

NIAGADS Update

September 2015 ADC Director's Meeting

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NIAGADS

New data at NIAGADS

ADSP Data and how to link to your
ADC information

NIAGADS Genomics DB

Datasets at NIAGADS

34 datasets | 49,000 subjects | 30 billion genotypes

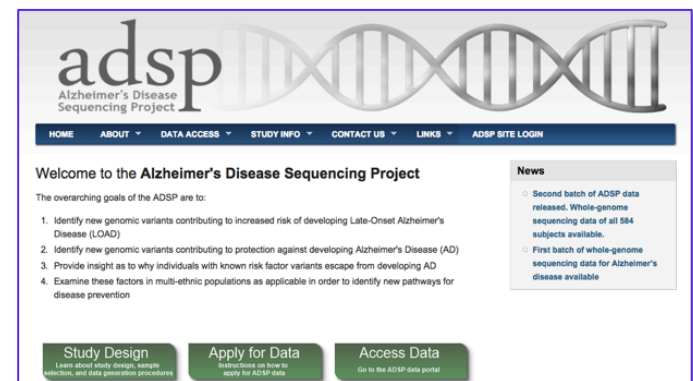
- ▣ **16 GWAS**
- ▣ 1 eGWAS
- ▣ 1 Expression
- ▣ 1 Linkage
- ▣ 9 Genotyping (<100k)
- ▣ 6 Summary Statistics
- ▣ 1 Whole Exome Sequencing
- ▣ 11 GWAS datasets with Imputation

Incoming Datasets:

- 2 Targeted Sequencing
- 3 GWAS
- 3 Summary Statistics
- 1 Exome Chip
- 1 PSP WES
- 2 Linkage

ADSP Data

- Raw data are available
 - WGS: 578 individuals / 111 multiplex families
 - WES: 10,939 samples/10,959 individuals
 - **3,264 WES are ADC subjects**
- Genotypes
 - WGS: July
 - WES: October/November
- See ADSP website
 (www.niagads.org/adsp)
 for more information on
 - Study design
 - Apply for data access



Apply for ADSP data access

Go to www.niagads.org/adsp , click **Apply for Data**



- ▣ All applications submitted to dbGaP, reviewed by NIH
- ▣ ADSP requires:
 - ▣ **Secondary/derived data return plan** that will be generated by your study and deposited into NIAGADS
 - ▣ Signed **NIA Data Sharing Plan** and **NIAGADS Data Distribution Agreement** for ADSP
- ▣ Contact NIAGADS (data@niagads.org) for data application, we'd be glad to help step-by-step

Linking ADSP WES ADC samples

- ADSP WES data are labeled using ADSP IDs

e.g. A-ADC-AD003257-BR-NCR-08AD11443

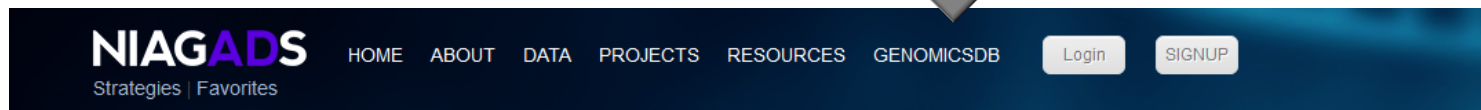
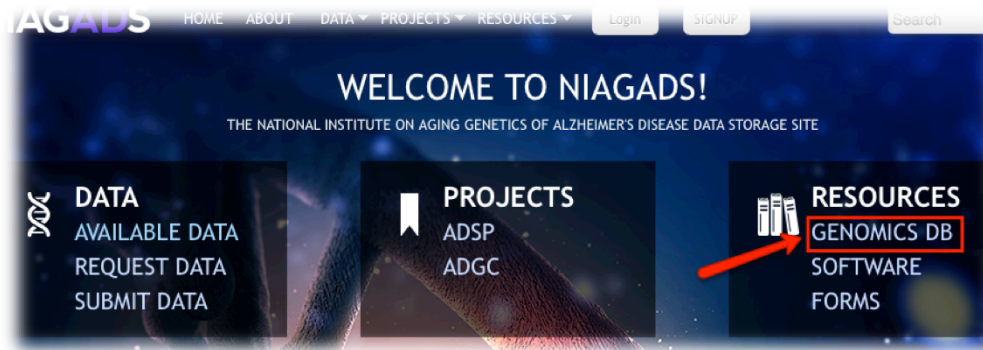
- ADCs can link with their own phenotypic data with these steps:



- Contact NIAGADS (data@niagads.org) if you plan to link the samples and we'll walk you through the process

NIAGADS Genomics Database

Available October 2015
at www.niagads.org/genomics



Welcome to the NIAGADS Genomics Database

A simple, but powerful, workspace for browsing and identifying genes, SNPs, and genomic regions
with special relevance to Alzheimer's Disease.



Search



View

New Search Page

GENES

FIND A SNP

Enter a dbSNP rs identifier to view details and curated annotations for a specific SNP.

SNPs

rs6656401

GENOMIC REGIONS

Enter a genomic region

SNP rs6656401

TTTCCTTCTCTGTCTCCATCTTCTC[G/A]TCGCCTTCTCCTCTGTGTGTGTCCT

Genomic Context

	207,692,000				207,692,125
NCBI Gene database					
dbSNP137					
	rs61034679			rs6656401	
	SNV C → T			SNV A → G	
	rs151110404			rs113531714	
	SNV T → C			SNV T → C	
				rs112003429	
				SNV C → T	

dbSNP137 SnpEff Effect

High
Moderate
Low
N/A

CHR1:207692049

- Allele: A
- Minor Allele/Frequency: G/0.9333

ADDITIONAL INFORMATION

NIAGADS datasets in which SNP rs6656401 has a GWAS significance supported by a p-value $\leq 1 \times 10^{-8}$.

Click on accession numbers to view a detailed report about the dataset or to request access to the data.

Use the provided links to **view the dataset on the GenomicsDB genome browser** or use the GenomicsDB to **search the dataset** for a complete list of significant SNPs.

With a single-click, **discover** SNPs with GWAS significance in published NIAGADS datasets

GWAS Significance in NIAGADS Datasets

Show 10 entries

Accession	Dataset		
NG00036	IGAP 2013: Stages 1 and 2		
		7.76e-15	G View Track Search
		3.39e-10	A View Track Search
		1.91e-08	A View Track Search
	Adjusted for Age, Sex and APOE	3.31e-08	A View Track Search
	Age, Sex and APOE	5.89e-08	A View Track Search
		2.57e-03	A View Track Search
NG00041	Neuropathologic features of AD and related dementias (case/control)	1.38e-02	A View Track Search
NG00041	Neuritic plaques (presence vs. absence): relaxed	3.98e-02	A View Track Search
NG00027	ADGC 2011: Stage 2 Adjusted for Age, Sex and APOE	5.25e-02	A View Track Search

Showing 1 to 10 of 22 entries

Previous 1 2 3 Next

New Gene and SNP Report Pages

APOE

apolipoprotein E

Also known as: APO-E, LPG, LDLQC5, AD2

Bookmark records or
add to a basket

Add to Basket  Add to Favorites 

CONTENTS

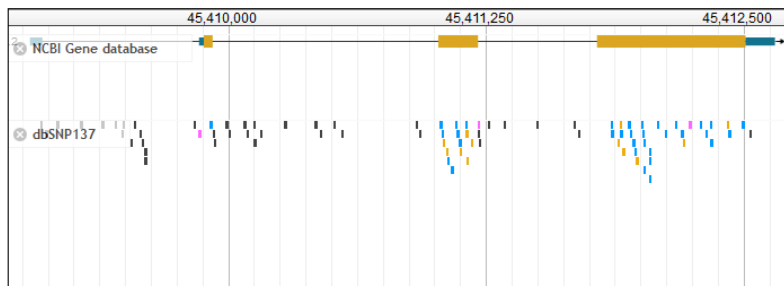
- Genomic Context
- Associated SNPs
- GO Terms
- KEGG Pathways

LINKS TO OTHER RESOURCES

- NCBI EntrezGene: 348
- HUGO: HGNC:613
- ENSEMBL: ENSG00000130203
- VEGA: OTTHUMG00000128901
- OMIM: 107741
- PUBMED

Link to other databases
with a single click.

Genomic Context



dbSNP137 SnpEff Effect

- High
- Moderate
- Low
- N/A

CHR19, (45409039..45412650)

- Explore annotations
- View on genome browser

Co-located SNPs

312 SNPs are co-located with APOE. Retrieve full listing.

With Clinical Significance

Associated with Alzheimer's Disease

Show 10 entries

Filter

SNP	Chromosome	Position	Disease Trait	p-value	Citation	Variant Type
rs429358	chr19	45411941	Cerebrospinal AB1-42 levels in Alzheimer's disease dementia	3.98e-17	25027320	missense variant
rs429358	chr19	45411941	Alzheimer's disease biomarkers	5.01e-14	23419831	missense variant
rs429358	chr19	45411941	Alzheimer's disease biomarkers	1.00e-06	21123754	missense

Quickly find
significant SNPs

Additional Search Functions

GENES

FIND A SNP

Enter a dbSNP rs identifier to view details and curated annotations for a specific SNP.

Go

More ↓

SNPs

rs6656401

Go

More ↓

GENOMIC REGIONS

Enter a genomic region

Go

Sample Strategies

Upload a list of locations

Expressed Enhancers

☒ Brain-specific expression? 

chr19:35409039..65412650

Transcription Factor Binding Sites

Histone Modifications

DNase I Hypersensitivity Sites

GWAS Significance

More ↑

Explore further to make novel discoveries

FIND EXPRESSED ENHANCERS WITHIN A REGION OF INTEREST

Search pre-defined enhancer sets for brain-relevant tissues and cells from [FANTOM5](#).

Enter a genomic location in the format chrN:start_end (e.g., chr19:35409039..65412650) to find all expressed enhancers within that region.

Explore and Analyze Gene Functions

My Strategies:
New
Opened (2)
All (2)
Basket
Public Strategies (0)

(Genes)
Strategy: Genes associated with SNPs with GWAS Significance in IGAP 2013*
Rename Duplicate Save As Share Delete

Dataset 1172 SNPs Step 1
->Genes 59 Genes Step 2
Add Step

59 Genes from Step 2
Strategy: Genes associated with SNPs with GWAS Significance in IGAP 2013
Add 59 Genes to Basket | Download 59 Genes

Gene Results
Genome View
Analyze Results BETA

To view additional details (e.g., annotations associated with column headers; click on the column header)

First 1 2 3 Next Last

Gene	Location
ABCA7	chr19:1040
ADGRF2	chr6:47624
APOC1	chr19:4541
APOC1P1	chr19:4543
APOC2	chr19:4544
APOC4	chr19:4544

Genes on forward strand;
Genes on reversed strand;

Showing 1 to 8 of 8 entries (filtered from 25 total entries) Show 25 entries
Search:
Previous

Sequence	Chromosome	#Genes	Length	Gene Locations
NC_000001.10	chr1	3	249250621	
NC_000002.11	chr2	1	243199373	
NC_000006.11	chr6	5	171115067	
NC_000007.13	chr7	5	159138663	
NC_000008.10	chr8	3	146364022	
NC_000011.9	chr11	8	135006516	
NC_000014.8	chr14	2	107349540	
NC_000019.9	chr19	28	59128983	

Sequence
Chromosome
#Genes
Length
Gene Locations

Showing 1 to 8 of 8 entries (filtered from 25 total entries)

Genome overview

New Result Pages: Explore and Analyze

My Strategies:
[New](#)
[Opened \(2\)](#)
[All \(2\)](#)
[Basket](#)
[Public Strategies \(0\)](#)

Dataset
1172 SNPs
Step 1

->Genes
59 Genes
Step 2

Add Step

Strategy: Genes associated with SNPs with GWAS Significance in IGAP 2013*

Rename
Duplicate
Save As
Share
Delete

59 Genes from Step 2
Strategy: Genes associated with SNPs with GWAS Significance in IGAP 2013

Add 59 Genes to Basket | Download 59 Genes

Gene Results
Genome View
Analyze Results BETA

To view additional details (e.g., annotation, external IDs) associated with column headers; columns can be expanded/collapsed.

First 1 2 3 Next Last

Advanced

Gene	Location
ABCA7	chr19:1040102-10658
ADGRF2	chr6:47624223-47668
APOC1	chr19:45417577-4542
APOC1P1	chr19:45430060-4543
APOC2	chr19:45449239-4545
APOC4	chr19:45445495-4544

Gene Ontology Enrichment

Pathway Enrichment

Genome Browser Tracks:

GWAS + ENCODE + FANTOM5



October Release

- ▣ Currently contains the following data
 - ▣ **Genes** and pathway annotations
 - ▣ **SNP** information (dbSNP v142) with population allele frequency and SNPEff impact predictions
 - ▣ Published **AD GWAS** summary statistics
 - ▣ NHGRI GWAS Catalog
 - ▣ **Functional genomics** data relevant to brain
 - ▣ ENCODE: DNaseI HS / Histone modification / TF Binding ChIP-Seq
 - ▣ FANTOM5: Enhancer-TSS associations / Cell-expressed enhancers
- ▣ Planned data
 - ▣ Gene-gene interactions
 - ▣ Gene expression tissue specificity
 - ▣ Cross-species conservation (PhastCons)
 - ▣ Genome interaction database
 - ▣ Structural variant calls (dbVar/DGV/CNVD)
 - ▣ GTex express QTL

Take-home message

-- please share with your ADC

- ▣ New datasets at NIAGADS
- ▣ **ADSP genotypes** for WGS (available now) and WES (October ~ November)
- ▣ **Linking ADSP WES samples** with ADC's own phenotype data – **contact NIAGADS so we can help you**
- ▣ Improved **NIAGADS Genomics Database** will be available in October

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Acknowledgements

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- **Patients and families**
- **NIA ADRC program and centers**
- **NACC and NCRAD**
- **ADSP**
- **IGAP/ADGC/CHARGE/EADI/GERAD**
- **Support from NIA/NHGRI/NIH**

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- | | |
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