

Supplementary Online Content

Table S1. Genes and pseudogenes associated with Alzheimer's disease.

Gene Symbol	Name	Gene Length	Onset of Alzheimer's Disease	ENSEMBL Gene ID
<i>APP</i>	amyloid beta (A4) precursor protein	2326.72	early	ENSG00000142192
<i>FKBP1B</i>	FK506 binding protein 1B	929.42	early	ENSG00000119782
<i>PSEN1</i>	presenilin 1	3941.76	early	ENSG00000080815
<i>PSEN2</i>	presenilin 2	1389.34	early	ENSG00000143801
<i>ABCA1</i>	ATP-binding cassette, sub-family A (ABC1), member 1	10494	late	ENSG00000165029
<i>ABCA7</i>	ATP-binding cassette, sub-family A (ABC1), member 7	1468.3	late	ENSG00000064687
<i>ANK1</i>	ankyrin 1, erythrocytic	2108.51	late	ENSG00000029534
<i>APOC1</i>	apolipoprotein C-I	446.35	late	ENSG00000130208
<i>APOE</i>	apolipoprotein E	1124.92	late	ENSG00000130203
<i>BACE2</i>	beta-site APP-cleaving enzyme 2	2372.29	late	ENSG00000182240
<i>BCR</i>	breakpoint cluster region	2509.52	late	ENSG00000186716
<i>BIN1</i>	bridging integrator 1	1549.99	late	ENSG00000136717
<i>CASS4</i>	Cas scaffolding protein family member 4	2883.85	late	ENSG00000087589
<i>CCL2</i>	chemokine (C-C motif) ligand 2	753.22	late	ENSG00000108691
<i>CD2AP</i>	CD2-associated protein	5412	late	ENSG00000198087
<i>CD33</i>	CD33 molecule	1613.85	late	ENSG00000105383
<i>CELF1</i>	CUGBP, Elav-like family member 1	4778.25	late	ENSG00000149187
<i>CLU</i>	clusterin	607.12	late	ENSG00000120885
<i>COX4I1</i>	cytochrome c oxidase subunit IV isoform 1	711.38	late	ENSG00000131143

<i>CR1</i>	complement component (3b/4b) receptor 1 (Knops blood group)	7442.25	late	ENSG00000203710
<i>CXCL8</i>	chemokine (C-X-C motif) ligand 8	1248.62	late	ENSG00000169429
<i>DSG2</i>	desmoglein 2	5831	late	ENSG00000046604
<i>EPHA1</i>	EPH receptor A1	2181.3	late	ENSG00000146904
<i>EPHA10</i>	EPH receptor A10	3964	late	ENSG00000183317
<i>FAM136A</i>	family with sequence similarity 136, member A	1794.23	late	ENSG00000035141
<i>FERMT2</i>	fermitin family member 2	2678.61	late	ENSG00000073712
<i>GAS7</i>	growth arrest-specific 7	4414.8	late	ENSG00000007237
<i>GRIK2</i>	glutamate receptor, ionotropic, kainate 2	4185	late	ENSG00000164418
<i>GRN</i>	granulin	1084.03	late	ENSG00000030582
<i>HAS3</i>	hyaluronan synthase 3	1342.72	late	ENSG00000103044
<i>HLA-A</i>	major histocompatibility complex, class I, A	5422	late	ENSG00000206503
<i>HLA-DRB1</i>	major histocompatibility complex, class II, DR beta 1	1229	late	ENSG00000196126
<i>HLA-DRB5</i>	major histocompatibility complex, class II, DR beta	1260	late	ENSG00000198502
<i>IL1RN</i>	interleukin 1 receptor antagonist	1776.01	late	ENSG00000136689
<i>IL6</i>	interleukin 6	885.33	late	ENSG00000136244
<i>ITGAL</i>	integrin, alpha L (antigen CD11A (p180), lymphocyte function-associated antigen 1; alpha polypeptide)	1875.14	late	ENSG00000005844
<i>KLK2</i>	kallikrein-related peptidase 2	528	late	ENSG00000167751
<i>LRP2</i>	low density lipoprotein receptor-related protein 2	3156	late	ENSG00000081479

<i>MAPT</i>	microtubule-associated protein tau	2987.74	late	ENSG00000186868
<i>MEF2C</i>	myocyte enhancer factor 2C	3003	late	ENSG00000081189
<i>MS4A4</i>	membrane-spanning 4- domains, subfamily A, member 8	1353	late	ENSG00000166959
<i>MS4A6E</i>	membrane-spanning 4- domains, subfamily A, member 6E phosphatidylinositol	711	late	ENSG00000166926
<i>PICALM</i>	binding clathrin assembly protein	1679.44	late	ENSG00000073921
<i>PIN1</i>	peptidylprolyl cis/trans isomerase, NIMA- interacting 1	1193.02	late	ENSG00000127445
<i>PILRA</i>	paired immunoglobulin-like type 2 receptor alpha	1302.4	late	ENSG00000085514
<i>PLD3</i>	phospholipase D family, member 3	1163.79	late	ENSG00000105223
<i>PRSS42</i>	protease, serine, 42	1280	late	ENSG00000178055
<i>PRSS45</i>	protease, serine, 45	3128	late	ENSG00000188086
<i>PTK2B</i>	protein tyrosine kinase 2 beta	3722.59	late	ENSG00000120899
<i>RIN3</i>	Ras and Rab interactor 3	3419.45	late	ENSG00000100599
<i>SEC31A</i>	SEC31 homolog A, COPII coat complex component	2083.44	late	ENSG00000138674
<i>SLC22A2</i>	solute carrier family 22 (organic cation transporter), member 2	2597	late	ENSG00000112499
<i>SLC24A4</i>	solute carrier family 24 (sodium/potassium/calcium exchanger), member 4	9950	late	ENSG00000140090
<i>SORL1</i>	sortilin-related receptor, L (DLR class) A repeats containing	10009.75	late	ENSG00000137642

<i>STOX2</i>	Storkhead Box 2	3626.57	late	ENSG00000173320
<i>THNSL2</i>	threonine synthase-like 2	1609.65	late	ENSG00000144115
<i>TMIE</i>	transmembrane inner ear	1824	late	ENSG00000181585
<i>TRDMT1</i>	TRNA aspartic acid methyltransferase 1	3705.83	late	ENSG00000107614
<i>TREM2</i>	triggering receptor expressed on myeloid cells 2	1044	late	ENSG00000095970
<i>ZCWPW1</i>	zinc finger, CW type with PWWP domain 1	1893.78	late	ENSG00000078487

Table S2. Summary of the expressions of 60 Alzheimer's disease-associated genes and pseudogenes in the severe OSA and non-severe OSA groups in descending order by probability.

Gene Symbol	Expression		Log ₂ (Fold Change)	Regulation	Probability
	Severe OSA	Non-Severe OSA			
<i>CCL2</i>	12.992	116.716	-3.167	Down	0.868 ^a
<i>IL6</i>	2.854	33.06	-3.534	Down	0.857 ^a
<i>CXCL8</i>	2.042	20.058	-3.296	Down	0.824 ^a
<i>HLA-A</i>	1.272	14.006	-3.460	Down	0.811 ^a
<i>IL1RN</i>	239.35	57.236	2.064	Up	0.806 ^a
<i>HLA-DRB1</i>	41.398	14.398	1.523	Up	0.716
<i>ITGAL</i>	6.81	1.944	1.808	Up	0.635
<i>HLA-DRB5</i>	22.194	10.358	1.099	Up	0.617
<i>CLU</i>	490.412	308.192	0.670	Up	0.522
<i>MS4A4</i>	2.176	4.908	-1.173	Down	0.512
<i>APP</i>	382.418	587.644	-0.619	Down	0.503
<i>TRDMT1</i>	2.702	5.57	-1.043	Down	0.502
<i>ANK1</i>	3.87	1.878	1.043	Up	0.464
<i>CR1</i>	1.076	0.214	2.329	Up	0.439
<i>EPHA1</i>	6.552	4.254	0.623	Up	0.408
<i>MS4A6E</i>	0.39	1.174	-1.590	Down	0.399
<i>BACE2</i>	69.39	90.6	-0.385	Down	0.390
<i>ABCA7</i>	3.636	2.218	0.713	Up	0.385
<i>MAPT</i>	1.134	0.408	1.475	Up	0.382
<i>PTK2B</i>	9.514	6.938	0.456	Up	0.376
<i>DSG2</i>	24.424	31.632	-0.373	Down	0.375
<i>GAS7</i>	5.698	3.952	0.528	Up	0.370
<i>PILRA</i>	1.406	2.452	-0.802	Down	0.370
<i>FERMT2</i>	14.036	17.708	-0.335	Down	0.348
<i>BIN1</i>	23.218	18.884	0.298	Up	0.335
<i>CASS4</i>	13.794	16.864	-0.290	Down	0.323
<i>APOE</i>	24.526	29.308	-0.257	Down	0.318
<i>SEC31A</i>	136.526	159.614	-0.225	Down	0.311
<i>CD33</i>	1.416	2.06	-0.541	Down	0.304
<i>PLD3</i>	121.136	139.682	-0.206	Down	0.300

<i>PIN1</i>	23.774	27.412	-0.205	Down	0.291
<i>GRN</i>	133.2	116.384	0.195	Up	0.289
<i>PSEN1</i>	12.776	14.876	-0.220	Down	0.286
<i>RIN3</i>	2.84	2.234	0.346	Up	0.276
<i>SORL1</i>	8.136	9.338	-0.199	Down	0.267
<i>PSEN2</i>	7.204	6.208	0.215	Up	0.265
<i>APOC1</i>	6.362	7.216	-0.182	Down	0.252
<i>ABCA1</i>	1.152	0.866	0.412	Up	0.248
<i>COX4I1</i>	142.382	153.196	-0.106	Down	0.240
<i>CELF1</i>	9.536	8.628	0.144	Up	0.240
<i>PICALM</i>	56.394	52.512	0.103	Up	0.233
<i>TREM2</i>	0.856	1.076	-0.330	Down	0.232
<i>FAM136A</i>	15.05	16.288	-0.114	Down	0.232
<i>BCR</i>	21.86	20.414	0.099	Up	0.228
<i>SLC22A2</i>	0.056	0.01	2.485	Up	0.224
<i>ZCWPW1</i>	1.442	1.674	-0.215	Down	0.223
<i>MEF2C</i>	16.674	15.664	0.090	Up	0.221
<i>CD2AP</i>	19.416	20.49	-0.078	Down	0.217
<i>FKBP1B</i>	3.786	4.126	-0.124	Down	0.216
<i>HAS3</i>	5.378	5.772	-0.102	Down	0.214
<i>EPHA10</i>	0.476	0.576	-0.275	Down	0.207
<i>SLC24A4</i>	0.202	0.274	-0.440	Down	0.205
<i>THNSL2</i>	8.034	7.658	0.069	Up	0.204
<i>LRP2</i>	0.288	0.22	0.389	Up	0.203
<i>PRSS45</i>	0.054	0.022	1.295	Up	0.196
<i>GRIK2</i>	0.312	0.368	-0.238	Down	0.196
<i>TMIE</i>	0.112	0.084	0.415	Up	0.190
<i>KLK2</i>	0.448	0.49	-0.129	Down	0.186
<i>STOX2</i>	2.428	2.48	-0.031	Down	0.180
<i>PRSS42</i>	0.036	0.022	0.710	Up	0.180

Abbreviations: OSA, obstructive sleep apnea. *Significantly up- and down-regulated genes were defined as FDR ≤ 0.001 (i.e. probability ≥ 0.8) and an absolute value of Log₂Ratio ≥ 1 .

Table S3. Results of Gene Ontology related to five Alzheimer's disease-associated differentially expressed genes in severe OSA patients.

Term	Count	Percentage	<i>p</i>-Value	Adjusted <i>p</i>-value
Biological process				
Immune response	5	1.3	<0.001	<0.001 ^a
Cellular response to interleukin-1	3	0.8	<0.001	0.01 ^a
Cellular response to tumor necrosis factor	3	0.8	<0.001	0.02 ^a
Cellular response to lipopolysaccharide	3	0.8	<0.001	0.01 ^a
Regulation of vascular endothelial growth factor production	2	0.5	0.001	0.04 ^a
Negative regulation of interleukin-1-mediated signaling pathway	2	0.5	0.001	0.04 ^a
PERK-mediated unfolded protein response	2	0.5	0.003	0.10
Inflammatory response	3	0.8	0.003	0.09
Cellular response to dexamethasone stimulus	2	0.5	0.007	0.17
Cellular response to fibroblast growth factor stimulus	2	0.5	0.007	0.16
Response to amino acid	2	0.5	0.007	0.15
Response to antibiotic	2	0.5	0.008	0.14
Acute-phase response	2	0.5	0.009	0.15
Monocyte chemotaxis	2	0.5	0.01	0.15
Response to heat	2	0.5	0.01	0.16
Humoral immune response	2	0.5	0.01	0.18
Response to glucocorticoid	2	0.5	0.02	0.19
Neutrophil chemotaxis	2	0.5	0.02	0.18
Chemokine-mediated signaling pathway	2	0.5	0.02	0.18
Defense response to Gram-positive bacterium	2	0.5	0.02	0.21
Chemotaxis	2	0.5	0.03	0.27
Cytokine-mediated signaling pathway	2	0.5	0.03	0.28
Regulation of cell shape	2	0.5	0.03	0.28
Aging	2	0.5	0.04	0.31

Positive regulation of ERK1 and ERK2 cascade	2	0.5	0.04	0.32
Angiogenesis	2	0.5	0.05	0.37
Negative regulation of cell proliferation	2	0.5	0.09	0.55
Cellular component				
Extracellular space	4	1.0	0.002	0.046 ^a
Intracellular	3	0.8	0.03	0.37
Extracellular region	3	0.8	0.04	0.35
Molecular function				
Chemokine activity	2	0.5	0.01	0.22
Cytokine activity	2	0.5	0.04	0.36
Receptor binding	2	0.5	0.08	0.45

Abbreviations: OSA, obstructive sleep apnea; ^a*P*-values <0.05 adjusted using the Benjamini method were statistically significant.