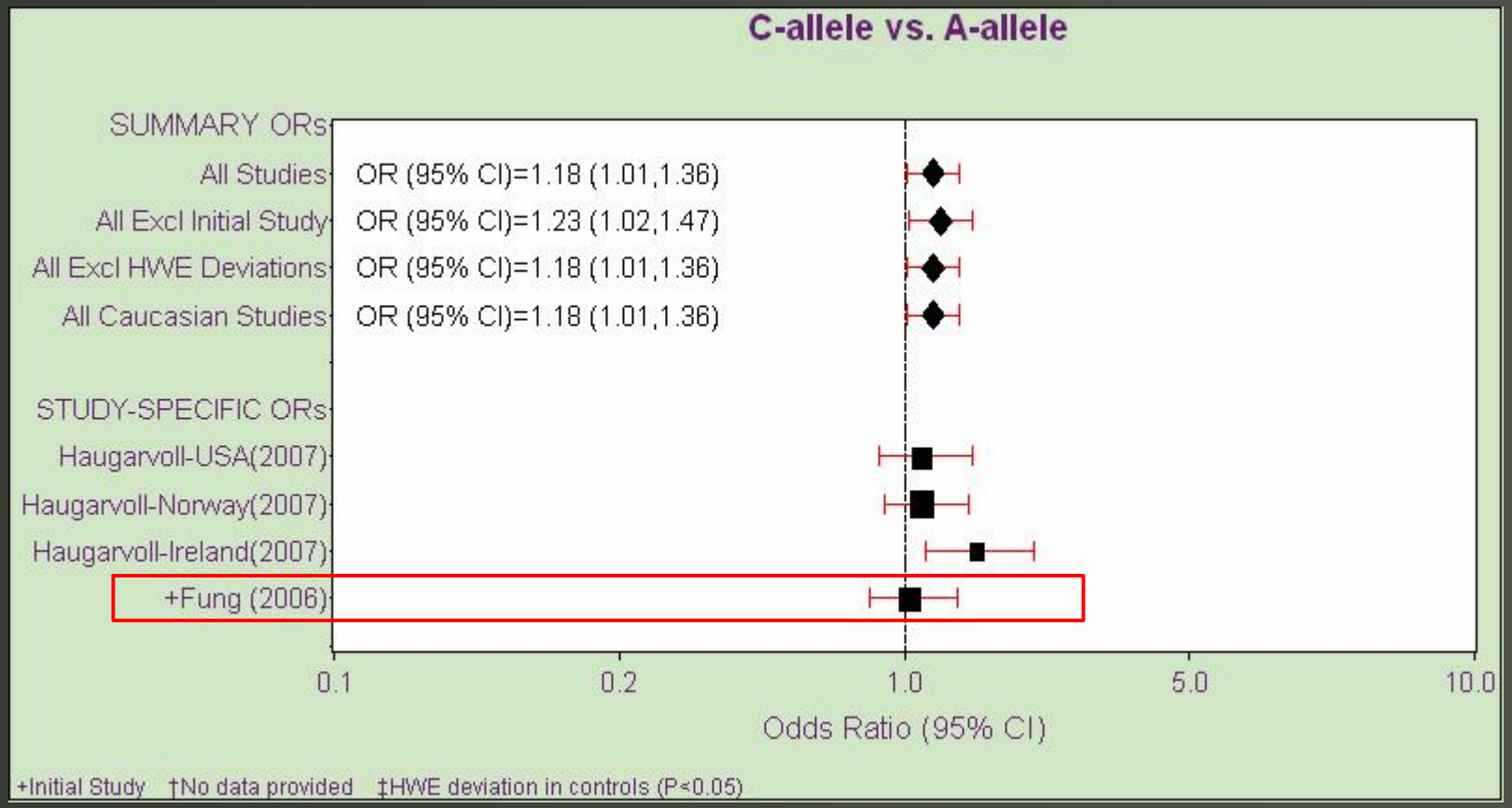
2. Add “negative” GWA genes to existing meta-analyses:

⇨ Adds potentially valuable “unbiased” data to existing results

⇨ Straightforward, if genotypes are publicly available

✓ *Implemented in AlzGene, PDGene (no public data for SzGene yet)*

Inclusion of “non-featured” GWA data



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3. Systematic meta-analyses across multiple GWA studies

⇨ Only on overlapping markers and if genotypes are publicly available

⇨ Display only markers with "significant" meta-analysis results

⇨ More challenging in terms of computation and interpretation

Analytic methods currently under development

Overview

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3. **Testing "Top Results" in family-based samples**
   - ⇨ Example: AlzGene (Alzheimer's disease)

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AlzGene *Updated 21 January 2008*

Chromosome: 1 2 3 4 5 6 7 8 9 10 11 1
14 15 16 17 18 19 20 21 22

Gene: -- Select -- Go

Protein: -- Select --

Polymorphism: -- Select --

Study: -- Select --

Keyword: Go

* New * View large scale studies (including GWA analys

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How to Cite Content on AlzGene:

Bertram L, McQueen MB, Mullin K, Blacker D, Tanzi RE "Systematic meta-analyses of Alzheimer disease genetic the AlzGene database." Nat Genet 39(1): 17-23. Abstract

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Top AlzGene Results

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1. *APOE (ε2/3/4)
2. *CHRNB2
3. CH25H
4. PGBD1
5. LMNA
6. MAPT
7. PCK1
8. *TFAM
9. *CST3
10. *ACE [close]
11. SORCS1
12. hCG2039140
13. GALP
14. SORL1
15. CTSD
16. TNK1
17. GWA 14q32.13
18. IL1B
19. *TF
20. LOC651924
21. GWA 7p15.2
22. LOC439999
23. DAPK1
24. *PRNP
25. *MTHFR
26. MYH13
27. BDNF
28. *PSEN1

*** Tested via FBAT plus:**

- *ESR1*
- *GAPDHS*
- *IDE*
- *NCSTN*
- *TNF*

Demographics of Alzheimer's families

Supplementary Table 1.

Sample	No. families (subjects)	No. women (%)	No. affecteds (AAO+SD [range])	No. unaffecteds (AAE+SD [range])
NIMH	436 (1,439)	992 (68.9%)	995 (72.4+7.7 [50-97])	411 (70.0+10.7 [31-93])
NIA	351 (1,111)	690 (62.1%)	803 (74.1+7.1 [52-98])	290 (73.3+9.5 [36-94])
NCRAD	340 (1,141)	730 (64.0%)	741 (71.3+7.6 [50-98])	300 (71.0+8.4 [39-93])
CAG	217 (489)	298 (61%)	222 (69.2+9.0 [50-89])	267 (72.9+8.8 [49-92)

The majority of families across all samples are of self-reported "Caucasian" ethnicity (NIMH = 94%, NIA = 94%, NCRAD = 97%, CAG = 99%). Numbers missing to total subjects when adding affecteds and unaffecteds = phenotype unknown.

Table. Comparison of AD association findings in case-control vs. family-based samples.

Gene/Variant	Ethnic group	Model	CASE-CONTROL (AlzGene)†		FAMILY-BASED (Combined samples)‡				
			OR (95% CI)	P-value	MAF	Fams	OR	X^2	P-value
ACE	All	I vs. D	1.11 (1.02-1.20)	0.01	0.46	469	0.96	7.3	0.50
rs179975 (intron 16)*	Caucasian	I vs. D	1.03 (0.96-1.11)	0.37	0.46	461	0.96	7.1	0.53
				* *					
				* *					
CST3	All	A vs. G	1.15 (1.02-1.31)	0.02	0.22	317	1.11	11.2	0.19
rs1064039 (A25T)*	Caucasian	A vs. G	1.16 (1.00-1.33)	0.04	0.22	309	1.08	10.1	0.26
ESR1	All	P vs. p	1.18 (1.00-1.39)	0.05	0.47	465	0.96	4.5	0.81
rs2234693	Caucasian	P vs. p	1.10 (0.93-1.29)	0.27	0.47	455	0.96	4.4	0.82
GAPDHS	All	G vs. C	0.82 (0.71-0.94)	0.004 *	0.40	450	1.06	3.9	0.87
rs12984928*	Caucasian	G vs. C	0.82 (0.71-0.94)	0.004 *	0.40	442	1.05	4.0	0.86
IDE	All	C vs. T	0.89 (0.79-1.00)	0.05	0.30	416	1.07	5.3	0.72
rs2251101	Caucasian	C vs. T	0.89 (0.79-1.00)	0.05	0.31	410	1.07	5.3	0.73
MTHFR	All	C vs. A	0.85 (0.73-1.00)	0.05	0.32	405	0.99	9.7	0.29
rs1801131	Caucasian	C vs. A	0.91 (0.76-1.10)	0.34	0.32	397	0.99	9.2	0.32
NCSTN	All	C vs. G	1.38 (1.03-1.83)	0.03	0.08	128	0.88	6.8	0.56
rs17370539*	Caucasian	C vs. G	1.38 (1.03-1.83)	0.03	0.08	120	0.98	8.3	0.40
PRNP	All	G vs. A	0.89 (0.81-0.98)	0.02	0.34	402	1.02	11.7	0.16
rs1799990 (M129V)*	Caucasian	G vs. A	0.89 (0.80-0.99)	0.03	0.34	395	1.02	12.7	0.15
				*					
				* *					
TFAM	All	G vs. A	0.78 (0.62-0.98)	0.03	0.45	433	1.10	2.3	0.97
rs2306604*	Caucasian	G vs. A	0.78 (0.62-0.98)	0.03	0.45	428	1.07	2.4	0.97
TNF	All	C vs. T	1.37 (1.05-1.78)	0.02	0.22	325	0.86	2.2	0.97
rs1799964 (-1031)‡‡	Caucasian	C vs. T	1.37 (1.05-1.78)	0.02	0.22	314	0.88	2.7	0.95

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