Supplementary Online Content

Lee JH, Cheng R, Vardarajan B, et al. Genetic modifiers of age at onset in carriers of the G206A mutation in *PSEN1* with familial Alzheimer disease among Caribbean Hispanics. *JAMA Neurol.* Published online July 27, 2015. doi:10.1001/jamaneurol.2015.1424.

eTable 1. Demographic and Clinical Characteristics of Participants in the Combined Late Onset Alzheimer Disease GWAS Datasets of Caribbean Hispanics*

eTable 2. Allelic Association Using Linear Mixed Model: Affecteds-Only Analysis

eFigure 1. Study Design Flow Chart

eFigure 2. Next-Generation Sequencing

eFigure 3. LD Flanking the Variant From the Original Discovery Set for *SORBS2* and *SH3RF3*

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Demographic and Clinical Characteristics of Participants in the Combined Late Onset Alzheimer Disease GWAS Datasets of Caribbean Hispanics*
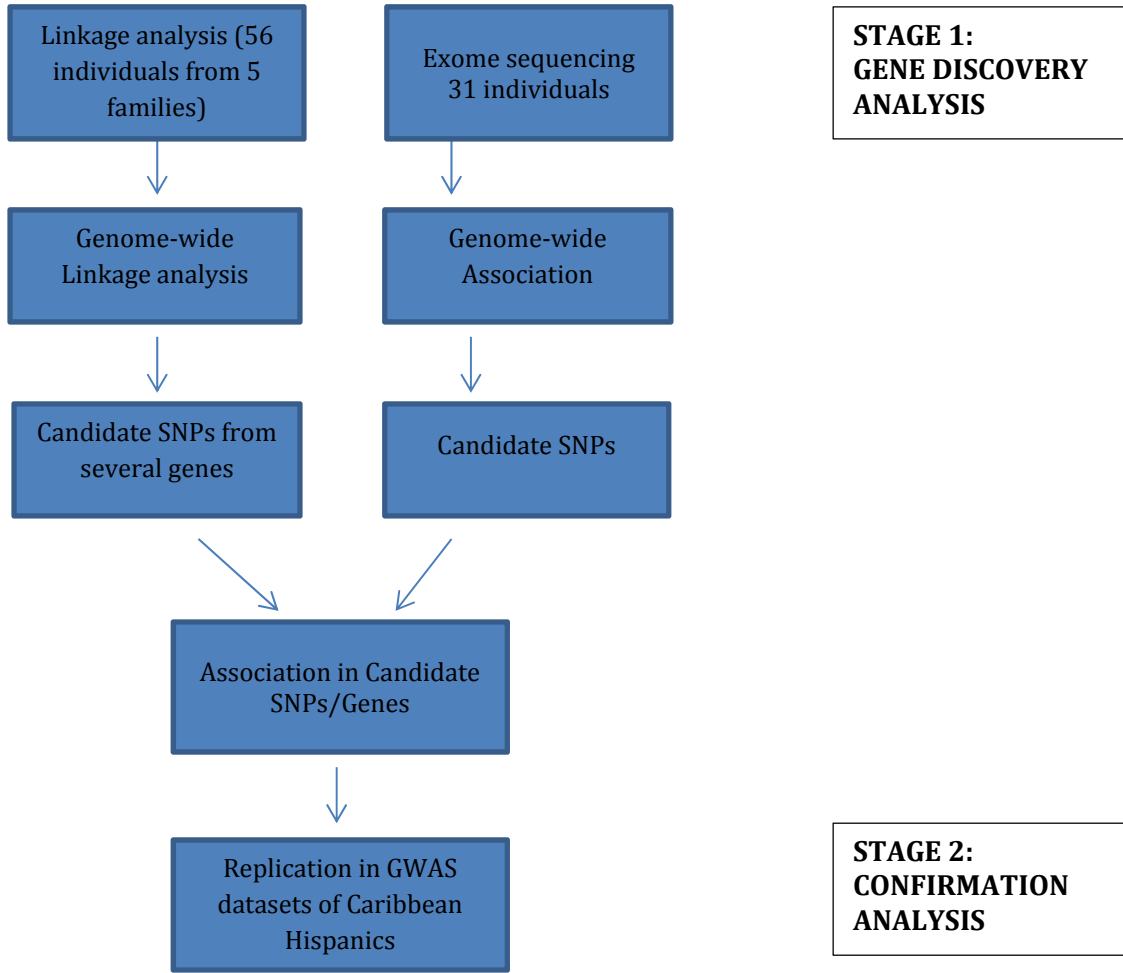
Number of subjects sequenced/genotyped +	2888		1062		763		1063	
Number of families			1062		196		1063	
Affection status								
Affected	1473	0.5	529	0.5	497	0.7	447	0.4
Unaffected	1408	0.5	532	0.5	265	0.3	611	0.6
Unknown	6	0.0	1	0.0	1	0.0	5	0.0
Proportion of males: females	970:1918	33.6:66.4	323:739	30.4:69.6	287:476	37.6:62.4	360:703	33.9:66.1
Age								
Age at onset or age at last examination		74.0±10.01		78.8±10.19		71.7±9.82		72.8±8.54
Education		5.7±4.73		6.4±4.68		5.8±4.93		5.1±4.54
APOE frequency								
E4	1238	23.0%	379	17.8%	452	29.7%	407	23.5%
E3	3849	71.5%	1599	75.3%	1021	66.9%	1229	71.0%
E2	293	5.5%	146	6.9%	51	3.4%	96	5.5%

*Three different batches of Caribbean Hispanic GWAS datasets were used.

eTable 2. Allelic Association Using Linear Mixed Model: Affecteds-Only Analysis
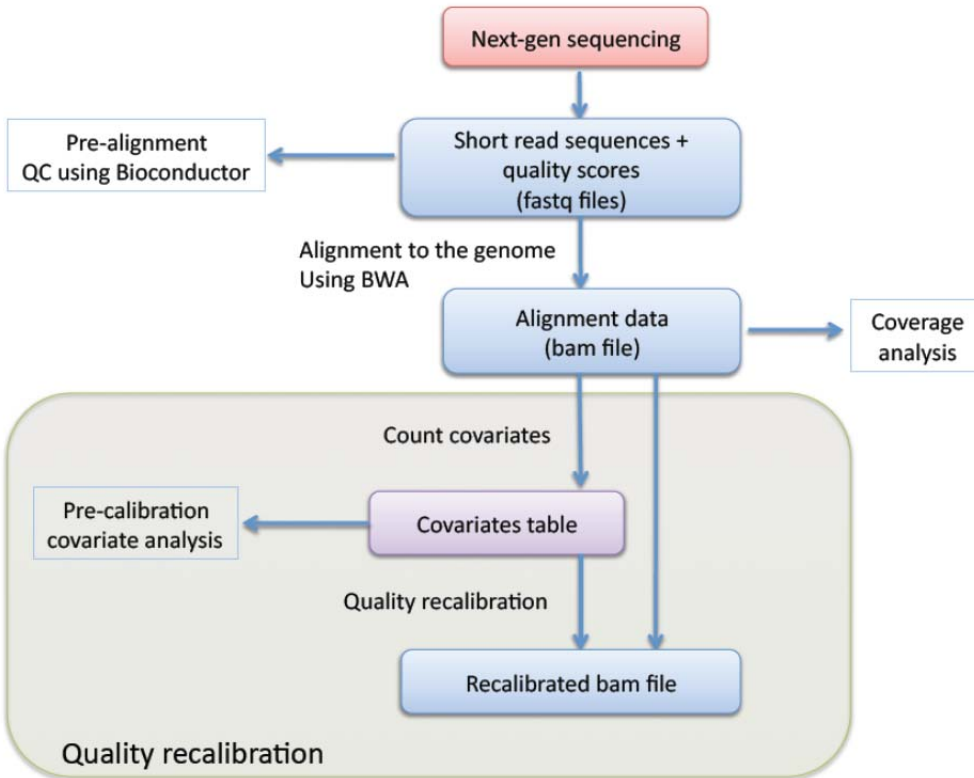
Cyto	Gene	SNP	Location (bp)	A1	A2	EOAD*		LOAD**	
						Beta	**P**	**# of SNPs**	**p gene-wise**
Linkage signal									
4q35	STOX2	rs28411264	184,908,447	G	A	13.20	0.05257	12	0.81696
4q35	ENPP6	rs13147555	185,074,686	C	A	-7.49	0.02959	28	0.23342
4q35	MLF1IP	rs1401359	185,640,216	C	T	-7.58	0.05502	58	0.09760
4q35	SNX25	rs11730401	186,268,129	G	A	8.83	0.00120	17	2.63E-06
4q35	PDLIM3	rs28522047	186,446,018	G	T	-11.37	0.18390	13	0.00532
4q35	SORBS2	rs13130022	186,678,161	C	T	14.26	0.00033	143	0.00313
4q35	FAM149A	rs2276920	187,078,938	A	G	7.24	0.02793	14	0.17919
Association signals									
2q13	SH3RF3	rs6542814	109,928,460	A	T	9.43	0.00276	157	0.00197
2q13	NPHP1	rs906815	110,942,496	A	G	-13.09	4.13E-06	12	0.01430
* Exome seuqencing, ** GWAS of Hispanics									

eFigure 1. Study Design Flow Chart.

| Linkage analysis (56 individuals from 5 families) | Exome sequencing 31 individuals | **STAGE 1: GENE DISCOVERY ANALYSIS** |

Genome-wide Linkage analysis

Genome-wide Association

Candidate SNPs from several genes

Candidate SNPs

Association in Candidate SNPs/Genes

Replication in GWAS datasets of Caribbean Hispanics

STAGE 2: CONFIRMATION ANALYSIS

eFigure 2. Next-Generation Sequencing

eFigure 3. LD Flanking the Variant From the Original Discovery Set for *SORBS2* and *SH3RF3*