

APPENDIX A. INCLUDED STUDIES

1. Adak S, Illouz K, Gorman W, et al. Predicting the rate of cognitive decline in aging and early Alzheimer disease. *Neurology*. 2004;63(1):108-114.
2. Altamura C, Squitti R, Pasqualetti P, et al. What is the relationship among atherosclerosis markers, apolipoprotein E polymorphism and dementia? *Eur J Neurol*. 2007;14(6):679-682.
3. Ampuero I, Ros R, Royuela A, et al. Risk factors for dementia of Alzheimer type and aging-associated cognitive decline in a Spanish population based sample, and in brains with pathology confirmed Alzheimer's disease. *J Alzheimers Dis*. 2008;14(2):179-191.
4. Attems J, Jellinger KA, Lintner F. Alzheimer's disease pathology influences severity and topographical distribution of cerebral amyloid angiopathy. *Acta Neuropathol*. 2005;110(3):222-231.
5. Aybek H, Ercan F, Aslan D, Sahiner T. Determination of malondialdehyde, reduced glutathione levels and APOE4 allele frequency in late-onset Alzheimer's disease in Denizli, Turkey. *Clin Biochem*. 2007;40(3-4):172-176.
6. Bahia VS, Kok F, Marie SN, Shinjo SO, Caramelli P, Nitrini R. Polymorphisms of APOE and LRP genes in Brazilian individuals with Alzheimer disease. *Alzheimer Dis Assoc Disord*. 2008;22(1):61-65.
7. Bennett DA, Wilson RS, Schneider JA, et al. Apolipoprotein E epsilon4 allele, AD pathology, and the clinical expression of Alzheimer's disease. *Neurology*. 2003;60(2):246-252.
8. Bian JT, Zhao HL, Zhang ZX, Bi XH, Zhang JW. Association of NAD(P)H:quinone oxidoreductase 1 polymorphism and Alzheimer's disease in Chinese. *J Mol Neurosci*. 2008;34(3):235-240.

9. Blazquez L, Juan DD, Ruiz-Martinez J, et al. Genes related to iron metabolism and susceptibility to Alzheimer's disease in Basque population. *Neurobiol Aging*. 2007;28(12):1941-1943.
10. Bosco P, Caraci F, Copani A, et al. The CDC2 I-G-T haplotype associated with the APOE epsilon4 allele increases the risk of sporadic Alzheimer's disease in Sicily. *Neurosci Lett*. 2007;419(3):195-198.
11. Bowirrat A, Oscar-Berman M, Logroscino G. Association of depression with Alzheimer's disease and vascular dementia in an elderly Arab population of Wadi-Ara, Israel. *Int J Geriatr Psychiatry*. 2006;21(3):246-251.
12. Bracco L, Piccini C, Baccini M, et al. Pattern and progression of cognitive decline in Alzheimer's disease: role of premorbid intelligence and ApoE genotype. *Dement Geriatr Cogn Disord*. 2007;24(6):483-491.
13. Bullock R, Bergman H, Touchon J, et al. Effect of age on response to rivastigmine or donepezil in patients with Alzheimer's disease. *Curr Med Res Opin*. 2006;22(3):483-494.
14. Chalmers K, Wilcock GK, Love S. APOE epsilon 4 influences the pathological phenotype of Alzheimer's disease by favouring cerebrovascular over parenchymal accumulation of A beta protein. *Neuropathol Appl Neurobiol*. 2003;29(3):231-238.
15. Chui HC, Zarow C, Mack WJ, et al. Cognitive impact of subcortical vascular and Alzheimer's disease pathology. *Ann Neurol*. 2006;60(6):677-687.
16. Chuu JY, Taylor JL, Tinklenberg J, et al. The brain-derived neurotrophic factor Val66Met polymorphism and rate of decline in Alzheimer's disease. *J Alzheimers Dis*. 2006;9(1):43-49.
17. Clarimon J, Bertranpetit J, Calafell F, Boada M, Tarraga L, Comas D. Joint analysis of candidate genes related to Alzheimer's disease in a Spanish population. *Psychiatr Genet*. 2003;13(2):85-90.

18. Cosentino S, Scarmeas N, Helzner E, et al. APOE epsilon 4 allele predicts faster cognitive decline in mild Alzheimer disease. *Neurology*. 2002;70(19 Pt 2):1842-1849.
19. Courtney C, Farrell D, Gray R, et al. Long-term donepezil treatment in 565 patients with Alzheimer's disease (AD2000): randomised double-blind trial. *Lancet*. 2004;363(9427):2105-2115.
20. Craig D, Hart DJ, McIlroy SP, Passmore AP. Association analysis of apolipoprotein E genotype and risk of depressive symptoms in Alzheimer's disease. *Dement Geriatr Cogn Disord*. 2005;19(2-3):154-157.
21. Davidson Y, Gibbons L, Pritchard A, et al. Apolipoprotein E epsilon4 allele frequency and age at onset of Alzheimer's disease. *Dement Geriatr Cogn Disord*. 2007;23(1):60-66.
22. Deniz-Naranjo MC, Munoz-Fernandez C, Alemany-Rodriguez MJ, et al. Cytokine IL-1 beta but not IL-1 alpha promoter polymorphism is associated with Alzheimer disease in a population from the Canary Islands, Spain. *Eur J Neurol*. 2008;15(10):1080-1084.
23. Drzezga A, Riemenschneider M, Strassner B, et al. Cerebral glucose metabolism in patients with AD and different APOE genotypes. *Neurology*. 2005;64(1):102-107.
24. Engelborghs S, Sleegers K, Cras P, et al. No association of CSF biomarkers with APOE epsilon4, plaque and tangle burden in definite Alzheimer's disease. *Brain*. 2007;130(Pt 9):2320-2326.
25. Flex A, Gaetani E, Proia AS, et al. Analysis of functional polymorphisms of metalloproteinase genes in persons with vascular dementia and Alzheimer's disease. *J Gerontol A Biol Sci Med Sci*. 2006;61(10):1065-1069.
26. Folin M, Baiguera S, Gallucci M, et al. A cross-sectional study of homocysteine-, NO- levels, and CT-findings in Alzheimer dementia, vascular dementia and controls. *Biogerontology*. 2005; 6(4):255-260.

27. Forero DA, Arboleda G, Yunis JJ, Pardo R, Arboleda H. Association study of polymorphisms in LRP1, tau and 5-HTT genes and Alzheimer's disease in a sample of Colombian patients. *J Neural Transm.* 2006;113(9):1253-1262.
28. Gacia M, Safranow K, Gabryelewicz T, et al. Two polymorphisms of presenilin-2 gene (PSEN2) 5' regulatory region are not associated with Alzheimer's disease (AD) in the Polish population. *J Neural Transm.* 2008;115(1):85-90.
29. Gold G, Blouin JL, Herrmann FR, et al. Specific BACE1 genotypes provide additional risk for late-onset Alzheimer disease in APOE epsilon 4 carriers. *Am J Med Genet B Neuropsychiatr Genet.* 2003;119B(1):44-47.
30. Greenberg SM, Tennis MK, Brown LB, et al. Donepezil therapy in clinical practice: a randomized crossover study. *Arch Neurol.* 2000;57(1):94-99.
31. Harwood DG, Barker WW, Ownby RL, George-Hyslop PS, Mullan M, Duara R. Apolipoprotein E polymorphism and age of onset for Alzheimer's disease in a bi-ethnic sample. *Int Psychogeriatr.* 2004;16(3):317-326.
32. He J, Gui JH, Zhang YH, et al. Relationship between apolipoprotein E gene and the risk for onset of Alzheimer disease in aged adults in Urumqi. *Chinese Journal of Clinical Rehabilitation.* 2005;9(25):207-209.
33. Hollingworth P, Hamshere ML, Moskvina V, et al. Four components describe behavioral symptoms in 1,120 individuals with late-onset Alzheimer's disease. *J Am Geriatr Soc.* 2006;54(9):1348-1354.
34. Jia L, Ye J, Haiyan LV, et al. Genetic association between polymorphisms of Pen2 gene and late onset Alzheimer's disease in the North Chinese population. *Brain Res.* 2007;1141:10-14.
35. Jicha GA, Parisi JE, Dickson DW, et al. Neuropathologic outcome of mild cognitive impairment following progression to clinical dementia. *Arch Neurol.* 2006;63(5):674-681.

36. Jo SA, Ahn K, Kim JH, et al. ApoE-epsilon 4-dependent association of the choline acetyltransferase gene polymorphisms (2384G>A and 1882G>A) with Alzheimer's disease. *Clin Chim Acta*. 2006;368(1-2):179-182.
37. Jones RW, Kivipelto M, Feldman H, et al. The Atorvastatin/Donepezil in Alzheimer's Disease Study (LEADe): design and baseline characteristics. *Alzheimers Dement*. 2008;4(2):145-153.
38. Kadir A, Andreassen N, Almkvist O, et al. Effect of phenserine treatment on brain functional activity and amyloid in Alzheimer's disease. *Ann Neurol*. 2008;63(5):621-631.
39. Kar S, Poirier J, Guevara J, et al. Cellular distribution of insulin-like growth factor-II/mannose-6-phosphate receptor in normal human brain and its alteration in Alzheimer's disease pathology. *Neurobiol Aging*. 2006;27(2):199-210.
40. Kim JM, Shin IS, Yoon JS. Correlates of dropout, efficacy, and adverse events in treatment with acetylcholinesterase inhibitors in Korean patients with Alzheimer's disease. *Int Psychogeriatr*. 2002;14(2):187-195.
41. Koivisto AM, Helisalmi S, Pihlajamaki J, et al. Interleukin-6 promoter polymorphism and late-onset Alzheimer's disease in the Finnish population. *J Neurogenet*. 2005;19(3-4):155-161.
42. Kuwano R, Miyashita A, Arai H, et al. Dynamin-binding protein gene on chromosome 10q is associated with late-onset Alzheimer's disease. *Hum Mol Genet*. 2006;15(13):2170-2182.
43. Lai MKP, Tsang SWY, Garcia-Alloza M, et al. Selective effects of the APOE (epsilon)4 allele on presynaptic cholinergic markers in the neocortex of Alzheimer's disease. *Neurobiol Dis*. 2006;22(3):555-561.
44. Lannfelt L, Blennow K, Zetterberg H, et al. Safety, efficacy, and biomarker findings of PBT2 in targeting Abeta as a modifying therapy for Alzheimer's disease: a phase

- Ia, double-blind, randomised, placebo-controlled trial. *Lancet Neurol.* 2008;7(9):779-786.
45. Liu HC, Hong CJ, Liu TY, Chi CW, Tsai SJ. Association analysis for the muscarinic M1 receptor genetic polymorphisms and Alzheimer's disease. *Dement Geriatr Cogn Disord.* 2005;19(1):42-45.
 46. Ma SL, Tang NL, Lam LC, Chiu HF. The association between promoter polymorphism of the interleukin-10 gene and Alzheimer's disease. *Neurobiol Aging.* 2005;26(7):1005-1010.
 47. Martins CA, Oulhaj A, de Jager CA, Williams JH. APOE alleles predict the rate of cognitive decline in Alzheimer disease: a nonlinear model. *Neurology.* 2005;65(12):1888-1893.
 48. Monastero R, Cefalu AB, Camarda C, et al. No association between Glu298Asp endothelial nitric oxide synthase polymorphism and Italian sporadic Alzheimer's disease. *Neurosci Lett.* 2003;341(3):229-232.
 49. Murrell JR, Price B, Lane KA, et al. Association of apolipoprotein E genotype and Alzheimer disease in African Americans. *Arch Neurol.* 2006;63(3):431-434.
 50. Orsitto G, Seripa D, Panza F, et al. Apolipoprotein E genotypes in hospitalized elderly patients with vascular dementia. *Dement Geriatr Cogn Disord.* 2007;23(5):327-333.
 51. Panza F, Solfrizzi V, Colacicco AM, et al. Apolipoprotein E (APOE) polymorphism influences serum APOE levels in Alzheimer's disease patients and centenarians. *Neuroreport.* 2003;14(4):605-608.
 52. Percy M, Moalem S, Garcia A, et al. Involvement of ApoE E4 and H63D in sporadic Alzheimer's disease in a folate-supplemented Ontario population. *J Alzheimers Dis.* 2008;14(1):69-84.

53. Perneczky R, Mosch D, Neumann M, et al. The Alzheimer variant of lewy body disease: a pathologically confirmed case-control study. *Dement Geriatr Cogn Disord.* 2005;20(2-3):89-94.
54. Piccardi M, Congiu D, Squassina A, et al. Alzheimer's disease: case-control association study of polymorphisms in ACHE, CHAT, and BCHE genes in a Sardinian sample. *Am J Med Genet B Neuropsychiatr Genet.* 2007;144B(7):895-899.
55. Piscopo P, Manfredi A, Malvezzi-Campeggi L, et al. Genetic study of Sardinian patients with Alzheimer's disease. *Neurosci Lett.* 2006;398(1-2):124-128.
56. Poli M, Gatta LB, Archetti S, Padovani A, Albertini A, Finazzi D. Association analysis between anterior-pharynx defective-1 genes polymorphisms and Alzheimer's disease. *Neurosci Lett.* 2003;350(2):77-80.
57. Ponomareva NV, Korovaitseva GI, Rogaev EI. EEG alterations in non-demented individuals related to apolipoprotein E genotype and to risk of Alzheimer disease. *Neurobiol Aging.* 2008;29(6):819-827.
58. Prince JA, Zetterberg H, Andreasen N, Marcusson J, Blennow K. APOE epsilon4 allele is associated with reduced cerebrospinal fluid levels of Abeta42. *Neurology.* 2004;62(11):2116-2118.
59. Profenno LA, Faraone SV. Diabetes and overweight associated with non-APOE4 genotype in an Alzheimer's disease population. *Am J Med Genet B Neuropsychiatr Genet.* 2008;147(6):822-829.
60. Quan W, Yasuda M, Hashimoto M, et al. Polymorphism of the regulatory region of the presenilin-2 gene in sporadic Alzheimer's disease: a case-control study. *J Neurol Sci.* 2006;240(1-2):71-75.
61. Rakonczay Z, Horvath Z, Juhasz A, Kalman J. Peripheral cholinergic disturbances in Alzheimer's disease. *Chem Biol Interact.* 2005;157-158:233-238.

62. Ramos EM, Lin MT, Larson EB, et al. Tumor necrosis factor alpha and interleukin 10 promoter region polymorphisms and risk of late-onset Alzheimer disease. *Arch Neurol.* 2006;63(8):1165-1169.
63. Raskind MA, Peskind ER, Wessel T, Yuan W. Galantamine in AD: A 6-month randomized, placebo-controlled trial with a 6-month extension. The Galantamine USA-1 Study Group. *Neurology.* 2000;54(12):2261-2268.
64. Raygani AV, Zahrai M, Soltanzadeh A, Doosti M, Javadi E, Pourmotabbed T. Analysis of association between butyrylcholinesterase K variant and apolipoprotein E genotypes in Alzheimer's disease. *Neurosci Lett.* 2004;371(2-3):142-146.
65. Reitz C, Tang MX, Luchsinger J, Mayeux R. Relation of plasma lipids to Alzheimer disease and vascular dementia. *Arch Neurol.* 2004;61(5):705-714.
66. Rodriguez-Rodriguez E, Llorca J, Mateo I, et al. No association of genetic variants of liver X receptor-beta with Alzheimer's disease risk. *Am J Med Genet B Neuropsychiatr Genet.* 2008;147B(5):650-653.
67. Sando SB, Melquist S, Cannon A, et al. APOE epsilon 4 lowers age at onset and is a high risk factor for Alzheimer's disease: a case control study from central Norway. *BMC Neurol.* 2008;8:9.
68. Seripa D, Matera MG, Andrea RPD, et al. Alzheimer disease risk associated with APOE4 is modified by STH gene polymorphism. *Neurology.* 2004;62(9):1631-1633.
69. Shi J, Zhang S, Tang M, et al. The 1239G/C polymorphism in exon 5 of BACE1 gene may be associated with sporadic Alzheimer's disease in Chinese Hans. *Am J Med Genet B Neuropsychiatr Genet.* 2004;124B(1):54-57.
70. Shibata N, Ohnuma T, Baba H, Higashi S, Nishioka K, Arai H. Genetic association between SORL1 polymorphisms and Alzheimer's disease in a Japanese population. *Dement Geriatr Cogn Disord.* 2008;26(2):161-164.

71. Smach MA, Charfeddine B, Lammouchi T, et al. CSF beta-amyloid 1-42 and tau in Tunisian patients with Alzheimer's disease: the effect of APOE epsilon4 allele. *Neurosci Lett.* 2008;440(2):145-149.
72. Souza DR, Godoy MRd, Hotta J, et al. Association of apolipoprotein E polymorphism in late-onset Alzheimer's disease and vascular dementia in Brazilians. *Braz J Med Biol Res.* 2003;36(7):919-923.
73. Spalletta G, Bernardini S, Bellincampi L, et al. Glutathione S-transferase P1 and T1 gene polymorphisms predict longitudinal course and age at onset of Alzheimer disease. *Am J Geriatr Psychiatry.* 2007;15(10):879-887.
74. Suh GH, Jung HY, Lee CU, et al. Effect of the apolipoprotein E epsilon4 allele on the efficacy and tolerability of galantamine in the treatment of Alzheimer's disease. *Dement Geriatr Cogn Disord.* 2006;21(1):33-39.
75. Sundermann EE, Gilbert PE, Murphy C. Apolipoprotein E epsilon4 genotype and gender: effects on memory. *Am J Geriatr Psychiatry.* 2007;15(10):869-878.
76. Suzuki Y, Yamamoto S, Umegaki H, et al. Smell identification test as an indicator for cognitive impairment in Alzheimer's disease. *Int J Geriatr Psychiatry.* 2004;19(8):727-733.
77. Tariot PN, Solomon PR, Morris JC, Kershaw P, Lilienfeld S, Ding C. A 5-month, randomized, placebo-controlled trial of galantamine in AD. The Galantamine USA-10 Study Group. *Neurology.* 2000;54(12):2269-2276.
78. Terreni L, Fogliarino S, Quadri P, et al. Tumor necrosis factor alpha polymorphism C-850T is not associated with Alzheimer's disease and vascular dementia in an Italian population. *Neurosci Lett.* 2003;344(2):135-137.
79. Tiraboschi P, Hansen LA, Masliah E, Alford M, Thal LJ, Corey-Bloom J. Impact of APOE genotype on neuropathologic and neurochemical markers of Alzheimer disease. *Neurology.* 2004;62(11):1977-1983.

80. Tsai SJ, Hong CJ, Liu HC, Liu TY, Liou YJ. The brain-derived neurotrophic factor gene as a possible susceptibility candidate for Alzheimer's disease in a Chinese population. *Dement Geriatr Cogn Disord*. 2006;21(3):139-143.
81. Vanhanen M, Koivisto K, Moilanen L, et al. Association of metabolic syndrome with Alzheimer disease: a population-based study. *Neurology*. 2006;67(5):843-847.
82. Ventriglia M, Chiavetto LB, Scassellati C, et al. Lack of association between MnSOD gene polymorphism and sporadic Alzheimer's disease. *Aging Clin Exp Res*. 2005;17(6):445-448.
83. Venturelli E, Galimberti D, Lovati C, et al. The T-786C NOS3 polymorphism in Alzheimer's disease: association and influence on gene expression. *Neurosci Lett*. 2005;382(3):300-303.
84. Vepsäläinen S, Helisalmi S, Koivisto AM, Tapaninen T, Hiltunen M, Soininen H. Somatostatin genetic variants modify the risk for Alzheimer's disease among Finnish patients. *J Neurol*. 2007;254(11):1504-1508.
85. Wang B, Zhou S, Yang Z, et al. Genetic analysis of tumor necrosis factor-alpha (TNF-alpha) G-308A and Saitohin Q7R polymorphisms with Alzheimer's disease. *J Neurol Sci*. 2008;270(1-2):148-151.
86. Wilcock GK, Lilienfeld S, Gaens E. Efficacy and safety of galantamine in patients with mild to moderate Alzheimer's disease: multicentre randomised controlled trial. Galantamine International-1 Study Group. *BMJ*. 2000;321(7274):1445-1449.
87. Williams MM, Xiong C, Morris JC, Galvin JE. Survival and mortality differences between dementia with Lewy bodies vs Alzheimer disease. *Neurology*. 2006;67(11):1935-1941.
88. Winblad B, Engedal K, Soininen H, et al. A 1-year, randomized, placebo-controlled study of donepezil in patients with mild to moderate AD. *Neurology*. 2001;57(3):489-495.

89. Yamagata H, Chen Y, Akatsu H, et al. Promoter polymorphism in fibroblast growth factor 1 gene increases risk of definite Alzheimer's disease. *Biochem Biophys Res Commun.* 2004;321(2):320-323.
90. Yang JD, Feng GY, Zhang J, et al. Apolipoprotein E -491 promoter polymorphism is an independent risk factor for Alzheimer's disease in the Chinese population. *Neurosci Lett.* 2003;350(1):25-28.
91. Yip AG, Green RC, Huyck M, Cupples LA, Farrer LA. Nonsteroidal anti-inflammatory drug use and Alzheimer's disease risk: The MIRAGE study. *BMC Geriatr.* 2005;5:2.
92. Yip AG, McKee AC, Green RC, et al. APOE, vascular pathology, and the AD brain. *Neurology.* 2005;65(2):259-265.
93. Yokes MB, Emre M, Harmanci H, et al. The apolipoprotein E (APOE) genotype in a Turkish population with Alzheimer's disease. *Balkan J Med Genet.* 2005;8(1-2):57-63.
94. Yu JT, Tan L, Ou JR, et al. Polymorphisms at the beta2-adrenergic receptor gene influence Alzheimer's disease susceptibility. *Brain Res.* 2008;1210:216-222.
95. Zappia M, Manna I, Serra P, et al. Increased risk for Alzheimer disease with the interaction of MPO and A2M polymorphisms. *Arch Neurol.* 2004;61(3):341-344.
96. Zetterberg M, Landgren S, Andersson ME, et al. Association of complement factor H Y402H gene polymorphism with Alzheimer's disease. *Am J Med Genet B Neuropsychiatr Genet.* 2008;147(6):720-726.
97. Zhang JW, Li XQ, Zhang ZX, et al. Association between angiotensin-converting enzyme gene polymorphism and Alzheimer's disease in a Chinese population. *Dement Geriatr Cogn Disord.* 2005;20(1):52-56.
98. Zhang Y, Londos E, Minthon L, et al. Usefulness of computed tomography linear measurements in diagnosing Alzheimer's disease. *Acta Radiol.* 2008;49(1):91-97.

99. Zhao FG, Wang YH, Yang JF, et al. Association between acyl-coenzyme A: cholesterol acyltransferase gene and risk for Alzheimer's disease in Chinese. *Neurosci Lett.* 2005;388(1):17-20.
100. Zhou W, Scott SA, Shelton SB, Crutcher KA. Cathepsin D-mediated proteolysis of apolipoprotein E: possible role in Alzheimer's disease. *Neuroscience.* 2006;143(3):689-701.