

Supplemental Table A1 Sleep Disruption

Significant Genes- Genomic Findings	Authors
<p>CLOCK (neurotrophic receptor tyrosine kinase 2) The results of this study indicate that polymorphisms in several circadian genes (i.e., <i>CLOCK</i>, <i>CRY1</i>, <i>PER1</i>, <i>PER2</i>, <i>PER3</i>) are associated with poor sleep maintenance and disturbed sleep-wake rhythms</p>	(Lee et al., 2015)
<p>CRY1 (Cryptochrome Circadian Clock 1) The results of this study indicate that polymorphisms in several circadian genes (i.e., <i>CLOCK</i>, <i>CRY1</i>, <i>PER1</i>, <i>PER2</i>, <i>PER3</i>) are associated with poor sleep maintenance and disturbed sleep-wake rhythms</p>	(Lee et al., 2015)
<p>PER1 (Period Circadian Clock 1) The results of this study indicate that polymorphisms in several circadian genes (i.e., <i>CLOCK</i>, <i>CRY1</i>, <i>PER1</i>, <i>PER2</i>, <i>PER3</i>) are associated with poor sleep maintenance and disturbed sleep-wake rhythms</p>	(Lee et al., 2015)
<p>PER2 (Period Circadian Clock 2) The results of this study indicate that polymorphisms in several circadian genes (i.e., <i>CLOCK</i>, <i>CRY1</i>, <i>PER1</i>, <i>PER2</i>, <i>PER3</i>) are associated with poor sleep maintenance and disturbed sleep-wake rhythms</p> <p>Using a standard approach to significance testing, there was a significant association between the PER2 SNP rs2304672 and sleep paralysis using an additive model of inheritance</p> <p>PER2 (and possibly for other circadian repressors), and this mode of regulation can also provide a highly sensitive system to track the timing of the clock</p>	(Lee et al., 2015) (Denis et al., 2015) (Jones, Huang, Ptacek, & Fu, 2013)
<p>PER3 (Period Circadian Clock 3) The results of this study indicate that polymorphisms in several circadian genes (i.e., <i>CLOCK</i>, <i>CRY1</i>, <i>PER1</i>, <i>PER2</i>, <i>PER3</i>) are associated with poor sleep maintenance and disturbed sleep-wake rhythms</p> <p>Rs10861688 harbored by PER3 displayed a trend of association with sleep disruption</p> <p>Participants with the 4/5 or 5/5 Per3 variable tandem repeat sequence had elevated IL-6 concentrations compared to those with the 4/4 genotype</p>	(Lee et al., 2015) (Drago, Monti, De Ronchi, & Serretti, 2015) (Guess et al., 2009)
<p>BDNF (Brain Derived Neurotrophic Factor) Met allele was associated with an interaction of GI and sleep quality.</p>	(Reddy et al., 2014)

HAT Tip60 (Tip60 histone acetyltransferase) Sleep disruption associated with AD is driven by epigenetic changes mediated by the histone acetyltransferase (HAT) Tip60	(Pirooznia & Elefant, 2013)
rs10861688 rs10861688 harbored by PER3 displayed a trend of association with sleep disruption	(Drago et al., 2015)
PERK (EIF2AK3 Eukaryotic Translation Initiation Factor 2 Alpha Kinase 3) Expression of PERK mRNA increases with 8 hours of sleep deprivation	(Cirelli, Gutierrez, & Tononi, 2004)
NTRK2 Neurotrophic Receptor Tyrosine Kinase 2) NTRK2 SNP rs1212171 was associated with sleep disturbance and fatigue in breast cancer patients.	(Young et al., 2017)
IL1B (interleukin 1 beta) Alzheimer's disease patients with the IL-1beta-31TT genotype plus homozygous APOEepsilon4 have an increased risk of developing AD with sleep disturbance	(Yin et al., 2016)
Significant Genes- Epigenomic Findings	Authors
HAT (Tip60) (Tip60 histone acetyltransferase) Sleep disruption associated with AD is driven by epigenetic changes mediated by the histone acetyltransferase (HAT) Tip60	(Pirooznia & Elefant, 2013)
CLOCK-BMAL1 (neurotrophic receptor tyrosine kinase 2-ARNTL Aryl Hydrocarbon Receptor Nuclear Translocator Like) Further observation revealed that activation of CCGs by CLOCK-BMAL1 is coupled to circadian changes in histone acetylation at their promoters	(EtcheGARay, Lee, Wade, & Reppert, 2003)
SIRT1 (Sirtuin 1) The activity of SIRT1 counterbalances the rhythmic HAT function of CLOCK, although other HATs are likely to be implicated	(Masri & Sassone-Corsi, 2010)
dTIP60 Changes in these sleep parameters with the dTip60 ^{RNAi} and dTip60 ^{E431Q} indicate that sleep becomes highly fragmented during the night	(Pirooznia, Chiu, Chan, Zimmerman, & Elefant, 2012)
Significant Genes- Transcriptomic Findings	Authors

<p>CLOCK (neurotrophic receptor tyrosine kinase 2) Core clock transcription factors CLOCK and BMAL1 promote expression by rhythmic binding to E-box motifs in the promoters of core clock genes</p> <p>Sleep disturbances and circadian misalignment have been associated with alterations of the physiological oscillations of CLOCK gene expression in humans, affecting the neurobiological response to stress</p> <p><i>Clock</i> gene expression was lower in CJL males than in control males</p>	<p>(Mohawk, Green, & Takahashi, 2012)</p> <p>(Ackermann et al., 2013)</p> <p>(Hadden, Soldin, & Massaro, 2012)</p>
<p>BMAL1 (ARNTL Aryl Hydrocarbon Receptor Nuclear Translocator Like) Core clock transcription factors CLOCK and BMAL1 promote expression by rhythmic binding to E-box motifs in the promoters of core clock genes</p> <p>In CJL females, <i>Bmal1</i> gene expression was lower than in controls</p>	<p>(Mohawk et al., 2012)</p> <p>(Hadden et al., 2012)</p>
<p>CRY2 (Cryptochrome Circadian Clock 2) <i>Cry2</i> gene expression was higher in CJL females, but not in CJL males</p> <p>Known clock genes classified as circadian while sleeping in phase included <i>ARNTL</i>, <i>NPAS2</i>, <i>PER2</i>, <i>PER3</i>, <i>CRY2</i>, <i>NR1D2</i>, and the protein kinase <i>CSKN1E</i></p>	<p>(Hadden et al., 2012)</p> <p>(Archer et al., 2014)</p>
<p>ARNTL (Aryl Hydrocarbon Receptor Nuclear Translocator Like) Known clock genes classified as circadian while sleeping in phase included <i>ARNTL</i>, <i>NPAS2</i>, <i>PER2</i>, <i>PER3</i>, <i>CRY2</i>, <i>NR1D2</i>, and the protein kinase <i>CSKN1E</i></p>	<p>(Archer et al., 2014)</p>
<p>NPAS2 (Neuronal PAS Domain Protein 2) Known clock genes classified as circadian while sleeping in phase included <i>ARNTL</i>, <i>NPAS2</i>, <i>PER2</i>, <i>PER3</i>, <i>CRY2</i>, <i>NR1D2</i>, and the protein kinase <i>CSKN1E</i></p>	<p>(Archer et al., 2014)</p>
<p>PER2 (Period Circadian Clock 2) Known clock genes classified as circadian while sleeping in phase included <i>ARNTL</i>, <i>NPAS2</i>, <i>PER2</i>, <i>PER3</i>, <i>CRY2</i>, <i>NR1D2</i>, and the protein kinase <i>CSKN1E</i></p>	<p>(Archer et al., 2014)</p>
<p>PER3 (Period Circadian Clock 3) Known clock genes classified as circadian while sleeping in phase included <i>ARNTL</i>, <i>NPAS2</i>, <i>PER2</i>, <i>PER3</i>, <i>CRY2</i>, <i>NR1D2</i>, and the protein kinase <i>CSKN1E</i></p>	<p>(Archer et al., 2014)</p>
<p>NR1D2 (Nuclear Receptor Subfamily 1 Group D Member 2) Known clock genes classified as circadian while sleeping in phase included <i>ARNTL</i>, <i>NPAS2</i>, <i>PER2</i>, <i>PER3</i>, <i>CRY2</i>, <i>NR1D2</i>, and the protein kinase <i>CSKN1E</i></p>	<p>(Archer et al., 2014)</p>
<p>CSKN1E (Casein Kinase 1 Epsilon) Known clock genes classified as circadian while sleeping in phase included <i>ARNTL</i>, <i>NPAS2</i>, <i>PER2</i>, <i>PER3</i>, <i>CRY2</i>, <i>NR1D2</i>, and the protein kinase <i>CSKN1E</i></p>	<p>(Archer et al., 2014)</p>

References

- Ackermann, K., Plomp, R., Lao, O., Middleton, B., Revell, V. L., Skene, D. J., & Kayser, M. (2013). Effect of sleep deprivation on rhythms of clock gene expression and melatonin in humans. *Chronobiol Int*, *30*(7), 901-909. doi:10.3109/07420528.2013.784773
- Archer, S. N., Laing, E. E., Moller-Levet, C. S., van der Veen, D. R., Bucca, G., Lazar, A. S., . . . Dijk, D. J. (2014). Mistimed sleep disrupts circadian regulation of the human transcriptome. *Proc Natl Acad Sci U S A*, *111*(6), E682-691. doi:10.1073/pnas.1316335111
- Cirelli, C., Gutierrez, C. M., & Tononi, G. (2004). Extensive and divergent effects of sleep and wakefulness on brain gene expression. *Neuron*, *41*(1), 35-43.
- Denis, D., French, C. C., Rowe, R., Zavos, H. M., Nolan, P. M., Parsons, M. J., & Gregory, A. M. (2015). A twin and molecular genetics study of sleep paralysis and associated factors. *J Sleep Res*, *24*(4), 438-446. doi:10.1111/jsr.12282
- Drago, A., Monti, B., De Ronchi, D., & Serretti, A. (2015). CRY1 Variations Impacts on the Depressive Relapse Rate in a Sample of Bipolar Patients. *Psychiatry Investig*, *12*(1), 118-124. doi:10.4306/pi.2015.12.1.118
- Etchegaray, J. P., Lee, C., Wade, P. A., & Reppert, S. M. (2003). Rhythmic histone acetylation underlies transcription in the mammalian circadian clock. *Nature*, *421*(6919), 177-182. doi:10.1038/nature01314
- Guess, J., Burch, J. B., Ogoussan, K., Armstead, C. A., Zhang, H., Wagner, S., . . . Hrushesky, W. J. (2009). Circadian disruption, Per3, and human cytokine secretion. *Integr Cancer Ther*, *8*(4), 329-336. doi:10.1177/1534735409352029
- Hadden, H., Soldin, S. J., & Massaro, D. (2012). Circadian disruption alters mouse lung clock gene expression and lung mechanics. *J Appl Physiol* (1985), *113*(3), 385-392. doi:10.1152/jappphysiol.00244.2012
- Jones, C. R., Huang, A. L., Ptacek, L. J., & Fu, Y. H. (2013). Genetic basis of human circadian rhythm disorders. *Exp Neurol*, *243*, 28-33. doi:10.1016/j.expneurol.2012.07.012
- Lee, K. A., Gay, C., Byun, E., Lerdal, A., Pullinger, C. R., & Aouizerat, B. E. (2015). Circadian regulation gene polymorphisms are associated with sleep disruption and duration, and circadian phase and rhythm in adults with HIV. *Chronobiol Int*, *32*(9), 1278-1293. doi:10.3109/07420528.2015.1087021
- Masri, S., & Sassone-Corsi, P. (2010). Plasticity and specificity of the circadian epigenome. *Nat Neurosci*, *13*(11), 1324-1329. doi:10.1038/nn.2668
- Mohawk, J. A., Green, C. B., & Takahashi, J. S. (2012). Central and peripheral circadian clocks in mammals. *Annu Rev Neurosci*, *35*, 445-462. doi:10.1146/annurev-neuro-060909-153128
- Pirooznia, S. K., Chiu, K., Chan, M. T., Zimmerman, J. E., & Elefant, F. (2012). Epigenetic regulation of axonal growth of Drosophila pacemaker cells by histone acetyltransferase tip60 controls sleep. *Genetics*, *192*(4), 1327-1345. doi:10.1534/genetics.112.144667
- Pirooznia, S. K., & Elefant, F. (2013). A HAT for sleep?: epigenetic regulation of sleep by Tip60 in Drosophila. *Fly (Austin)*, *7*(2), 99-104. doi:10.4161/fly.24141
- Reddy, S. Y., Rasmussen, N. A., Fourie, N. H., Berger, R. S., Martino, A. C., Gill, J., . . . Henderson, W. A. (2014). Sleep quality, BDNF genotype and gene expression in individuals with chronic abdominal pain. *BMC Med Genomics*, *7*, 61. doi:10.1186/s12920-014-0061-1
- Yin, Y., Liu, Y., Pan, X., Chen, R., Li, P., Wu, H. J., . . . Zhao, Z. X. (2016). Interleukin-1beta Promoter Polymorphism Enhances the Risk of Sleep Disturbance in Alzheimer's Disease. *PLoS One*, *11*(3), e0149945. doi:10.1371/journal.pone.0149945
- Young, E. E., Kelly, D. L., Shim, I., Baumbauer, K. M., Starkweather, A., & Lyon, D. E. (2017). Variations in COMT and NTRK2 Influence Symptom Burden in Women Undergoing Breast Cancer Treatment. *Biol Res Nurs*, *19*(3), 318-328. doi:10.1177/1099800417692877

Supplemental Table A2 Cognitive Impairment

Significant Genes – Genomic Findings	Authors
<p>11βHSD1 (11 beta-Hydroxysteroid dehydrogenase type 1) Polymorphisms in the 11βHSD1 and NR3C1 genes were associated with impaired cognitive function in Cushing's Syndrome</p>	(Ragnarsson et al., 2014)
<p>5-HTTLPR (SLC6A4 Solute Carrier Family 6 Member 4) We observed a significant interaction between 5-HTTLPR variants and childhood trauma across cognitive domains; here, homozygotic s-carriers exposed to high levels of childhood trauma (physical neglect and abuse) had significantly poorer cognitive functioning than all other groups.</p> <p>Participants homozygous for the Met allele of the COMT polymorphism showed impaired inhibition of prepotent responses, whereas individuals homozygous for the s-allele of the 5-HTTLPR showed a restricted ability to update information in working memory.</p>	(Aas et al., 2012) (Weiss et al., 2014)
<p>ABCA7 (ATP Binding Cassette Subfamily A Member 7) ABCA7 SNP rs3752232 correlated with Rey Complex Figure Test (RCFT) copy score in Alzheimer's Disease patients</p> <p>Significant associations with cognitive performance were observed for APOE ϵ4 allele, ABCA7-rs3764650, CR1-rs3818361, MS4A4E-rs6109332, BDNF-rs6265, COMT-rs4680, CTNBL-rs6125962, FRMD4A-rs17314229, FRMD4A-rs17314229, intergenic SNP chrX-rs12007229, PDE7A-rs10808746, SORL1-rs668387, and ZNF224-rs3746319</p>	(Chung et al., 2014) (Andrews, Das, Cherbuin, Anstey, & Easteal, 2016)
<p>ACE (Angiotensin I Converting Enzyme) A significant difference in the serum ACE level was observed among the three genotypes(DD>DI>II) in both the aMCI (mild cognitive impairment) and the control groups (all p<0.01)</p> <p>The findings indicated that ACE genotype was associated with episodic memory, serum levels of ACE, and resting-state brain activity in aMCI (mild cognitive impairment) patients, and the findings of cognitive function and brain activity further suggests that the ACE D allele may have a specific role in semantic memory dysfunction and brain activity in aMCI (mild cognitive impairment).</p> <p>The ACE DD genotype carriers had an increased risk of cognitive impairment</p> <p>The cognitive results suggest that Apo E or ACE genotypes may modify the effects of ethanol on cognitive deterioration in alcoholic patients</p>	(Z. Zhang et al., 2012) (Z. Zhang et al., 2010) (Amouyel et al., 1996) (Bartres-Faz, Clemente, et al., 2002)

The ACE-DD genotype may be associated with post-stroke cognitive decline while the APOE-epsilon4 allele is not	(Bour et al., 2010)
Results suggest that ACE D alleles are associated with memory impairment in the elderly.	(Bartres-Faz et al., 2000)
Subjects carrying the Apo E epsilon4 allele exhibit lower memory performance on tests of both declarative and procedural memory.	(Bartres-Faz et al., 1999)
D allele carrier patients performed worse than those with I/I polymorphism on tests involving attention and processing speed.	(Ariza et al., 2006)
The ACE-DD genotype may be associated with post-stroke cognitive decline while the APOE-epsilon4 allele is not	(Bour et al., 2010)
The finding suggests that ACE might be involved in the pathophysiology of cognitive dysfunction in remitted geriatric depression patients	(Hou et al., 2010)
ACT (Actin-Like Protein (ACT) Gene) APOE is a risk gene for amnesic MCI (mild cognitive impairment) and that ACT and CHRNA7 may act in these patients as modifier genes for the time of progression to AD.	(Barabash et al., 2009)
ADD1, ADD2, ADD3 (Adducin 1,2,3) The analysis showed significant effects of ADD2 genotype on almost every cognitive domain. Moreover, significant interactions between ADD1 and ADD3 were also observed on some BACS (brief assessment of cognition in Schizophrenia) subtests, namely Symbol Coding and Verbal Memory	(Bosia et al., 2016)
ADRA2B (Adrenoceptor Alpha 2B) Our data demonstrate for the first time an independent contribution of the ADRA2B genetic polymorphism to memory impairment	(Koutroumani et al., 2013)
AKT1 (AKT Serine/Threonine Kinase 1) DRD2 and AKT1 polymorphisms altered dose-response effects of anti-psychotic drugs on cognition in schizophrenia	(Tan et al., 2012)
AMPK (PRKAA1 Protein Kinase AMP-Activated Catalytic Subunit Alpha 1) These findings collectively support a hypothesis that AMPK has a role not only in metabolic functioning but also in cognitive functioning in humans.	(Kim et al., 2012)
ANK3 (Ankyrin 3) The ANK3 risk allele rs1938526 appears to be associated with general cognitive impairment and widespread cortical thinning in patients with first episode psychosis.	(Cassidy et al., 2014)
Post-hoc analyses showed that patients with rs10994336T/T genotype had significantly lower accuracy rate and more reaction time at 2-back task than those with T/C and C/C genotypes	(C. Zhang et al., 2014)

<p>APBB2 (Amyloid Beta Precursor Protein Binding Family B Member 2) After stratification of centenarians upon their cognitive performance, the APBB2 rs13133980 G allele was over-represented in centenarians with severe cognitive impairment compared to individuals without this disability. Also the hCV1558625-rs13133980 AG haplotype increased relative risk for severe cognitive impairment in centenarians</p>	(Golanska et al., 2013)
<p>APOA1 (Apolipoprotein A1) APOA1 A-allele carriers displayed superior overall cognitive performance compared with non-carriers (P 0.008) and had a three-fold decrease in the relative risk of overall cognitive impairment</p> <p>Our results suggest an impact of the G-->A polymorphism at position -75 bp in the APOA1 gene on cognitive impairment, but not on the risk of Alzheimer's Disease</p>	(Koutsis et al., 2009) (Helbecque, Codron, Cottel, & Amouyel, 2008)
<p>APOC1 (Apolipoprotein C1) We found significant associations both for APOE and APOC1 loci and their combinations with the AAMI (age-associated memory impairment) condition.</p>	(Bartres-Faz et al., 2001)
<p>APOE (Apolipoprotein E) Presence of the epsilon4 allele poses a minor risk for late cognitive impairment after the subacute phase of aneurysmal SAH.</p> <p>Apolipoprotein E ε4 significantly accelerated rates of cognitive decline, and women in all cohorts had higher rates of decline than men</p> <p>The patients exhibited amnesic mild cognitive impairment across multiple domains. Cognitive performance was worse in patients who carried the ApoE ε4 allele.</p> <p>Among the elderly veterans, people who carry APOE ε4 were found to have worse performance on the total Cognitive Ability Screening Instrument scores, the abstraction/judgment subscores and the list-generating fluency subscores</p> <p>APOE SNP rs2075650 correlated with the percentile of Rey Complex Figure Test (RCFT) copy score in Alzheimer's Disease patients</p> <p>Mild Cognitively Impaired individuals with an ε4 allele showed increased cognitive decline across a range of cognitive tasks, putatively reflecting early cognitive signs of Alzheimer's disease.</p> <p>These findings suggest that nondemented APOE ε4 allele carriers with memory complaints may have a greater genetic risk for AD and should be monitored more closely</p>	(Louko, Vilkki, & Niskakangas, 2006) (Holland, Desikan, Dale, McEvoy, & Alzheimer's Disease Neuroimaging, 2013) (Suarez et al., 2014) (C. S. Chu et al., 2014) (Chung et al., 2014) (Albrecht et al., 2015) (X. Wang, Wang, Li, Li, & Yu, 2014)

APOE ϵ 4 carriers and participants with the AA allele of CYP46 have decreased mental manipulation ability	(Lai, Liou, Liu, Yang, & Lin, 2014)
An effect of BDNF genotype was found in APOE E4 carriers for episodic memory (logical memory and ADAS-Cog) and semantic fluency measures, with Met carriers performing worse cognitively in all cases	(Gomar et al., 2016)
MTHFR C677T TT was associated with higher tHcy but did not affect cognitive performance per se. However, when combined with the apolipoprotein E (APOE)- ϵ 4 allele, it was a risk factor for lower executive performance, independently of tHcy levels.	(Polito et al., 2016)
Specific neurodegenerative-related genetic polymorphisms (i.e. APOE and CLU) moderate and magnify the risk contributed by selected personality trait levels (i.e. openness to experience, extraversion) on declarative memory performance in non-demented aging	(Sapkota, Wiebe, Small, & Dixon, 2016)
In MCI (mild cognitive impairment), the risk of cognitive decline, hippocampal volumetric loss and progression to AD seems to be the greatest in individuals who carry at least one copy of both the BCHE-K and APOE epsilon4 alleles.	(Lane et al., 2008)
The APOE ϵ 4 allele related to worsening in executive function, as well as visuospatial function, activation retrieval, and performance on the Mini-Mental State Examination.	(Gomperts et al., 2013)
The study suggests that amnesic cognitive impairment is characterized by memory impairment and associated with SNPs in three systems relating to the pathogenesis of AD—those of the amyloid cascade, tau and cholesterol metabolism pathways	(X. Liu et al., 2012)
Severe WMHs (white matter hyperintensity) appear to be predominantly associated with frontal/executive dysfunction, irrespective of APOE ϵ 4 allele presence. WMH severity and APOE ϵ 4 had an interactive effect on memory function, with WMH severity affecting memory impairment only in APOE ϵ 4 noncarriers.	(Son et al., 2012)
Individuals with at least one APOE- ϵ 2 allele showed less functional decline over time and better performance on neuropsychological measures than those without an ϵ 2 allele, even after controlling for potential confounders	(Bonner-Jackson, Okonkwo, Tremont, & Alzheimer's Disease Neuroimaging, 2012)
Follow up showed higher conversion to Alzheimer's disease in mild cognitive impairment ϵ 4 carriers than in non ϵ 4 carriers.	(Biundo et al., 2011)

We provide further evidence of both independent and interactive influences of APOE ϵ 4+ and A β on cognitive function in mild cognitive impairment, with APOE ϵ 4+ and A β showing dissociable effects on executive and non-executive functions, respectively.	(Seo et al., 2016)
APOE ϵ 4 carriers performed more poorly on all spatial navigation subtasks	(Laczo et al., 2014)
In the mild cognitive impairment group, ϵ 4 carriers had elevated current frontal systems behavior Scale Executive Dysfunction scores in comparison with noncarriers.	(Mikos, Piryatinsky, Tremont, & Malloy, 2013)
APOE- ϵ 4 allele is protective against attention deficit and especially against poor working memory in HCV-infected subjects with mild liver disease. The results indicated the APOE epsilon 4 allele was associated with increased risk for cognitive dysfunction in Non-Hispanic white and white Hispanics after controlling for the effects of age, education, and gender	(Wozniak et al., 2016) (Harwood, Barker, Ownby, Mullan, & Duara, 2002)
Subjects with Apo-E(4) genotype did significantly worse in scores of intentional memory test (sensory memory) when compared with other genotypes.	(Elwan et al., 2003)
Increased risk for global cognitive dysfunction and poorer verbal recall performance were linked with the APOE epsilon4 allele	(Harwood et al., 2002)
Higher urinary albumin to creatinine ratio values were significantly associated with cognitive dysfunction in the general Korean population, with cognition in APOE E4 carriers being more severely affected.	(Shin et al., 2014)
This study provides further support for the medial temporal lobe dysfunction and relative integrity of fronto-striatal systems in mild cognitive impairment, and indicates the influence of ApoE genotype on implicit learning even in healthy older individuals without cognitive impairment.	(Negash et al., 2007)
The PI (A2) -allele of the platelet glycoprotein-IIIa (ITGB-3) gene was present in 13 (42%) and 25 (20%) patients with and without cognitive dysfunction, respectively, $p = 0.012$. The apolipoprotein E- ϵ 4 allele was present in 9 (29%) and 24 (19%) patients with and without cognitive dysfunction, respectively, $p = 0.24$. Both the PI(A2) and apolipoprotein- ϵ 4 alleles were present together in 6 (19%) and 5 (4%) patients with and without cognitive dysfunction, respectively, $p = 0.003$	(A. Stewart et al., 2013)
APOE4 is significantly associated with dementia and cognitive impairment no dementia due to AD pathology, but not with vascular cognitive impairment.	(Chai et al., 2016)

The results show an increase of amyloid accumulation and allele frequency of APOE4 in the mTBI patients with cognitive impairment	(S. T. Yang et al., 2015)
Four variables were found to be independent risk factors for cognitive impairment after stroke: ApoE epsilon4, Informant Questionnaire on Cognitive Decline in the Elderly score > or =3.44, total or partial anterior stroke syndromes, and National Institutes of Health Stroke Scale total score >5	(Wagle et al., 2009)
Only in Middle Europe was the APOE ε4 allele significantly associated with poor performance on tests of delayed recall and learning, as well as with the amnesic subtype of mild cognitive impairment.	(Norberg et al., 2011)
Cognitive impairment was negatively associated with epsilon2 and positively but more weakly associated with epsilon4. Effects of both alleles increased markedly after age 70.	(R. Stewart et al., 2001)
Apo E ε4 positively predicted four cognitive scores measured every 6 months over 30 months.	(Regal, Nair, & Hetherington, 2013)
In older stroke patients with early cognitive impairment, the presence of an APOE epsilon4 allele is associated with greater progression of cognitive decline	(Ballard et al., 2004)
The ApoE epsilon4-allele constitutes an independent risk factor for cognitive impairment at 13 months post-stroke, and is associated with progression of cognitive decline in tasks related to verbal learning and memory.	(Wagle et al., 2010)
A strong association was found between the presence of APOE epsilon 4 and cognitive deficits in patients with Multiple Sclerosis, particularly in the domains of learning and memory.	(J. Shi, Zhao, Vollmer, Tyry, & Kuniyoshi, 2008)
ApoE epsilon4 allele-bearing individuals had greater risk of having late-onset AD or non-vascular cognitive impairment	(Traykov et al., 1999)
APOE is a risk gene for amnesic mild cognitive impairment and ACT and CHRNA7 may act in these patients as modifier genes for the time of progression to Alzheimer's Disease.	(Barabash et al., 2009)
This study suggests that apolipoprotein E genotype is related to cognitive dysfunction after cardiopulmonary bypass	(Tardiff et al., 1997)
There was a strong association between the apolipoprotein E ε4 and postoperative cognitive dysfunction in elderly patients undergoing inhalation anesthetics.	(Cai et al., 2012)

The presence of Met-BDNF allele, particularly in association with APOE*E4, may predict a worse cognitive outcome in patients with mild cognitive impairment.	(Forlenza et al., 2010)
The AA homozygous state of the -491 A/T polymorphism of the APOE regulatory region is associated with cognitive impairment in patients with Multiple Sclerosis	(Oliveri et al., 1999)
While the APOE epsilon4 allele was associated with slightly lower memory test performance for persons without cognitive impairment at baseline, it only increased their risk of developing dementia if their memory was below average.	(Klages & Fisk, 2002)
In The Chinese Han population, APOE ε4 increased the risk of Alzheimer's Disease and mild cognitive impairment in a dose-dependent manner and ε2 decreased the risk of Alzheimer's Disease as reported previously	(K. L. Chen et al., 2016)
This study confirms in a population sample that the epsilon 4 allele is a risk factor for dementia, but refutes the suggestion that homozygosity for the epsilon 4 allele is sufficient for the development of Alzheimer's disease	(Henderson et al., 1995)
Higher cortisol levels, lower high-density lipoprotein (HDL-c) and very low-density lipoprotein (VLDL-c), presence of ε4 allele of APOE, and aging were associated with cognitive impairment and dementia	(Lara et al., 2016)
APOE genotype may influence the cognitive phenotype of Parkinson's Disease, and specifically that absence of the epsilon4 allele is associated with working memory impairment.	(Troster, Fields, Paolo, & Koller, 2006)
The APOE E4 allele was observed to have a dramatic effect on cognitive impairment, especially in homozygotes	(S. R. Quintino-Santos et al., 2012)
While ApoE4(+) status appears to be a sex neutral risk factor for dementia, its association with verbal memory and learning decline and impairment was stronger among women	(Beydoun et al., 2012)
The apoE-ε4 polymorphism is an independent risk factor for cognitive dysfunction as early as 1 day after carotid endarterectomy and at 1 month as well	(Heyer et al., 2014)
(1) Patients with mild cognitive impairment can be clinically defined, (2) many members of this group progress to Alzheimer's disease, and (3) APOE epsilon 4 allele status appears to be a strong predictor of clinical progression	(Petersen et al., 1995)

At least two genetic loci affect the rate of A β -related cognitive decline. A β (+)ε4(+)/BDNF(Met) individuals can expect to show clinically significant memory impairment after 3 years, whereas A β (+)ε4(+)/BDNF(Val/Val) individuals can expect a similar degree of impairment after 10 years.	(Lim et al., 2015)
The epsilon4 group was significantly slower in performing all of the Cognometer memory tasks	(O'Hara et al., 2008)
The results of this study suggest that, among these Puerto Rican non-demented nonagenarians, being an APOE epsilon4 allele carrier is associated with better cognition	(Carrion-Baralt et al., 2009)
The data indicates that the APOE-rs405509 interaction impairs elderly's cognitive performance through brain functional network.	(C. Ma et al., 2016)
APOE-epsilon4 is associated with cognitive decline among a high-functioning elderly cohort, with effects most pronounced after 7 years of follow-up	(Bretsky et al., 2003)
The APOE epsilon4 allele was associated with increased risk for cognitive deficits, whereas the MBL2 O/O genotype was associated with increased risk for progressive cognitive decline in Chinese individuals infected with HIV through contaminated blood products.	(Spector et al., 2010)
Carriage of APOE ε4 in cognitively normal older adults with low A β was associated with a significantly increased rate of decline in learning and unexpectedly, improved cognitive performance on measures of verbal episodic memory over 18 months.	(Thai et al., 2015)
Those who remained cognitively intact had better memory at entry and were less likely to have APOE4 than those who developed cognitive decline.	(Howieson et al., 2003)
The cognitive results suggest that Apo E or ACE genotypes may modify the effects of ethanol on cognitive deterioration in alcoholic patients	(Bartres-Faz, Clemente, et al., 2002)
The negative effect of ApoE4 on episodic memory and hippocampal volume in subjective memory impairment supports this as a prodromal condition of Alzheimer's Disease.	(Stripens et al., 2011)
The main finding is a strong negative association between the presence of APOE ε4 allele and memory dimension in the MMSE	(S. Quintino-Santos et al., 2015)
APOE E4 may have a more robust cognitive influence on female than on male individuals with age associated memory impairment.	(Bartres-Faz, Junque, et al., 2002)

Older professional football players who possessed the APOE epsilon4 allele scored lower on cognitive tests than did players without this allele or less experienced players of any genotype

(Kutner, Erlanger, Tsai, Jordan, & Relkin, 2000)

APOE-epsilon4 predicts longitudinal memory decline in healthy controls and that MRI morphometry of hippocampus adds slightly to predictive value.

(Tupler et al., 2007)

Relatively higher levels of CSF APOE in ϵ 4+ HIV+ (having primarily APOE4 isoforms) may negatively impact the brain and lead to poorer cognitive outcomes, while those individuals without the ϵ 4 allele (with primarily APOE2 or APOE3 isoforms) may show compensatory responses that lead to better cognitive performance.

(Andres et al., 2011)

HIMS replication analysis supported rs439401 (APOE regulatory region), and rs2297660 and rs3737983 (APOER2), with an effect on memory performance in normal aging subjects consistent with the findings in schizophrenia cases.

(Verbrugghe et al., 2012)

The APOE ϵ 4 group exhibited greater activation than the Low Risk group at baseline, but they subsequently showed a progressive decline in activation during the follow-up periods with corresponding emergence of episodic memory loss and hippocampal atrophy

(Rao et al., 2015)

This study and meta-analysis suggest an association between delirium and the APOE sigma4 allele.

(van Munster, Korevaar, Zwinderman, Leeflang, & de Rooij, 2009)

APOE (*3) was associated with overall severe dysfunction on cognitive performance

(Soeira-de-Souza et al., 2010)

Drinking was associated with a decreased risk of cognitive deterioration in non-ApoE epsilon4 carriers, whereas an opposite association was observed in ApoE epsilon4 carriers.

(Dufouil et al., 2000)

In combined Alzheimer's Disease + mild cognitive impairment analyses, epsilon 4 homozygosity was associated with poorer retention, learning, and verbal comprehension at a given disease duration

(Smith et al., 1998)

Data demonstrate that SIGMAR1 and APOE interact to influence Alzheimer's Disease severity across ethnic populations.

(Huang et al., 2011)

Subjects carrying the Apo E epsilon4 allele exhibit lower memory performance on tests of both declarative and procedural memory.

(Bartres-Faz et al., 1999)

Behaviorally, epsilon4+ subjects performed significantly worse than epsilon4- subjects in item memory and spatial context retrieval.	(Kukulja, Thiel, Eggermann, Zerres, & Fink, 2010)
The APOE ε4 allele segregated dose-dependently and selectively with worse episodic memory performance in a pool of older subjects across a cognitive spectrum.	(Kerchner et al., 2014)
Findings support the hypothesis of the beneficial effect of APOε2 and education, both which seem to act as contributing factors in delaying or forestalling the clinical manifestations of Alzheimer's Disease despite consistent levels of pathology	(Iacono et al., 2015)
APOE ε4 homozygotes declined more quickly than non-carriers on mental arithmetic tests related to frontal lobe-mediated working memory ability.	(Caselli et al., 2011)
Single polymorphisms within the saitojin and APOE genes were associated with increased cognitive impairment and functional dependence.	(Schutte, Reed, Decrane, & Ersig, 2011)
APOE4 on episodic memory was modest in women, the risk for impairment was found to occur in about 30%. APOE4 was observed to have a dramatic effect on episodic memory in men, but only in homozygotes.	(Lehmann et al., 2006)
The APOE-ε4 allele is associated with a moderately increased risk for progression from mild cognitive impairment to Alzheimer's Disease-type dementia The results suggest that the APOE epsilon 4 allele influences risk of Alzheimer's Disease by a relatively selective effect on episodic memory.	(Elias-Sonnenschein, Viechtbauer, Ramakers, Verhey, & Visser, 2011) (Wilson et al., 2002)
Persons with one or two epsilon 4 alleles were more likely to have a family history of dementia than those with none	(Henderson et al., 1995)
This work provides evidence for an alteration in cognitive performance as a function of the presence of the ApoE epsilon4 allele, and points to the critical role of disease duration itself for cognitive impairment in temporal lobe epilepsy	(Gambardella et al., 2005)
We found significant associations both for APOE and APOC1 loci and their combinations with age-associated memory impairment.	(Bartres-Faz et al., 2001)
In early stages of Alzheimer's Disease, patients from the epsilon4+ group had greater deficits in delayed recall of new information. On the other hand, working memory appeared to be more impaired in the epsilon4- group of patients	(Luczywek et al., 2002)

Memory declined in APOE ϵ 4 carriers before the symptomatic presentation of mild cognitive impairment in a cohort whose mean age was 60 years over a median period of 33 months	(Caselli et al., 2004)
APOE-epsilon4 was associated with memory decline in subjects with cognitive impairment, but not in normally functioning subjects.	(Dik et al., 2000)
Our data indicate that the APOE ϵ 4 allele is an important predictor of cognitive function in Parkinson's Disease across multiple domains	(Mata et al., 2014)
Our data confirm a specific effect caused by the presence and amount of ApoE epsilon4 allele.	(Nacmias et al., 2004)
E4 carriers had a sixfold increase in the relative risk of impairment in verbal learning vs noncarriers	(Koutsis et al., 2007)
In Alzheimer's Disease and vascular dementia groups epsilon4 present patients showed impairment in selective attention.	(McGuinness, Carson, Barrett, Craig, & Passmore, 2010)
APOE E4 allele frequency was significantly higher in cognitive impairment, no dementia patients versus healthy controls	(Dube et al., 2013)
The data suggests that the PICALM genotype modulates both brain atrophy and cognitive performance in APOE ϵ 4 carriers.	(Morgen et al., 2014)
The findings suggest that patients with brain tumors who are carriers of the APOE ϵ 4 allele may have increased vulnerability to developing memory and executive dysfunction, and that additional SNPs in the APOE gene may be associated with cognitive outcome	(Correa et al., 2014)
Significant associations with cognitive performance were observed for APOE ϵ 4 allele, ABCA7-rs3764650, CR1-rs3818361, MS4A4E-rs6109332, BDNF-rs6265, COMT-rs4680, CTNBL-rs6125962, FRMD4A-rs17314229, FRMD4A-rs17314229, intergenic SNP chrX-rs12007229, PDE7A-rs10808746, SORL1-rs668387, and ZNF224-rs3746319	(Andrews et al., 2016)
In the Western Australian Family Study of Schizophrenia sample, we observed significant association of APOE, APOER2, VLDLR, and DAB1 SNPs with pre-morbid intelligence and verbal memory in cases. Health in Men Study replication analysis supported rs439401 (APOE regulatory region), and rs2297660 and rs3737983 (APOER2), with an effect on memory performance in normal aging subjects consistent with the findings in schizophrenia cases	(Verbrugge et al., 2012)

<p>Across mild cognitive impairment and Alzheimer's Disease patients, carriers of the apolipoprotein E ϵ4 allele displayed a leftward spatial bias, which was the more pronounced in younger age and in earlier disease onset</p>	(Redel et al., 2012)
<p>Results are showing the association of apathy and APOE4 with reduced serum BDNF levels in Alzheimer's Disease, and are suggesting that BDNF reductions might contribute to the worse cognitive performance exhibited by Alzheimer's Disease apathetic patients and female APOE4 carriers.</p>	(Alvarez, Aleixandre, Linares, Masliah, & Moessler, 2014)
<p>Older age, a lower Mini-Mental State Examination recall score, APOE4 carrier, and a lower verbal delayed recall score were the most relevant predictors of progression in memory impairment</p>	(Hong et al., 2015)
<p>During low-working memory-load tasks, the APOE4 carriers recruited significantly greater additional processing resources than the non-APOE4 carriers. During moderate- and high-working memory-load tasks, the APOE4 carrier group displayed fewer increases in activation than the non-APOE4 carrier group, suggest possible subclinical impairment of WM capacity in APOE4 carriers</p>	(C. J. Chen et al., 2013)
<p>APOER2 (LRP8 LDL Receptor Related Protein 8) In the Western Australian Family Study of Schizophrenia sample, we observed significant association of APOE, APOER2, VLDLR, and DAB1 SNPs with disease outcome</p>	(Verbrugge et al., 2012)
<p>AR (Androgen Receptor) Greater CAG repeat length was associated with lower scores on three cognitive tests</p>	(Yaffe et al., 2003)
<p>BCHE-K (Butyrylcholinesterase) K variant: In mild cognitive impairment, the risk of cognitive decline, hippocampal volumetric loss and progression to Alzheimer's Disease seems to be the greatest in individuals who carry at least one copy of both the BCHE-K and APOE epsilon4 alleles.</p>	(Lane et al., 2008)
<p>Sex and BuChE genotype seem to differentially influence the type of decline in mild cognitive impairment patients, with more rapid progression of cognitive decline in male BuChE-K, and more incident AD and functional decline in female BuChE wt/wt</p>	(Ferris, Nordberg, Soininen, Darreh-Shori, & Lane, 2009)
<p>BDNF (brain-derived neurotrophic factor) At least two genetic loci affect the rate of Aβ-related cognitive decline. Aβ(+)ϵ4(+)/BDNF(Met) individuals can expect to show clinically significant memory impairment after 3 years, whereas Aβ(+)ϵ4(+)/BDNF(Val/Val) individuals can expect a similar degree of impairment after 10 years</p>	(Chung et al., 2014)

Participants with the Met allele performed significantly more poorly than participants with the Val allele, and a group by allele interaction was observed, the BDNF Met allele being associated with a poorer executive factor score in the healthy adult children of alcoholics group.	(Benzerouk et al., 2013)
An effect of BDNF genotype was found in APOE E4 carriers for episodic memory (logical memory and ADAS-Cog) and semantic fluency measures, with Met carriers performing worse in all cases	(Gomar et al., 2016)
Significant associations with cognitive performance were observed for APOE ϵ 4 allele, ABCA7-rs3764650, CR1-rs3818361, MS4A4E-rs6109332, BDNF-rs6265, COMT-rs4680, CTNBL-rs6125962, FRMD4A-rs17314229, FRMD4A-rs17314229, intergenic SNP chrX-rs12007229, PDE7A-rs10808746, SORL1-rs668387, and ZNF224-rs3746319	(Andrews et al., 2016)
In individuals with amnesic mild cognitive impairment and high A β , Met carriers showed significant and large decline in episodic memory	(Lim et al., 2014)
Among patients with only a mild stage of Alzheimer's Disease, the Frontal Assessment Battery total and go/no-go scores were significantly lower ($p < 0.05$) among the subjects with the Val/Val genotype than among the Met carriers	(Nagata, Shinagawa, Nukariya, Yamada, & Nakayama, 2012)
Of the known BDNF polymorphisms, the C270T SNP may influence executive dysfunction as a non-memory cognitive impairment in Japanese patients with Alzheimer's Disease	(Nagata, Shinagawa, Nukariya, Ochiai, et al., 2011)
Found a positive association between the BDNF(Met) variant and poor medial temporal lobe-related memory performance	(B. C. Ho et al., 2006)
The presence of Met-BDNF allele, particularly in association with APOE*E4, may predict a worse cognitive outcome in patients with mild cognitive impairment.	(Forlenza et al., 2010)
The BDNF(AA) homozygote genotype is over-represented in Parkinson's Disease patients compared with normal individuals; this genotype was significantly correlated to cognitive impairment, age and disease severity	(Guerini et al., 2009)
At least two genetic loci affect the rate of A β -related cognitive decline. A β (+) ϵ 4(+)/BDNF(Met) individuals can expect to show clinically significant memory impairment after 3 years, whereas A β (+) ϵ 4(+)/BDNF(Val/Val) individuals can expect a similar degree of impairment after 10 years. The BDNF Met66 allele was associated with better cognitive functioning in the psychomotor and motor domains	(Lim et al., 2015)
	(Oroszi et al., 2006)

<p>We found a statistically significant association between genotypic variation and memory function at both baseline (NRSF: rs1105434, rs2227902 and BDNF: rs1491850, rs2030324, rs11030094) and in our longitudinal analysis (NRSF: rs2227902 and BDNF: rs12273363).</p>	(Warburton et al., 2016)
<p>The mean age of Parkinson's Disease onset among BDNF Met/Met carriers was later (65.00±6.13) in comparison to Val/Val (57.45±10.68) and Val/Met (56.33±10.91) subjects and patients with Met/Met alleles demonstrated better delayed recall of information than patients with Val/Val alleles.</p>	(Gill et al., 2016)
<p>Carriers of at least one BDNF 66Met allele presented a higher prevalence of cognitive impairment</p>	(Altmann et al., 2016)
<p>Carriers of the BDNF Met allele are protected against chemotherapy-associated cognitive impairment.</p>	(Ng et al., 2016)
<p>The association between decreased BDNF serum levels and cognitive impairment in schizophrenia is dependent on the BDNF Val66Met polymorphism</p>	(X. Y. Zhang et al., 2012)
<p>We demonstrated significant impairment on some aspects of cognitive function and increased BDNF levels in methamphetamine-dependent patients as well as genotypic differences in the relationships between BDNF levels and Repeatable battery for Assessment of Neuropsychological status scores on the BDNF Val66Met polymorphism only in these patients</p>	(Su et al., 2015)
<p>In healthy adults with high Aβ, Met carriers showed significant and moderate-to-large declines in episodic memory, executive function, and language, and greater hippocampal atrophy over 36 months, compared with Val/Val homozygotes</p>	(Lim et al., 2013)
<p>At least two genetic loci affect the rate of Aβ-related cognitive decline. Aβ(+)ε4(+)/BDNF(Met) individuals can expect to show clinically significant memory impairment after 3 years, whereas Aβ(+)ε4(+)/BDNF(Val/Val) individuals can expect a similar degree of impairment after 10 years</p>	(Lim et al., 2015)
<p>Our results further implicate variation in putative regulatory regions in the DYX2 locus, particularly in DCDC2, influencing language and cognitive traits</p>	(Eicher et al., 2015)
<p>C2ORF3 (GCFC2 GC-Rich Sequence DNA-Binding Factor 2) These findings suggest that this locus, originally identified as being associated with dyslexia, is likely to harbor genetic variants associated with general cognitive abilities by influencing white matter structure in localized neuronal regions.</p>	(Scerri et al., 2012)
<p>CACNA1C (Calcium Voltage-Gated Channel Subunit Alpha1 C) In patients with Bipolar Disorder, the CACNA1C genotype Met/Met was associated with worse performance on all four executive function tests compared to Val/Val.</p>	(Soeiro-de-Souza et al., 2013)

<p>CAMK2A (Calcium/Calmodulin Dependent Protein Kinase II Alpha) A significant association between the genotypes RELN (rs528528 and rs2299356), PLK2 (rs15009 and rs702723), and CAMK2A (rs3756577 and rs3822606) and Alzheimer's Disease or mild cognitive impairment was found</p>	(Bufill et al., 2015)
<p>CAMTA1 (Calmodulin Binding Transcription Activator 1) Results indicate that CAMTA1 genotype is associated with cognitive function in older adults with cardiovascular disease, because carriers of the T allele performed more poorly on tests of attention, executive function, and psychomotor speed</p>	(Miller et al., 2011)
<p>CASP1 (Caspase 1) CASP1 is a modifier gene for the time of progression from mild cognitive impairment to Alzheimer's Disease, in that it might identify patients with mild cognitive impairment who are more likely to rapidly convert to Alzheimer's Disease during a short follow-up period</p>	(Pozueta et al., 2011)
<p>CASP7 (Caspase 7) Among these genes, APOE and APOC1 are known AD risk genes. For the other five genes TNFRSF1A, CDH1, CASP7, LRP1B and TG, this is the first genetic association study which showed the significant association between these five genes and Alzheimer's Disease susceptibility in Caribbean Hispanic individuals.</p>	(Shang et al., 2015)
<p>CBP (CREBBP CREB Binding Protein) The intron 4CT and intron 3AC polymorphisms in the CBP gene were associated with better cognitive performance at baseline and during follow-up. Genetic variation in the CBP gene is associated with better cognitive performance in an elderly population.</p>	(Trompet et al., 2011)
<p>CD33 (CD33 Molecule) CR1, TOMM40, BIN1, and CD33 contribute to late-onset Alzheimer's Disease susceptibility and cognitive impairment, in addition to apolipoprotein E.</p>	(Omoumi et al., 2014)
<p>CDH1 (Cadherin 1) Among these genes, APOE and APOC1 are known AD risk genes. For the other five genes TNFRSF1A, CDH1, CASP7, LRP1B and TG, this is the first genetic association study which showed the significant association between these five genes and Alzheimer's Disease susceptibility in Caribbean Hispanic individuals.</p>	(Shang et al., 2015)
<p>CETP (Cholesteryl Ester Transfer Protein) Subjects with MMSE (Mini Mental status exam) > 25 were twice as likely to have the CETP VV Genotype, and those with the VV genotype were more likely to have MMSE > 25. Subjects with the VV genotype had lower levels of CETP, higher high-density lipoprotein (HDL) levels, and larger lipoprotein particles</p>	(Barzilai, Atzmon, Derby, Bauman, & Lipton, 2006)
<p>CHAT (Choline O-Acetyltransferase) Results demonstrated that sequence variants of CHAT were associated with human cognitive ability in not only patients with psychiatric disorders but also normal healthy individuals</p> <p>ChAT 2384 A allele is a risk factor for Alzheimer's Disease and mild cognitive impairment</p>	(X. Liu et al., 2016) (Tang et al., 2008)

<p>CHRFAM7A(CHRNA7 (Exons 5-10) And FAM7A (Exons A-E) Fusion) Meta-analysis of CHRFAM7A indicated a significant association of the gene with Alzheimer's Disease and/or mild cognitive impairment</p>	(Swaminathan et al., 2012)
<p>CHRNA7 (Cholinergic Receptor Nicotinic Alpha 7 Subunit) APOE is a risk gene for amnesic mild cognitive impairment and that ACT and CHRNA7 may act in these patients as modifier genes for the time of progression to Alzheimer's Disease.</p>	(Barabash et al., 2009)
<p>CLU (Clusterin) The Alzheimer's Disease risk variant CLU influences longitudinal changes in brain function in asymptomatic individuals and is associated with faster cognitive decline in presymptomatic stages of disease progression</p> <p>Specific neurodegenerative-related genetic polymorphisms (i.e. APOE and CLU) moderate and magnify the risk contributed by selected personality trait levels (i.e. openness to experience, extraversion) on declarative memory performance in non-demented aging</p>	(Thambisetty et al., 2013) (Sapkota et al., 2016)
<p>CNP (2',3'-Cyclic Nucleotide 3' Phosphodiesterase) Combined genetics and neuroimaging data showed that variants from the MAG, OLIG2, and CNP genes influenced white matter tract integrity and cognitive performance</p>	(Voineskos et al., 2013)
<p>CNR1 (Cannabinoid Receptor 1) Our findings suggest that heavy cannabis use in the context of specific CNR1 genotypes may contribute to greater white matter volume deficits and cognitive impairment</p>	(B. C. Ho, Wassink, Ziebell, & Andreasen, 2011)
<p>CNTNAP2 (Contactin Associated Protein-Like 2) A new male-specific association with cognitive impairment in aging is reported for a CNV in the CNTNAP2 gene</p>	(Iakoubov, Mossakowska, Szwed, & Puzianowska-Kuznicka, 2015)
<p>COMT (Catechol-O-Methyltransferase) Patients undergoing mania and mixed episodes carrying the COMT allele G had better performance on executive function, memory, verbal fluency, and intelligence tests. Moreover, an interaction was detected between the COMT allele G and the Young Mania Rating Scale in Bipolar disorder and cognitive dysfunction</p> <p>Analyses of covariance revealed that Met-hemizygous patients performed significantly better on a composite measure of executive function (comprising set-shifting, verbal fluency, attention, and working memory) than did Val-hemizygous patients.</p> <p>Among COMT-Val/Val participants, MTHFR-C/C made more spatial working memory errors ($p=0.033$) and solved fewer attentional flexibility and planning problems ($p=0.025$) than MTHFR-T carriers. In patients, there was a significant COMT×MTHFR interaction on full scale IQ ($p=0.035$): among COMT-Met carriers, MTHFR-T carriers performed significantly worse than MTHFR-C/C ($p=0.021$), which was driven by a COMT×MTHFR interaction involving performance IQ ($p=0.047$).</p>	(Soeiro-de-Souza, Machado-Vieira, Soares Bio, Do Prado, & Moreno, 2012) (Bearden et al., 2004) (Kontis et al., 2013)

<p>We found significant associations between COMT and variability in the Signal Detection Theory indices d' and $\ln\beta$ across blocks, as well as a statistical trend for association between COMT and commission errors. Higher externalizing psychopathology was associated with general impairment on AX-CPT performance, and for some indices (i.e., d' variability and $\ln\beta$ variability) the effect of COMT was stronger at higher levels of psychopathology.</p>	<p>(Park & Waldman, 2014)</p>
<p>The Val/Val COMT group was also associated with significantly more gambling disorder diagnostic criteria being met, greater frequency of gambling behavior, and significantly worse cognitive performance on the Cambridge Gamble Task (risk adjustment and delay aversion) and the Spatial Working Memory task (total errors).</p>	<p>(Grant, Leppink, Redden, Odlaug, & Chamberlain, 2015)</p>
<p>COMT genotype modulates cognitive functioning in Parkinson's Disease</p>	<p>(Fallon et al., 2015)</p>
<p>Significant associations with cognitive performance were observed for APOE ϵ4 allele, ABCA7-rs3764650, CR1-rs3818361, MS4A4E-rs6109332, BDNF-rs6265, COMT-rs4680, CTNBL-rs6125962, FRMD4A-rs17314229, FRMD4A-rs17314229, intergenic SNP chrX-rs12007229, PDE7A-rs10808746, SORL1-rs668387, and ZNF224-rs3746319</p>	<p>(Andrews et al., 2016)</p>
<p>Infections with HSV-1 and the COMT Val158Val genotype are risk factors for cognitive deficits in non-elderly persons without a psychiatric disorder.</p>	<p>(F. Dickerson et al., 2008)</p>
<p>Genotype had a critical impact on task strategy: whilst patients with high activity COMT genotypes (val/val) adopted a typical approach of preferentially shifting attention within rather than between dimensions, those with low activity genotypes (met/met) failed to adopt such a strategy, suggesting an inability to form an attentional 'set'. Moreover, this behavior was associated with significant underactivation across the frontoparietal attentional network.</p>	<p>(Williams-Gray, Hampshire, Barker, & Owen, 2008)</p>
<p>COMT Val(158)Met polymorphism influences executive functions in schizophrenia and the neuromotor performance in the deficit subtype only. Both the COMT Val158Met polymorphism and serological evidence of HSV-1 infection affect cognitive functioning in individuals with bipolar disorder.</p>	<p>(Galderisi et al., 2005) (F. B. Dickerson et al., 2006)</p>
<p>Data showed significantly impaired performance in several neuro-cognitive tests in carriers of Met/Met genotype in patients with dementia compared to either Met/Val or Val/Val genotype carriers</p>	<p>(Nedic et al., 2011)</p>
<p>Participants homozygous for the Met allele of the COMT polymorphism showed impaired inhibition of prepotent responses, whereas individuals homozygous for the s-allele of the 5-HTTLPR showed a restricted ability to update information in working memory.</p>	<p>(Weiss et al., 2014)</p>

COMT genotype impacts on executive function in Parkinson's Disease through directly influencing frontoparietal activation	(Williams-Gray, Hampshire, Robbins, Owen, & Barker, 2007)
For Parkinson's Disease patients, the met homozygous group performed differently on tests of executive function compared with the val homozygous group	(Leroi et al., 2013)
COMT genetic variation at SNP rs165599 is associated with BPD (bipolar disorder 1) I and influences prefrontal aspects of verbal memory in bipolar patients and healthy controls	(Burdick et al., 2007)
We found a Met advantage for tasks requiring cognitive stability in both schizophrenia patients and healthy controls	(Rosa, Dickinson, Apud, Weinberger, & Elvevag, 2010)
Our data support a potentially critical role of the Met allele of the Catechol-O-methyltransferase (COMT) Val158Met polymorphism in externally paced sequential recall	(Hill et al., 2013)
Significant effects of the COMTp.Val158Met polymorphism were identified for attention and cognitive flexibility in the younger but not the older cohort	(Degen et al., 2016)
Cortical synaptic dopamine monitored by the COMT Val158Met polymorphism influenced prefrontal control of both parietal processing in working memory maintenance and striatal processing in working memory manipulation.	(Tan et al., 2012)
COX2 (Prostaglandin-Endoperoxide Synthase 2) Cognitive impairment in Mexican patients with diabetes is associated with less exposure to the CG genotype of the c.1-765G>C polymorphism of COX2	(Diaz De Leon Gonzalez et al., 2014)
CPLX2 (Complexin 2) Six single-nucleotide polymorphisms, distributed over the whole CPLX2 gene, were found to be highly associated with current cognition of schizophrenic subjects but only marginally with premorbid intelligence	(Begemann et al., 2010)
CR1 (Complement C3b/C4b Receptor 1 (Knops Blood Group)) CR1 SNP rs11803956 correlated with Mini-Mental State Examination (MMSE) score in Alzheimer's Disease patients	(Chung et al., 2014)
Significant associations with cognitive performance were observed for APOE ε4 allele, ABCA7-rs3764650, CR1-rs3818361, MS4A4E-rs6109332, BDNF-rs6265, COMT-rs4680, CTNBL-rs6125962, FRMD4A-rs17314229, FRMD4A-rs17314229, intergenic SNP chrX-rs12007229, PDE7A-rs10808746, SORL1-rs668387, and ZNF224-rs3746319	(Andrews et al., 2016)
CR1, TOMM40, BIN1, and CD33 contribute to late-onset Alzheimer's Disease susceptibility and cognitive impairment, in addition to apolipoprotein E.	(Omoumi et al., 2014)

<p>CREB1 (CAMP Responsive Element Binding Protein 1) There was an effect of CREB1 polymorphism on selective attention and retrieval of long-term memory, but not on immediate memory for Chinese patients with major depression.</p>	(Guo et al., 2014)
<p>CRHR1 (Corticotropin Releasing Hormone Receptor 1) Our data indicate that GG-homozygotes of CRHR1 rs110402 and rs242924 represent a genetically driven subtype of early working memory impairments due to alterations in hippocampal CRHR1 activation</p>	(Grimm et al., 2015)
<p>CRP (C-reactive Protein) Elevated serum levels of C-reactive protein in schizophrenia are associated with the severity of cognitive impairment but not of psychiatric symptoms</p>	(F. Dickerson, Stallings, Origoni, Boronow, & Yolken, 2007)
<p>CTNBL (catenin beta 1) Significant associations with cognitive performance were observed for APOE ϵ4 allele, ABCA7-rs3764650, CR1-rs3818361, MS4A4E-rs6109332, BDNF-rs6265, COMT-rs4680, CTNBL-rs6125962, FRMD4A-rs17314229, FRMD4A-rs17314229, intergenic SNP chrX-rs12007229, PDE7A-rs10808746, SORL1-rs668387, and ZNF224-rs3746319</p>	(Andrews et al., 2016)
<p>CYP46 (Cytochrome P450 Family 46 Subfamily A Member 1) Apoϵ4 carriers and participants with the AA allele of CYP46 have decreased mental manipulation ability</p>	(Lai et al., 2014)
<p>CYP46A1 gene may act to modulate the course of cognitive deterioration in late life</p>	(B. Y. Fu et al., 2009)
<p>CYTB (MT-CYB Mitochondrially Encoded Cytochrome B) The m.15244A>G, p.G166G, CytB variant was associated with a significant decline in Digit Symbol Substitution Test score for elderly adults</p>	(Tranah et al., 2012)
<p>DAOA (D-Amino Acid Oxidase Activator) The DAOA haplotype GAGGCT was associated with worse scores in Trail making test B in schizophrenic patients only</p>	(Soler et al., 2016)
<p>DARS2 (Aspartyl-TRNA Synthetase 2, Mitochondrial) Cognitive impairment seems to be common among patients with LBSL and DARS2 mutations. The cognitive profile in LBSL shares similarities with that reported in multiple sclerosis</p>	(Martikainen, Ellfolk, & Majamaa, 2013)
<p>DAT1 (SLC6A3 Solute Carrier Family 6 Member 3) The minor allele was more common in Alzheimer's Disease patients than in both individuals with mild cognitive impairment and healthy elderly controls</p>	(Roussotte et al., 2015)
<p>Results suggest that DAT1 is a QTL for cognitive endophenotype of response inhibition.</p>	(Cornish et al., 2005)
<p>Findings confirm a significant effect of the SLC6A3 genotype on the neurophysiological correlates of cognitive response control in ADHD</p>	(Dresler et al., 2010)

<p>DBH (Dopamine Beta-Hydroxylase) The 19bp insertion/deletion polymorphism of the DBH gene influences cognition in elderly women and might have a stronger effect than APOE epsilon4 allele status on mild cognitive impairment</p>	(Togsverd et al., 2007)
<p>DCDC2 (Doublecortin Domain Containing 2) BV677278 interacts nonadditively with KIAA0319, an Dyslexia-associated gene, to adversely affect several reading and cognitive phenotypes</p> <p>Our results further implicate variation in putative regulatory regions in the DYX2 locus, particularly in DCDC2, influencing language and cognitive traits</p>	(Powers et al., 2013) (Eicher et al., 2015)
<p>DISC1 (Disrupted In Schizophrenia 1) Patients carrying the A allele of rs1000731 exhibited a significant improvement in Working Memory and Attention domains, and the homozygosity of the A allele of rs821616 showed a significant improvement in Motor Dexterity performance over 3 years of follow-up post psychosis</p> <p>ZNF804A, DISC1 and KIAA0319 were associated with language and speech, verbal learning and recall processes, and processing speed in schizophrenic patients</p>	(Vazquez-Bourgon et al., 2015) (Nicodemus et al., 2014)
<p>DNM2 (Dynamain 2) We found a significant association of late-onset Alzheimer's Disease with single nucleotide polymorphism markers of the DNM2 gene, especially in non-carriers of the apolipoprotein E-epsilon4 allele</p>	(Aidaraliev et al., 2008)
<p>DP (dystrophin isoform 140) Comparison of molecular and psychometric findings demonstrated that deletions and duplications that were localized in the distal part of the gene seemed to be preferentially associated with cognitive impairment in Duchenne's muscular dystrophy</p> <p>Impairment of cognitive abilities in Duchenne muscular dystrophy and Becker muscular dystrophy patients might be related to a dysfunction of Dp140 brain isoform.</p>	(Moizard et al., 1998) (Bardoni et al., 2000)
<p>DRB1 (HLA-DRB1 Major Histocompatibility Complex, Class II, DR Beta 1) We observed that both DRB1*0801 and DRB1*1101 were significantly associated with vocabulary ability (cross-sectional and longitudinal scores) and that the effects were in opposite directions with DRB1*0801 associated with lower score and faster cognitive decline</p>	(Payton et al., 2016)
<p>DRD2 (Dopamine Receptor D2) The DRD2 and AKT1 polymorphisms altered dose-response effects of anti-psychotic drugs on cognition in schizophrenia</p> <p>The study shows that variants (rs6277 DRD2 gene and DRD4 48 bp VNTR) may be risk factors for deficits in executive function and cognitive flexibility.</p>	(Tan et al., 2012) (Villalba, Devieux, Rosenberg, & Cadet, 2015)

<p>DRD4 (Dopamine Receptor D4) The study shows that variants (rs6277 DRD2 gene and DRD4 48 bp VNTR) may be risk factors for deficits in executive function and cognitive flexibility.</p>	(Villalba et al., 2015)
<p>DTNBP1 (Dystrobrevin Binding Protein 1) The present study supports the involvement of DTNBP1 in the regulation of cognitive processes and demonstrates association in particular with sustained attention and set-shifting in schizophrenia patients.</p> <p>We report an association between DTNBP1 genotype and general cognitive ability</p>	(Bakanidze et al., 2016) (Burdick et al., 2006)
<p>DYX2 (Dyslexia Susceptibility 2 KIAA0319) Our results further implicate variation in putative regulatory regions in the DYX2 locus, particularly in DCDC2, influencing language and cognitive traits</p> <p>ZNF804A, DISC1 and KIAA0319 were associated with language and speech, verbal learning and recall processes, and processing speed in schizophrenic patients</p> <p>Analyses of covariance revealed that individuals with the TT genotype of the rs12193738 polymorphism exposed to high maternal stress during pregnancy possessed significantly poorer reading ability during adolescence compared with TT carriers exposed to low maternal stress. TT carriers of the rs12193738 SNP also obtained lower IQ scores at age 7 than C allele carriers</p>	(Eicher et al., 2015) (Nicodemus et al., 2014) (D'Souza et al., 2016)
<p>EAAT (SLC1A3 Solute Carrier Family 1 Member 3 and SLC1A2 member 2) ANOVA showed a significant difference among both EAAT1 and EAAT2 genotype groups on different cognitive measures. Worse performances were observed among carriers of the genotypes associated with lower EAAT expression</p>	(Spangaro et al., 2014)
<p>ESR1 (estrogen receptor 1) We found that among non-demented community elders, several SNPs in the ESR1 and ESR2 genes were associated with risk of developing cognitive impairment</p> <p>Estrogen receptor 1 polymorphisms are associated with risk of developing cognitive impairment in older women</p>	(Yaffe et al., 2009) (Yaffe, Lui, Grady, Stone, & Morin, 2002)
<p>ESR2 (estrogen receptor 2) Our large multicenter prospective study provides preliminary evidence that ESR2 genetic variants may be associated with specific cognitive domains and suggests that further examination of the role of this gene in cognitive function is warranted.</p> <p>We found that among non-demented community elders, several SNPs in the ESR1 and ESR2 genes were associated with risk of developing cognitive impairment</p>	(Ryan et al., 2013) (Yaffe et al., 2009)

<p>FASTKD2 (FAST Kinase Domains 2) Using a genome-wide screen, we discovered a novel association of a polymorphism in the pro-apoptotic gene FASTKD2 (fas-activated serine/threonine kinase domains 2; rs7594645-G) and in the MTOR pathway with better memory performance and replicated this finding in independent samples.</p>	(Ramanan, Nho, et al., 2015)
<p>FMR1 (Fragile X Mental Retardation 1) Male carriers of midsize to large premutation alleles had a sixfold increased risk of developing cognitive decline and the risk increases with allele size. In addition, it was observed that cognitive impairment may precede motor symptoms.</p> <p>FXTAS (fragile X-associated tremor/ataxia syndrome) involves impairment of general intellectual functioning, with marked impairment of executive cognitive abilities.</p> <p>Our findings indicate a specific vulnerability in premutation males on tasks that require simultaneous manipulation and storage of new information</p>	(Sevin et al., 2009) (Grigsby et al., 2007) (Cornish et al., 2009)
<p>FRMD4A (FERM Domain Containing 4A) Significant associations with cognitive performance were observed for APOE ε4 allele, ABCA7-rs3764650, CR1-rs3818361, MS4A4E-rs6109332, BDNF-rs6265, COMT-rs4680, CTNBL-rs6125962, FRMD4A-rs17314229, FRMD4A-rs17314229, intergenic SNP chrX-rs12007229, PDE7A-rs10808746, SORL1-rs668387, and ZNF224-rs3746319</p>	(Andrews et al., 2016)
<p>FTO (FTO, Alpha-Ketoglutarate Dependent Dioxygenase) These findings suggest that the FTO risk allele is associated with reduced memory performance, particularly on aspects of memory encoding and delayed recall.</p> <p>Obese and overweight but not normal weight FTO A allele carriers showed a lower performance on verbal fluency than non-carriers</p>	(Alosco et al., 2013) (Benedict et al., 2011)
<p>GABRR2 (Gamma-Aminobutyric Acid Type A Receptor Rho2 Subunit) Results showed a significant influence of GABRR2 gene polymorphism on individuals' Raven's Standard Progressive Matrices</p>	(Z. Ma et al., 2017)
<p>GBA (Glucosylceramidase Beta) Both GBA mutations and E326K are associated with a distinct cognitive profile characterized by greater impairment in working memory/executive function and visuospatial abilities in Parkinson's Disease patients</p> <p>GBA mutation carriers performed more poorly than noncarriers on the Mini-Mental State Examination, and on the memory and visuospatial domains. The most prominent differences were observed in nonverbal memory performance.</p>	(Mata et al., 2016) (Alcalay et al., 2012)

<p>The results showed that GBA mutation carriers were more likely to receive a diagnosis of mild cognitive impairment or dementia and performed worse than noncarrier patients on the Mini-Mental State Examination and on tasks assessing visual memory and visuospatial abilities</p>	(Daniele & Albanese, 2012)
<p>The N370S GBA mutation is the risk factor for cognitive impairment in Parkinson's Disease patients</p>	(Malec-Litwinowicz et al., 2014)
<p>GHRL (Ghrelin And Obestatin Prepropeptide) Glucose impairment and L90G Ghrelin gene variant influence cognitive function in old dwelling individuals participating in the Mataró Ageing Study</p>	(Mora et al., 2014)
<p>GIGYF2 (GRB10 Interacting GYF Protein 2) A novel genetic variant (p.Arg610Gly) in the GIGYF2 gene, previously known to be associated with Parkinson's Disease, was identified as potential disease-causing mutation with cognitive impairment.</p>	(Ruiz-Martinez et al., 2015)
<p>GRN (Granulin Precursor) Measurable cognitive differences exist before the development of frontotemporal dementia in subjects with GRN mutations.</p>	(Hallam et al., 2014)
<p>GSTM1 (Glutathione S-Transferase Mu 1) GSTM1 and GSTT1 polymorphisms may predict adverse events, including cognitive impairment after therapy, in patients with medulloblastoma</p>	(Barahmani et al., 2009)
<p>GSTT1 (Glutathione S-Transferase Theta 1) GSTM1 and GSTT1 polymorphisms may predict adverse events, including cognitive impairment after therapy, in patients with medulloblastoma</p>	(Barahmani et al., 2009)
<p>GTF2IRD2 (GTF2I Repeat Domain Containing 2) Cognitive, behavioral and psychological functioning in Williams-Beuren syndrome patients showed that those with slightly larger deletions encompassing GTF2IRD2 were significantly more cognitively impaired in the areas of spatial functioning, social reasoning, and cognitive flexibility</p>	(Porter et al., 2012)
<p>H2AFZ (H2A Histone Family Member Z) Our findings suggest that the H2AFZ gene may confer a risk for schizophrenia and contribute to the impairment of executive function in Han Chinese patients with schizophrenia</p>	(Chang, Sun, Liu, Sun, & You, 2015)
<p>HD (HTT Huntingtin) Participants with CAG expansions showed significant worsening in motor, cognitive, and functional measures compared with those without expansion</p> <p>We found distinct group differences in frequency of impairment on measures of Executive functions and psychomotor speed in manifest and premanifest Huntington's Disease gene-expansion carriers</p>	(Huntington Study Group et al., 2016) (Unmack Larsen, Vinther-Jensen, Gade, Nielsen, & Vogel, 2015)

Cognitive decline appears to start before clinical onset of Huntington disease and is correlated with the number of trinucleotide repeats	(Jason et al., 1997)
A broad neuropsychological assessment battery was administered to 24 asymptomatic gene carriers (HD+) and 31 noncarriers (HD-). The gene carriers revealed inferior cognitive functioning as compared with the noncarriers in memory and executive functions.	(Robins Wahlin, Lundin, & Dear, 2007)
HLA-DQA1 (Major Histocompatibility Complex, Class II, DQ Alpha 1) The most strongly associated single nucleotide polymorphism (SNP) in the CAM pathway (rs9272105 within HLA-DQA1) explained 1-3% of the variance in attentional control	(Hargreaves et al., 2014)
HSPA8 (Heat Shock Protein Family A (Hsp70) Member 8) One SNP (rs1136141) in HSPA8 met these criteria, yielding a significant allelic frequency difference between cases with mental impairment and normal controls for individual genotyping and a significant correlation within the control group	(Butcher et al., 2005)
IL6 (interleukin 6) GG genotype was more frequent among global cognitive score non-decliners while carriers of at least one C allele were more frequent in the group with global cognitive score decliners	(Fraga et al., 2015)
Our results suggest that elevated IL-6 levels may play the role in cognitive impairment and serve as potential inflammatory biomarker of deterioration in schizophrenia	(Frydecka et al., 2015)
IL10 (interleukin 10) Logistic regression analysis showed that the IL-10 1082G/A (AA) genotype decreased (Odds ratio=0.440, p=0.042), while the IL-117A rs8193036 (CC) genotype increased the risk of cognitive impairment in Parkinson's disease (OR=1.838, p=0.048).	(Nie et al., 2013)
IL-17A (interleukin 17A) Logistic regression analysis showed that the IL-10 1082G/A (AA) genotype decreased (Odds ratio=0.440, p=0.042), while the IL-117A rs8193036 (CC) genotype increased the risk of cognitive impairment in Parkinson's disease (OR=1.838, p=0.048).	(Nie et al., 2013)
IL1RAP (Interleukin 1 Receptor Accessory Protein) IL1RAP rs12053868-G carriers were more likely to progress from mild cognitive impairment to Alzheimer's disease and exhibited greater longitudinal temporal cortex atrophy on MRI	(Ramanan, Risacher, et al., 2015)
INOS (NOS2 nitric oxide synthase 2) iNOS promoter polymorphism variant provides protection against moderate/severe cognitive dysfunction 1 month after carotid endarterectomy	(Yocum et al., 2009)
IRS1 (Insulin Receptor Substrate 1) The Arg972 IRS1 polymorphism is an independent risk factor for Alzheimer's Disease and the A allele has a gene dosage effect on severity in Han Chinese	(W. Wang et al., 2014)

<p>ITGB3 (integrin subunit beta 3) The PI(A2) -allele of the platelet glycoprotein-IIIa (ITGB-3) gene was present in 13 (42%) and 25 (20%) patients with and without cognitive dysfunction, respectively, $p = 0.012$. The apolipoprotein E-$\epsilon 4$ allele was present in 9 (29%) and 24 (19%) patients with and without cognitive dysfunction, respectively, $p = 0.24$. Both the PI(A2) and apolipoprotein-$\epsilon 4$ alleles were present together in 6 (19%) and 5 (4%) patients with and without cognitive dysfunction, respectively, $p = 0.003$</p>	(A. Stewart et al., 2013)
<p>KIBRA (WW And C2 Domain Containing 1) An association between the KIBRA gene and episodic memory (immediate free recall) and suggests a differential effect of this genetic variant in early onset schizophrenia and healthy siblings</p>	(Vyas et al., 2014)
<p>rs17070145 associates with cognitive function in depression</p>	(J. J. Liu, Lavebratt, Lou, & Forsell, 2015)
<p>KLOTHO (KL Klotho) GA+AA genotype subjects had a significantly lower risk of cognitive impairment (odds ratio 0.66; 95 % confidence interval 0.44 to 0.98) than GG genotype individuals after adjusting for age, gender, and other relevant risk factors.</p>	(Hao, Ding, Gao, Yang, & Dong, 2016)
<p>LDLR (Low Density Lipoprotein Receptor) The study suggests that amnesic cognitive impairment is characterized by memory impairment and associated with SNPs in three systems relating to the pathogenesis of AD—those of the amyloid cascade, tau and cholesterol metabolism pathways</p>	(X. Liu et al., 2012)
<p>LRP1 (LDL Receptor Related Protein 1) We identified haplotypes within the region containing the LRP1 gene. Of these, haplotype TAA (T: rs1800194; A: rs11837145; A: rs10876967) was significantly associated with amnesic mild cognitive impairment</p>	(Y. M. Shi et al., 2009)
<p>LRP1B (LDL Receptor Related Protein 1B) Among these genes, APOE and APOC1 are known AD risk genes. For the other five genes TNFRSF1A, CDH1, CASP7, LRP1B and TG, this is the first genetic association study which showed the significant association between these five genes and Alzheimer's Disease susceptibility in Caribbean Hispanic individuals.</p>	(Shang et al., 2015)
<p>LRRK2 (Leucine Rich Repeat Kinase 2) Subjects with G2019S and R1441G mutations of the LRRK-2 gene showed less impairment on scales for general cognition (Mattis dementia rating scale 131.2 ± 10.9 vs. 119 ± 24.0, $p = 0.022$), episodic verbal memory (Rey's auditory verbal learning test, immediate recall 39.2 ± 9.5 vs. 27.6 ± 12.8 $p < 0.001$, delayed recall 7.2 ± 3.7 vs. 4.7 ± 4.0 $p = 0.022$), and the Neuropsychiatric Inventory (9.7 ± 9.2 vs. 20.5 ± 14.3, $p = 0.004$, significant differences for apathy and hallucinations).</p>	(Somme et al., 2015)

<p>These results indicate that non-manifesting carriers of the G2019S mutation in the LRRK2 gene have a specific cognitive profile with executive functions, demonstrating significant impairment but with working memory remaining relatively intact Parkinson's Disease patients who carried A419V have a lower Minimum-Mental State Examination scores than PD patients who did not ($p = 0.04$)</p>	(Thaler et al., 2016)
<p>LTA (Lymphotoxin Alpha) The LTA Cys13Arg polymorphism may represent a risk factor for cognitive impairment in individuals with schizophrenia.</p>	(F. Dickerson, Boronow, Stallings, Origoni, & Yolken, 2007)
<p>MAG (Myelin Associated Glycoprotein) Combined genetics and neuroimaging data showed that variants from the MAG, OLIG2, and CNP genes influenced white matter tract integrity and cognitive performance</p>	(Voineskos et al., 2013) v
<p>MAPT (Myelin Associated Glycoprotein) MAPT H1/H1 genotype was an independent predictor of dementia risk.</p> <p>These results firstly suggest that the risk of mild cognitive impairment is influenced by tau protein gene variations and that mild cognitive impairment shares a common genetic background with Alzheimer's disease</p> <p>Cognitive decline and the development of Parkinson's disease dementia are strongly associated with the inversion polymorphism containing MAPT. We also found a novel synergistic interaction between the MAPT inversion polymorphism and the single nucleotide polymorphism rs356219 from the 3' region of SNCA</p> <p>Common variation in MAPT is not only associated with the dementia of Parkinson's disease but also differences in the neural circuitry underlying aspects of cognition in normal aging</p> <p>The study suggests that amnesic cognitive impairment is characterized by memory impairment and associated with SNPs in three systems relating to the pathogenesis of AD—those of the amyloid cascade, tau and cholesterol metabolism pathways</p>	<p>(Williams-Gray et al., 2009)</p> <p>(Di Maria et al., 2010)</p> <p>(Goris et al., 2007)</p> <p>(Winder-Rhodes et al., 2015)</p> <p>(X. Liu et al., 2012)</p>
<p>MBL2 (Mannose Binding Lectin 2) The APOE epsilon4 allele was associated with increased risk for cognitive deficits, whereas the MBL2 O/O genotype was associated with increased risk for progressive cognitive decline in Chinese individuals infected with HIV through contaminated blood products.</p>	(Spector et al., 2010)
<p>MRPL19 (Mitochondrial Ribosomal Protein L19) MRPL19/C2ORF3 locus showed statistically significant association with measures of general cognitive abilities</p>	(Scerri et al., 2012)

<p>MS (MTR 5-Methyltetrahydrofolate-Homocysteine Methyltransferase) The A2756G polymorphism in the MS gene was shown to be an independent risk factor for mild cognitive impairment in the Xinjiang Uyghur population. The A>G mutation in the MS gene at the rs1805087 locus was another independent risk factor for mild cognitive impairment in the Uyghur population. The risk of mild cognitive impairment in G allele carriers was 2.265 times higher than that in matched control individuals</p>	(Luo, Ji, Zhou, Liang, & Zou, 2015)
<p>MS4A4E (Membrane Spanning 4-Domains A4E) Significant associations with cognitive performance were observed for APOE ε4 allele, ABCA7-rs3764650, CR1-rs3818361, MS4A4E-rs6109332, BDNF-rs6265, COMT-rs4680, CTNBL-rs6125962, FRMD4A-rs17314229, FRMD4A-rs17314229, intergenic SNP chrX-rs12007229, PDE7A-rs10808746, SORL1-rs668387, and ZNF224-rs3746319</p>	(Andrews et al., 2016)
<p>MSRA (Methionine Sulfoxide Reductase A) Allele frequencies of the rs4840463 polymorphism were significantly different between bipolar disorder patients and controls, and between patients with psychotic symptoms and controls. BD I patients performed more poorly in 11 of the 13 neurocognitive measurements compared with controls</p>	(Ni et al., 2015)
<p>MTHFR (Methylenetetrahydrofolate Reductase) Compared with the wild CC genotype, participants with the MTHFR-TT genotype had 46% greater odds of cognitive impairment (OR 1.46, 95% CI 1.01-2.11, P=0.043) Among COMT-Val/Val participants, MTHFR-C/C made more spatial working memory errors (p=0.033) and solved fewer attentional flexibility and planning problems (p=0.025) than MTHFR-T carriers. In patients, there was a significant COMT×MTHFR interaction on full scale IQ (p=0.035): among COMT-Met carriers, MTHFR-T carriers performed significantly worse than MTHFR-C/C (p=0.021), which was driven by a COMT×MTHFR interaction involving performance IQ (p=0.047).</p> <p>When MTHFR C677T TT was combined with the apolipoprotein E (APOE)-ε4 allele, it was a risk factor for lower executive performance.</p> <p>Compared with the wild CC genotype, participants with the MTHFR-TT genotype had 46% greater odds of cognitive impairment</p> <p>T/T subjects exhibited significantly greater deficits on the Verbal Fluency Test and had more difficulty achieving the first category on the Wisconsin Card Sort Test</p>	<p>(Ford et al., 2012)</p> <p>(Kontis et al., 2013)</p> <p>(Polito et al., 2016)</p> <p>(Ford et al., 2012)</p> <p>(Roffman et al., 2007)</p>
<p>MTOR (Mechanistic Target Of Rapamycin) Using a genome-wide screen, we discovered a novel association of a polymorphism in the proapoptotic gene FASTKD2 (fas-activated serine/threonine kinase domains 2; rs7594645-G) and in the MTOR pathway with better memory performance and replicated this finding in independent samples.</p>	(Ramanan, Nho, et al., 2015)

<p>MTR (5-Methyltetrahydrofolate-Homocysteine Methyltransferase) People with late life depression carrying MTR2756 AA genotype have higher risk of cognitive impairment than those carrying G allele.</p>	(Yang et al., 2017)
<p>MYD88 (Myeloid Differentiation Primary Response 88) Carriers of the MYD88 rs6853 variant were half as likely to have cognitive dysfunction than wild-type patients.</p>	(Barratt, Klepstad, Dale, Kaasa, & Somogyi, 2015)
<p>ND6 (Mitochondrially Encoded NADH:Ubiquinone Oxidoreductase Core Subunit 6) m.14178T>C, p.I166V, ND6 variant was associated with a significant decline in the modified mini mental state score in elderly adults</p>	(Tranah et al., 2012)
<p>NEDD9 (Neural Precursor Cell Expressed, Developmentally Down-Regulated 9) Our study identified rs760678 within NEDD9 gene in association with the risk of Alzheimer disease and cognitive performance in Chinese older persons.</p>	(Y. Fu et al., 2012)
<p>NGF (Nerve Growth Factor) A significant difference was noted for the go/no-go scores ($p < 0.01$) between C/C and T carriers. The NGF gene rs6330 might influence the inhibition task in Japanese patients with early-stage Alzheimer's Disease or mild cognitive impairment</p>	(Nagata, Shinagawa, Nukariya, Nakayama, et al., 2011)
<p>NOS3 (nitric oxide synthase 3) Though no association between NOS3 gene variation and mild cognitive impairment status was observed, cases carrying the Asp variant (T+) performed worse in the Mini-Mental State Examination, Wechsler Memory Scale (Revised) long-term visual memory and the phonetic verbal fluency tests.</p>	(Sole-Padulles et al., 2004)
<p>NOTCH3 (Notch 3) CADASIL subjects carrying mutations in NOTCH 3 had pronounced impairments of the timed measures (Stroop II and III, Trail Making Test, symbol digit, digit cancellation).</p> <p>The 2 mutation carrier groups without dementia and the controls could be reliably distinguished using 3 tests that assessed working memory/attention, executive function, and mental speed.</p> <p>The NOTCH3 R544C is associated with lower frequency of anterior temporal involvement, later age at onset and higher frequency of cognitive dysfunction.</p>	(Peters et al., 2005) (Amberla et al., 2004) (Liao et al., 2015)
<p>NOX (NAPDH oxidase) Polymorphisms within the NOX gene or its functional subunits may account for important components of the variance in cognitive function deficits associated with obstructive sleep apnea in children.</p>	(Gozal et al., 2012)
<p>NPC1 (NPC Intracellular Cholesterol Transporter 1) Patients with mutations in the gene coding for the cholesterol trafficking protein NPC1 had more marked deficits in verbal working memory than in visuospatial working memory.</p>	(Klarner, Klunemann, Lurding, Aslanidis, & Rupprecht, 2007)
<p>NR3C1(Nuclear Receptor Subfamily 3 Group C Member 1) Polymorphisms in the 11βHSD1 and NR3C1 genes were associated with impaired cognitive function in Cushing's Syndrome</p>	(Ragnarsson et al., 2014)

<p>NRG1 (Neuregulin 1) NRG1 (SNP8NRG221533; rs35753505) status was determined and correlated with a linear effect on semantic but not on lexical verbal fluency.</p>	(Kircher et al., 2009)
<p>NRSF (REST RE1 Silencing Transcription Factor) We found a statistically significant association between genotypic variation and memory function at both baseline (NRSF: rs1105434, rs2227902 and BDNF: rs1491850, rs2030324, rs11030094) and in our longitudinal analysis (NRSF: rs2227902 and BDNF: rs12273363).</p>	(Warburton et al., 2016)
<p>NT3 (3'-Nucleotidase) These results suggested that an NT-3 polymorphism, rs6332, may significantly influence executive function, reflecting interference performances among patients with mild-stage Alzheimer's Disease.</p>	(Kobayashi et al., 2012)
<p>OLIG2 (Oligodendrocyte Transcription Factor 2) Combined genetics and neuroimaging data showed that variants from the MAG, OLIG2, and CNP genes influenced white matter tract integrity and cognitive performance</p>	(Voineskos et al., 2013)
<p>PDE4D (Phosphodiesterase 4D) The C/C genotype of SNP 83 is significantly associated with the highest incidence of cognitive dysfunction 1 day following carotid endarterectomy in comparison with the C/T and T/T genotypes</p>	(Heyer et al., 2013)
<p>PDE7A (Phosphodiesterase 7A) Significant associations with cognitive performance were observed for APOE ε4 allele, ABCA7-rs3764650, CR1-rs3818361, MS4A4E-rs6109332, BDNF-rs6265, COMT-rs4680, CTNBL-rs6125962, FRMD4A-rs17314229, FRMD4A-rs17314229, intergenic SNP chrX-rs12007229, PDE7A-rs10808746, SORL1-rs668387, and ZNF224-rs3746319</p>	(Andrews et al., 2016)
<p>PGRN (Granulin Precursor) The clinical presentation of an Alzheimer disease-like phenotype of cognitive impairment was associated with the c.154delA mutation in progranulin.</p>	(Kelley et al., 2010)
<p>PICALM (Phosphatidylinositol Binding Clathrin Assembly Protein) The data suggest a neural mechanism for APOE-PICALM interactions in patients with manifest Alzheimer's Disease and indicate that the PICALM genotype modulates both brain atrophy and cognitive performance in APOE ε4 carriers.</p> <p>PICALM rs3851179 was associated with cognitive impairment (MMSE < 24) in Parkinson's Disease subjects > 70 years old (OR=2.3; adjusted p-value=0.017; n=250) but not in Parkinson's Disease subjects ≤ 70 years old.</p>	(Morgen et al., 2014) (Barrett, Koeppl, Flanigan, Turner, & Worrall, 2016)
<p>PLAU (Plasminogen Activator, Urokinase) The study suggests that amnesic cognitive impairment is characterized by memory impairment and associated with SNPs in three systems relating to the pathogenesis of AD—those of the amyloid cascade, tau and cholesterol metabolism pathways</p>	(X. Liu et al., 2012)

<p>PLK2 (Polo Like Kinase 2) A significant association between the genotypes RELN (rs528528 and rs2299356), PLK2 (rs15009 and rs702723), and CAMK2A (rs3756577 and rs3822606) and Alzheimer's Disease or mild cognitive impairment was found</p>	(Bufill et al., 2015)
<p>PPARG (Peroxisome Proliferator Activated Receptor Gamma) The PPAR-gamma Ala12 allele carriers may have less risk of developing cognitive decline</p> <p>These data suggest that although the Ala variant is associated with a reduced risk of type 2 diabetes, it may increase the risk of cognitive impairment in individuals once diabetes has developed. Male Ala carriers may also have a greater risk of dementia and cognitive impairment.</p>	(Yaffe et al., 2008) (West, Haan, & Morgenstern, 2010)
<p>PRNP (Prion Protein) The 6-OPRI polymorphism variant patients had more widespread and severe cognitive dysfunction than the P102L group in inherited prion disease.</p> <p>Variability of the PRNP locus may be associated with cognitive performance in the elderly</p> <p>These findings provide evidence that variability of the PRNP gene at codon 129 might contribute to accelerating the rate of earlier cognitive decline in Down Syndrome subjects.</p>	(Alner et al., 2012) (Berr et al., 1998) (Del Bo et al., 2003)
<p>PSEN1 (Presenilin 1) The familial AD carriers showed significant dual memory task decrements compared to those family members without the variation in presenilin-1.</p> <p>The presence of the Glu318Gly mutation was associated with significantly lower cognitive performance when compared to controls</p> <p>Clinical deterioration can be detected as measurable cognitive impairment around two decades before dementia onset in PSEN1 E280A carriers</p> <p>The PSEN1 F177S mutation leads to typical Alzheimer's Disease starting at age 30 and a homogeneous phenotype with rapid cognitive decline and prominent neurological symptoms</p> <p>Variation in the third transmembrane domain of PSEN1 is characterized by fast cognitive decline with progressive memory impairment, early involvement of executive functions, behavioral disturbances, and extrapyramidal signs</p>	(MacPherson, Parra, Moreno, Lopera, & Della Sala, 2015) (Laws et al., 2002) (Acosta-Baena et al., 2011) (Hausner et al., 2014) (Piscopo et al., 2010)
<p>RELN (Reelin) A significant association was found between the genotypes RELN (rs528528 and rs2299356), PLK2 (rs15009 and rs702723), and CAMK2A (rs3756577 and rs3822606) and Alzheimer's Disease or mild cognitive impairment</p>	(Bufill et al., 2015)

<p>RNASE13 (Ribonuclease A Family Member 13 (Inactive)) Gene-based analyses found a genome-wide significant association between RNASE13 and executive function resilience</p>	(Mukherjee et al., 2014)
<p>SELP (Selectin P) Older patients with cardiovascular disease and the SELP 1087A allele performed more poorly on neuropsychological testing.</p>	(Gunstad et al., 2009)
<p>SHANK (SHANK group SH3 And Multiple Ankyrin Repeat Domains 1, 2, 3) Mutations of the SHANK genes were detected in the whole spectrum of autism with a gradient of severity in cognitive impairment</p>	(Leblond et al., 2014)
<p>SIGMAR1 (Sigma Non-Opioid Intracellular Receptor 1) Data demonstrate that SIGMAR1 and APOE interact to influence Alzheimer's Disease severity across ethnic populations.</p>	(Huang et al., 2011)
<p>SLC1A2 (Solute Carrier Family 1 Member 2) Genetic variation (rs4354668 and its haplotypes) in SLC1A2 may be involved in impaired executive function for schizophrenic patients</p>	(B. Zhang et al., 2015)
<p>SLC5A7 (Solute Carrier Family 5 Member 7) These results are the first to demonstrate a specific impairment in cognitive control associated with the Ile89Val polymorphism</p>	(Berry et al., 2014)
<p>SLC6A4 (Solute Carrier Family 6 Member 4) We found that elderly volunteers homozygous for the VNTR2 12 allele had a faster rate of decline for all cognitive tests.</p> <p>The presence of STin2.10 and absence of STin2.12 allele may be related to a possible genetic endophenotype for characteristic cognitive dysfunctions detected in major depressive disorder</p>	(Payton et al., 2005) (Sarosi et al., 2008)
<p>SNAP25 (Synaptosome Associated Protein 25) Results showed that the intronic rs363050 (A) and rs363043 (T) alleles, as well as the rs363050/rs363043 A-T haplotype are significantly more frequent in Alzheimer's Disease and amnesic mild cognitive impairment and are associated with pathological scores of categorical fluency in AD.</p> <p>Homozygote T/T allele carriers of the Ddel polymorphism showed significant better neuropsychological test results in cognitive domains verbal memory and executive functions than those with the combined T/C and C/C genotypes (P < 0.01)</p>	(Guerini et al., 2014) (Spellmann et al., 2008)
<p>SNCA (Synuclein Alpha) Cognitive decline and the development of Parkinson's Disease dementia are strongly associated with the inversion polymorphism containing MAPT. We also found a novel synergistic interaction between the MAPT inversion polymorphism and the single nucleotide polymorphism rs356219 from the 3' region of SNCA</p>	(Goris et al., 2007)

<p>SORL1 (Sortilin Related Receptor 1) Significant associations with cognitive performance were observed for APOE ε4 allele, ABCA7-rs3764650, CR1-rs3818361, MS4A4E-rs6109332, BDNF-rs6265, COMT-rs4680, CTNBL-rs6125962, FRMD4A-rs17314229, FRMD4A-rs17314229, intergenic SNP chrX-rs12007229, PDE7A-rs10808746, SORL1-rs668387, and ZNF224-rs3746319</p> <p>The strongest gene-phenotype association was between SORL1 (rs1131497; $p = 3.2 \times 10^{-6}$) and abstract reasoning</p>	<p>(Andrews et al., 2016)</p> <p>(Seshadri et al., 2007)</p>
<p>SPG11 (SPG11, Spatacsin Vesicle Trafficking Associated) This study reveals the high frequency of SPG11 mutations in patients with hereditary spastic paraplegias, a thin corpus callosum, and cognitive impairment and extends the associated phenotype</p>	<p>(Stevanin et al., 2008)</p>
<p>SPG4 (SPAST Spastin) Asymptomatic cognitive impairment mostly affecting executive functions is present in SPG4 mutation carriers and is more frequent in those with missense mutations This data demonstrates that cognitive decline and dementia is a feature of SPG4-HSP due to a deletion of exon 17 of the spastin gene</p> <p>Haplotype carriers affected by HSP had lower total Cambridge Cognitive exam scores than control subjects</p>	<p>(Tallaksen et al., 2003)</p> <p>(Murphy et al., 2009)</p> <p>(Byrne et al., 2000)</p>
<p>STH (Saitohin) Among the patients with schizophrenia, stratified for age and gender, the STH polymorphism resulted in a significant predictor of Wisconsin Card Scoring Test performance</p>	<p>(Bosia et al., 2012)</p>
<p>SYNPO (Synaptopodin) From the gene SYNPO, rs6579797 (MAF = 0.032) shows significant associations with abstraction and mental flexibility ($P = .015$) and schizophrenia ($P = .040$), as well as jointly ($P = .0027$). In the Mexican American pedigrees, rs6579797 exhibits significant associations with IQ ($P = .011$), indicating more global effects on neurocognition.</p>	<p>(Kos et al., 2016)</p>
<p>TG (thyroglobulin) Among these genes, APOE and APOC1 are known AD risk genes. For the other five genes TNFRSF1A, CDH1, CASP7, LRP1B and TG, this is the first genetic association study which showed the significant association between these five genes and Alzheimer's Disease susceptibility in Caribbean Hispanic individuals.</p>	<p>(Shang et al., 2015)</p>
<p>TNFRSF1A (TNF Receptor Superfamily Member 1A) Among these genes, APOE and APOC1 are known AD risk genes. For the other five genes TNFRSF1A, CDH1, CASP7, LRP1B and TG, this is the first genetic association study which showed the significant association between these five genes and Alzheimer's Disease susceptibility in Caribbean Hispanic individuals.</p>	<p>(Shang et al., 2015)</p>

<p>TOMM40 (Translocase Of Outer Mitochondrial Membrane 40) These results suggest that previous findings of an association of the TOMM40 short allele with better cognitive performance, independently from the APOE variant status, are pertinent to elderly with diabetes.</p> <p>The study suggests that amnesic mild cognitive Impairment is associated with SNPs in three systems relating to the pathogenesis of AD—those of the amyloid cascade, tau and cholesterol metabolism pathways</p> <p>CR1, TOMM40, BIN1, and CD33 contribute to late-onset Alzheimer's Disease susceptibility and cognitive impairment, in addition to apolipoprotein E.</p>	<p>(Greenbaum et al., 2014)</p> <p>(X. Liu et al., 2012)</p> <p>(Omoumi et al., 2014)</p>
<p>UBR5 (Ubiquitin Protein Ligase E3 Component N-Recognin 5) rs7840202 at chr8 in UBR5 was associated with a significant decline in cognition as well as the conversion of subjects with mild cognitive impairment to a diagnosis of Alzheimer's Disease.</p>	<p>(Hu et al., 2011)</p>
<p>YWHAE (Tyrosine 3-Monooxygenase/Tryptophan 5-Monooxygenase Activation Protein Epsilon) Individuals who are HIV-seropositive and heterozygous at the rs4790084/rs1204828 loci in the YWHAE gene were 3x more likely to display reduced cognitive functioning</p>	<p>(Morales, Hechavarria, Wojna, & Acevedo, 2013)</p>
<p>ZNF224 (Zinc Finger Protein 224) Significant associations with cognitive performance were observed for APOE ε4 allele, ABCA7-rs3764650, CR1-rs3818361, MS4A4E-rs6109332, BDNF-rs6265, COMT-rs4680, CTNND1-rs6125962, FRMD4A-rs17314229, FRMD4A-rs17314229, intergenic SNP chrX-rs12007229, PDE7A-rs10808746, SORL1-rs668387, and ZNF224-rs3746319</p>	<p>(Andrews et al., 2016)</p>
<p>ZNF804A (Zinc Finger Protein 804A) ZNF804A, DISC1 and KIAA0319 were associated with language and speech, verbal learning and recall processes, and processing speed in schizophrenic patients</p> <p>A significant ZNF804A genotype-diagnosis interaction was found for visual memory performance. Patients with the high-risk T/T genotype scored significantly lower on visual memory tasks than G carriers did</p>	<p>(Nicodemus et al., 2014)</p> <p>(Hashimoto et al., 2010)</p>
<p style="text-align: center;">Significant Genes – Epigenomic Findings</p>	<p style="text-align: center;">Authors</p>
<p>BACE1 (Beta-Secretase 1) BACE1 promoter region was less accessible due to histone H3 acetylation in peripheral blood mononuclear cells from individuals with mild cognitive impairment.</p>	<p>(Marques et al., 2012)</p>
<p>FMR1 (Fragile X Mental Retardation 1) The data suggest that hypermethylation of the FMR1 intron 1 sites in blood is predictive of cognitive impairment in Fragile X carrier females.</p>	<p>(Godler et al., 2012)</p>

HMOX1 (Heme Oxygenase 1) We observed lower methylation of HMOX1 at the -374 promoter CpG site in Alzheimer's disease patients compared to mild cognitive impairment and control individuals	(Sung et al., 2016)
KLOTHO (KL Klotho) Our results showed that KLOTHO promoter hypermethylation contributed to the risk of mild cognitive impairment in Xinjiang Han Chinese but not in Xinjiang Uygur Chinese.	(Luo, Zhou, et al., 2015)
NCAPH2/LMF2 (Non-SMC Condensin II Complex Subunit H2/ Lipase Maturation Factor 2) DNA methylation in the NCAPH2/LMF2 promoter region was significantly decreased in the AD (n = 30) and aMCI (n = 28) groups as compared to the NC group (n = 30) (P < 0.0001, ANCOVA)	(Kobayashi et al., 2016)
SORL1 (Sortilin Related Receptor 1) The methylation ratio (86.9%) of SORL1 in mild cognitive impairment patients was significantly higher than in patients without cognitive impairment patients (35.9%, P<0.05) and in the control group (11.3%, P<0.05). These results suggested that the DNA methylation of the SORL1 5'-flanking region may significantly influence the manifestation of mild cognitive impairment in Type 2 diabetes, and might be associated with its neurocognitive presentation	(Yu et al., 2016)
Significant Genes – Transcriptomic Findings	Authors
ABCB1 (ATP Binding Cassette Subfamily B Member 1) ABCB1 gene expression exhibited significantly positive correlation with mini mental state exam scores among normal controls, mild cognitive impairment, and Alzheimer's Disease subjects	(K. D. Chen et al., 2011)
APOE (Apolipoprotein E) Activation of peripheral circulating GSK-3 β , expression of ApoE ϵ 4 and increase of olfactory score are diagnostic for the mild cognitive impairment in Type 2 diabetes patients, and combination of these biomarkers can improve the diagnostic accuracy.	(Xu et al., 2016)
APP (Amyloid Beta Precursor Protein) Differential gene expression measurements revealed a significant up-regulation in expression of APP in both Alzheimer's disease and frontotemporal lobar degeneration patients compared to the controls	(Vignini et al., 2013)
ASMT (Acetylserotonin O-Methyltransferase) Data suggest a relationship between decreased mRNA and protein expression levels of ASMT and cognitive impairment.	(Talarowska, Szemraj, Zajackowska, & Galecki, 2014)
ATM (ATM Serine/Threonine Kinase) The expression of CCL-checkpoint and DNA damage response genes: MDM4, ATM and ATR was strongly upregulated and associated with progression of dementia (cognitive dementia rating, CDR), appearing as early as questionable or mild dementia (CDRs 0.5-1).	(Katsel, Tan, Fam, Purohit, & Haroutunian, 2013)

<p>ATR (ATR Serine/Threonine Kinase) The expression of CCL-checkpoint and DNA damage response genes: MDM4, ATM and ATR was strongly upregulated and associated with progression of dementia (cognitive dementia rating, CDR), appearing as early as questionable or mild dementia (CDRs 0.5-1).</p>	(Katsel et al., 2013)
<p>BACE1 (Beta-Secretase 1) BACE1 mRNA levels tended to increase as miR-107 levels decreased in the progression of Alzheimer's disease</p>	(W. X. Wang et al., 2008)
<p>BAX (BCL2 Associated X, Apoptosis Regulator) Results show that Bax and Sod1 mRNA levels are altered in PBMCs from both mild cognitive impairment and Alzheimer's Disease patients and indicate these changes as potential biomarkers in the early diagnosis of cognitive impairment</p>	(Gatta et al., 2009)
<p>BDNF (brain derived neurotrophic factor) Higher brain BDNF expression is associated with slower cognitive decline and may also reduce the deleterious effects of Alzheimer's Disease pathology on cognitive decline</p> <p>A marked decrease in the expression of miR-29c was observed in the Alzheimer's Disease group compared with the normal control group, accompanied by a decrease in the expression of BDNF. Additionally, a significant increase in the expression of DNMT3 was observed in the CSF from the patients with Alzheimer's Disease</p> <p>Associative and logical verbal memory improved significantly and showed a significant correlation with changes in PMC BDNF and GABA-A beta3 receptor mRNA, which increased during SSRI treatment.</p>	(Buchman et al., 2016) (G. Yang et al., 2015) (Silver et al., 2015)
<p>BIN1 (Bridging Integrator 1) We found that temporal lobe epilepsy patients with severe memory impairment carried the single nucleotide polymorphism rs744373 C-allele, which was also associated with high mRNA levels of bridging integrator 1 (BIN1)/Amphiphysin 2, i.e. a major component of the endocytotic machinery and located in a crucial genetic Alzheimer's Disease risk locus.</p>	(Bungenberg et al., 2016)
<p>CCR2 (C-C Motif Chemokine Receptor 2) CCR2 expression is associated with lower MMSE scores in an older human population.</p>	(Harries et al., 2012)
<p>CD36 (CD36 Molecule) Data indicate that the reduction of CD36 expression in leukocytes is a disease-related phenomenon, occurring since the early stages of Alzheimer's disease/mild cognitive impairment</p>	(Giunta et al., 2007)
<p>CHRNA7 (Cholinergic Receptor Nicotinic Alpha 7 Subunit) Cholinergic nucleus basalis neurons displayed a statistically significant up-regulation of alpha7 nicotinic receptor messenger RNA expression in subjects with mild to moderate Alzheimer's Disease compared with those with no cognitive impairment and mild cognitive impairment</p>	(Counts et al., 2007)
<p>DNM2 (Dynamain 2) Expression of DNM2 mRNA in the hippocampus was decreased in the patients compared to non-demented controls.</p>	(Aidaraliev et al., 2008)

<p>DNMT3 (DNA methyltransferase 3) A marked decrease in the expression of miR-29c was observed in the Alzheimer's Disease group compared with the normal control group, accompanied by a decrease in the expression of BDNF. Additionally, a significant increase in the expression of DNMT3 was observed in the CSF from the patients with Alzheimer's Disease</p>	(G. Yang et al., 2015)
<p>EPHB2 (EPH Receptor B2) Cognitive associations were limited to the cingulate, where decreased levels of EPHB2 mRNA were associated with better global cognitive status for HIV subjects.</p>	(Yuferov et al., 2013)
<p>FMR1 (Fragile X Mental Retardation 1) There was a significant reduction in FMRP expression and an elevated FMR1 mRNA expression level associated with moderate cognitive deficit</p>	(Tassone et al., 2000)
<p>FMRP (fragile X mental retardation protein also FMR1) There was a significant reduction in FMRP expression and an elevated FMR1 mRNA expression level associated with moderate cognitive deficit</p>	(Tassone et al., 2000)
<p>GABRB3 (Gamma-Aminobutyric Acid Type A Receptor Beta3 Subunit) Associative and logical verbal memory improved significantly and showed a significant correlation with changes in PMC BDNF and GABA-A beta3 receptor mRNA, which increased during SSRI treatment.</p>	(Silver et al., 2015)
<p>GHRL (Ghrelin And Obestatin Prepropeptide) We found a striking reduction in mRNA levels for ghrelin, and its newly discovered In2-ghrelin variant, as well as for the enzyme responsible for ghrelin acylation, ghrelin-O-acyltransferase and GHS-R1a, while expression of GHS-R1b was markedly increased. In addition, expression levels of NTSR1 and NTSR2 were profoundly decreased in Alzheimer's Disease, whereas mRNA levels of NTS only declined slightly, and those of NTSR3 (which is involved in neuronal apoptosis) did not vary.</p>	(Gahete et al., 2010)
<p>GHS-R1a (Growth Hormone Secretagogue Receptor) We found a striking reduction in mRNA levels for ghrelin, and its newly discovered In2-ghrelin variant, as well as for the enzyme responsible for ghrelin acylation, ghrelin-O-acyltransferase and GHS-R1a, while expression of GHS-R1b was markedly increased. In addition, expression levels of NTSR1 and NTSR2 were profoundly decreased in Alzheimer's Disease, whereas mRNA levels of NTS only declined slightly, and those of NTSR3 (which is involved in neuronal apoptosis) did not vary.</p>	(Gahete et al., 2010)
<p>GHS-R1b (Growth Hormone Secretagogue Receptor) We found a striking reduction in mRNA levels for ghrelin, and its newly discovered In2-ghrelin variant, as well as for the enzyme responsible for ghrelin acylation, ghrelin-O-acyltransferase and GHS-R1a, while expression of GHS-R1b was markedly increased. In addition, expression levels of NTSR1 and NTSR2 were profoundly decreased in Alzheimer's Disease, whereas mRNA levels of NTS only declined slightly, and those of NTSR3 (which is involved in neuronal apoptosis) did not vary.</p>	(Gahete et al., 2010)

<p>HLA-DQ/HLA-DR (Major Histocompatibility Complex, Class II, DQ and DR) Compared to non-demented high-pathology controls, the hippocampus of AD cases with mild/moderate dementia had increased gene expression of the inflammatory molecule major histocompatibility complex (MHC) II, as assessed with microarray analysis. MHC II protein levels were also increased and inversely correlated with cognitive ability.</p>	(Parachikova et al., 2007)
<p>HO-1 (Heme Oxygenase 1) Astroglial HO-1 expression in the temporal cortex was associated with decreased scores for global cognition, episodic memory, semantic memory and working memory. Hippocampal astroglial HO-1 expression was associated with lower scores for global cognition, semantic memory and perceptual speed.</p>	(Schipper et al., 2006)
<p>LR11 (SORL1 Sortilin Related Receptor 1) LR11 expression in brain tissue was heterogeneous in mild cognitive impairment, forming low- and high-level LR11 subgroups. Those subjects with low LR11 were significantly more cognitively impaired than the high LR11 subjects. We also found a significant correlation between cognitive performance and LR11 levels across all clinical groups examined (normal, Alzheimer's disease, mild cognitive impairment).</p>	(Sager et al., 2007)
<p>MAPT (SORL1 Sortilin Related Receptor 1) Results revealed a shift in the ratio of three-repeat tau (3Rtau) to four-repeat tau (4Rtau) mRNAs within individual human cholinergic basal forebrain neurons within nucleus basalis and CA1 hippocampal neurons during the progression of Alzheimer's Disease, but not during normal aging</p>	(Ginsberg, Che, Counts, & Mufson, 2006)
<p>MCP-1 (C-C Motif Chemokine Ligand 2) Data showed elevated MCP-1 expression in the frontal cortex of mild cognitive impairment cases that are at high risk for developing Alzheimer's disease</p>	(L. Ho et al., 2012)
<p>MDM4 (MDM4, P53 Regulator) The expression of CCL-checkpoint and DNA damage response genes: MDM4, ATM and ATR was strongly upregulated and associated with progression of dementia (cognitive dementia rating, CDR), appearing as early as questionable or mild dementia (CDRs 0.5-1).</p>	(Katsel et al., 2013)
<p>miR-193b (MicroRNA 193b) Dementia of Alzheimer type patients had lower exosomal miR-193b levels in blood as compared with the mild cognitive impairment group. A decreased exosomal miR-193b expression level was additionally observed in the cerebral spinal fluid (CSF) of dementia of Alzheimer type patients</p>	(C. G. Liu, Song, Zhang, & Wang, 2014)
<p>miR-29c (MicroRNA 29c) A marked decrease in the expression of miR-29c was observed in the Alzheimer's Disease group compared with the normal control group, accompanied by a decrease in the expression of BDNF. Additionally, a significant increase in the expression of DNMT3 was observed in the CSF from the patients with Alzheimer's Disease</p>	(G. Yang et al., 2015)

<p>miRNA107 (MicroRNA 107) The miRNA107 expression in plasma has a high capability to discriminate between patients with amnesic mild cognitive impairment and healthy controls.</p> <p>BACE1 mRNA levels tended to increase as miR-107 levels decreased in the progression of Alzheimer's disease</p>	<p>(T. Wang et al., 2015)</p> <p>(W. X. Wang et al., 2008)</p>
<p>NEP (MME Membrane Metalloendopeptidase) NEP expression was correlated with Aβ accumulation and clinical diagnosis, being lower in Alzheimer's Disease than in no cognitive impairment.</p>	<p>(S. Wang et al., 2010)</p>
<p>NTS (Neurotensin) We found a striking reduction in mRNA levels for ghrelin, and its newly discovered In2-ghrelin variant, as well as for the enzyme responsible for ghrelin acylation, ghrelin-O-acyltransferase and GHS-R1a, while expression of GHS-R1b was markedly increased. In addition, expression levels of NTSR1 and NTSR2 were profoundly decreased in Alzheimer's Disease, whereas mRNA levels of NTS only declined slightly, and those of NTSR3 (which is involved in neuronal apoptosis) did not vary.</p>	<p>(Gahete et al., 2010)</p>
<p>NTSR1 (Neurotensin Receptor 1) We found a striking reduction in mRNA levels for ghrelin, and its newly discovered In2-ghrelin variant, as well as for the enzyme responsible for ghrelin acylation, ghrelin-O-acyltransferase and GHS-R1a, while expression of GHS-R1b was markedly increased. In addition, expression levels of NTSR1 and NTSR2 were profoundly decreased in Alzheimer's Disease, whereas mRNA levels of NTS only declined slightly, and those of NTSR3 (which is involved in neuronal apoptosis) did not vary.</p>	<p>(Gahete et al., 2010)</p>
<p>NTSR2 (Neurotensin Receptor 1) We found a striking reduction in mRNA levels for ghrelin, and its newly discovered In2-ghrelin variant, as well as for the enzyme responsible for ghrelin acylation, ghrelin-O-acyltransferase and GHS-R1a, while expression of GHS-R1b was markedly increased. In addition, expression levels of NTSR1 and NTSR2 were profoundly decreased in Alzheimer's Disease, whereas mRNA levels of NTS only declined slightly, and those of NTSR3 (which is involved in neuronal apoptosis) did not vary.</p>	<p>(Gahete et al., 2010)</p>
<p>OGG1 (8-Oxoguanine DNA Glycosylase) The data suggest oxidative damage to nucleic acids and a compensatory increase in OGG1 expression occur early in the pathogenesis of Alzheimer's disease</p>	<p>(Lovell, Soman, & Bradley, 2011)</p>
<p>RAB5 (RAB5A, Member RAS Oncogene Family) Expression levels of genes regulating early endosomes (rab5) and late endosomes (rab7) are selectively upregulated in homogeneous populations of CA1 neurons from individuals with mild cognitive impairment and Alzheimer's Disease. The levels of these genes are selectively increased as antemortem measures of cognition decline during Alzheimer's Disease progression. Elevation of select rab GTPases regulating endocytosis paralleled the downregulation of genes encoding the neurotrophin receptors TrkB and TrkC.</p>	<p>(Ginsberg et al., 2010)</p>

<p>RAB7 (RAB5A, Member RAS Oncogene Family) Expression levels of genes regulating early endosomes (rab5) and late endosomes (rab7) are selectively upregulated in homogeneous populations of CA1 neurons from individuals with mild cognitive impairment and Alzheimer's Disease. The levels of these genes are selectively increased as antemortem measures of cognition decline during Alzheimer's Disease progression. Elevation of select rab GTPases regulating endocytosis paralleled the downregulation of genes encoding the neurotrophin receptors TrkB and TrkC.</p>	(Ginsberg et al., 2010)
<p>RIG1 (DDX58 DExD/H-Box Helicase 58) Retinoic acid-inducible gene-I (RIG-1) is significantly elevated in the temporal cortex and plasma in patients with mild cognitive impairment.</p>	(de Rivero Vaccari et al., 2014)
<p>RYR2 (Ryanodine Receptor 2) We find an increase in RyR2 transcripts in mild cognitive impairment brains compared with no cognitive impairment. In addition, there is a reduction in a RyR2 splice variant, associated with an antiapoptotic function, in mild cognitive impairment and Alzheimer's Disease brains.</p>	(Bruno et al., 2012)
<p>SOD1 (Superoxide Dismutase 1) Results show that Bax and Sod1 mRNA levels are altered in PBMCs from both mild cognitive impairment and Alzheimer's Disease patients and indicate these changes as potential biomarkers in the early diagnosis of cognitive impairment</p>	(Gatta et al., 2009)
<p>TNF (tumor necrosis factor) Results show increased expression of the TNF, TNFRSF1A and TNFRSF1B genes on both mRNA and protein levels in depression</p>	(Bobinska, Galecka, Szemraj, Galecki, & Talarowska, 2017)
<p>TNFRSF1A (TNF Receptor Superfamily Member 1A) Results show increased expression of the TNF, TNFRSF1A and TNFRSF1B genes on both mRNA and protein levels in depression</p>	(Bobinska et al., 2017)
<p>TNFRSF1B (TNF Receptor Superfamily Member 1B) Results show increased expression of the TNF, TNFRSF1A and TNFRSF1B genes on both mRNA and protein levels in depression</p>	(Bobinska et al., 2017)
<p>TRKA (NTRK1 Neurotrophic Receptor Tyrosine Kinase 1) Individual cholinergic NB neurons displayed a significant down regulation of trkA, trkB, and trkC expression during the progression of Alzheimer's Disease. An intermediate reduction was observed in mild cognitive impairment, with the greatest decrement in mild to moderate Alzheimer's Disease as compared to controls. Importantly, trk down regulation is associated with cognitive decline measured by the Global Cognitive Score (GCS) and the Mini-Mental State Examination (MMSE).</p> <p>Reduced trkA mRNA levels were associated with poorer global cognitive performance and higher Braak scores in the female subjects.</p> <p>Individuals with mild cognitive impairment and Alzheimer's Disease displayed significant reductions in trkA mRNA relative to aged-matched controls, indicating that alterations in trkA</p>	<p>(Ginsberg, Che, Wu, Counts, & Mufson, 2006)</p> <p>(Ikemoto, Yoshida, & Oda, 1992)</p> <p>(Y. Chu, Cochran, Bennett, Mufson, & Kordower, 2001)</p>

gene expression occur early in the disease process.	
<p>TRKB (NTRK2 Neurotrophic Receptor Tyrosine Kinase 2) Neurotrophin receptor tyrosine kinase receptor B (TrkB) and is differentially expressed in the cortex of demented AIDS patients vs those without cognitive impairment +/- AIDS or HIV.</p> <p>Individual cholinergic NB neurons displayed a significant down regulation of trkA, trkB, and trkC expression during the progression of Alzheimer's Disease. An intermediate reduction was observed in mild cognitive impairment, with the greatest decrement in mild to moderate Alzheimer's Disease as compared to controls. Importantly, trk down regulation is associated with cognitive decline measured by the Global Cognitive Score (GCS) and the Mini-Mental State Examination (MMSE).</p> <p>Expression levels of genes regulating early endosomes (rab5) and late endosomes (rab7) are selectively upregulated in homogeneous populations of CA1 neurons from individuals with mild cognitive impairment and Alzheimer's Disease. The levels of these genes are selectively increased as antemortem measures of cognition decline during Alzheimer's Disease progression. Elevation of select rab GTPases regulating endocytosis paralleled the downregulation of genes encoding the neurotrophin receptors TrkB and TrkC.</p>	<p>(Wildemann et al., 2001)</p> <p>(Ginsberg, Che, Wu, et al., 2006)</p> <p>(Ginsberg et al., 2010)</p>
<p>TRKC (NTRK3 Neurotrophic Receptor Tyrosine Kinase 3) Individual cholinergic NB neurons displayed a significant down regulation of trkA, trkB, and trkC expression during the progression of Alzheimer's Disease. An intermediate reduction was observed in mild cognitive impairment, with the greatest decrement in mild to moderate Alzheimer's Disease as compared to controls. Importantly, trk down regulation is associated with cognitive decline measured by the Global Cognitive Score (GCS) and the Mini-Mental State Examination (MMSE).</p> <p>Expression levels of genes regulating early endosomes (rab5) and late endosomes (rab7) are selectively upregulated in homogeneous populations of CA1 neurons from individuals with mild cognitive impairment and Alzheimer's Disease. The levels of these genes are selectively increased as antemortem measures of cognition decline during Alzheimer's Disease progression. Elevation of select rab GTPases regulating endocytosis paralleled the downregulation of genes encoding the neurotrophin receptors TrkB and TrkC.</p>	<p>(Ginsberg, Che, Wu, et al., 2006)</p> <p>(Ginsberg et al., 2010)</p>

References

- Aas, M., Djurovic, S., Athanasiu, L., Steen, N. E., Agartz, I., Lorentzen, S., . . . Melle, I. (2012). Serotonin transporter gene polymorphism, childhood trauma, and cognition in patients with psychotic disorders. *Schizophr Bull*, *38*(1), 15-22. doi:10.1093/schbul/sbr113
- Acosta-Baena, N., Sepulveda-Falla, D., Lopera-Gomez, C. M., Jaramillo-Elorza, M. C., Moreno, S., Aguirre-Acevedo, D. C., . . . Lopera, F. (2011). Pre-dementia clinical stages in presenilin 1 E280A familial early-onset Alzheimer's disease: a retrospective cohort study. *Lancet Neurol*, *10*(3), 213-220. doi:10.1016/S1474-4422(10)70323-9
- Aidaraliev, N. J., Kamino, K., Kimura, R., Yamamoto, M., Morihara, T., Kazui, H., . . . Takeda, M. (2008). Dynamin 2 gene is a novel susceptibility gene for late-onset Alzheimer disease in non-APOE-epsilon4 carriers. *J Hum Genet*, *53*(4), 296-302. doi:10.1007/s10038-008-0251-9
- Albrecht, M. A., Szoek, C., Maruff, P., Savage, G., Lautenschlager, N. T., Ellis, K. A., . . . Group, A. R. (2015). Longitudinal cognitive decline in the AIBL cohort: The role of APOE epsilon4 status. *Neuropsychologia*, *75*, 411-419. doi:10.1016/j.neuropsychologia.2015.06.008
- Alcalay, R. N., Caccappolo, E., Mejia-Santana, H., Tang, M., Rosado, L., Orbe Reilly, M., . . . Marder, K. (2012). Cognitive performance of GBA mutation carriers with early-onset PD: the CORE-PD study. *Neurology*, *78*(18), 1434-1440. doi:10.1212/WNL.0b013e318253d54b
- Alner, K., Hyare, H., Mead, S., Rudge, P., Wroe, S., Rohrer, J. D., . . . Cipolotti, L. (2012). Distinct neuropsychological profiles correspond to distribution of cortical thinning in inherited prion disease caused by insertional mutation. *J Neurol Neurosurg Psychiatry*, *83*(1), 109-114. doi:10.1136/jnnp-2011-300167
- Alosco, M. L., Benitez, A., Gunstad, J., Spitznagel, M. B., McCaffery, J. M., McGeary, J. E., . . . Cohen, R. A. (2013). Reduced memory in fat mass and obesity-associated allele carriers among older adults with cardiovascular disease. *Psychogeriatrics*, *13*(1), 35-40. doi:10.1111/j.1479-8301.2012.00424.x
- Altmann, V., Schumacher-Schuh, A. F., Rieck, M., Callegari-Jacques, S. M., Rieder, C. R., & Hutz, M. H. (2016). Val66Met BDNF polymorphism is associated with Parkinson's disease cognitive impairment. *Neurosci Lett*, *615*, 88-91. doi:10.1016/j.neulet.2016.01.030
- Alvarez, A., Aleixandre, M., Linares, C., Masliah, E., & Moessler, H. (2014). Apathy and APOE4 are associated with reduced BDNF levels in Alzheimer's disease. *J Alzheimers Dis*, *42*(4), 1347-1355. doi:10.3233/JAD-140849
- Amberla, K., Waljas, M., Tuominen, S., Almkvist, O., Poyhonen, M., Tuisku, S., . . . Viitanen, M. (2004). Insidious cognitive decline in CADASIL. *Stroke*, *35*(7), 1598-1602. doi:10.1161/01.STR.0000129787.92085.0a
- Amouyel, P., Richard, F., Cottel, D., Amant, C., Codron, V., & Helbecque, N. (1996). The deletion allele of the angiotensin I converting enzyme gene as a genetic susceptibility factor for cognitive impairment. *Neurosci Lett*, *217*(2-3), 203-205.
- Andres, M. A., Feger, U., Nath, A., Munsaka, S., Jiang, C. S., & Chang, L. (2011). APOE epsilon 4 allele and CSF APOE on cognition in HIV-infected subjects. *J Neuroimmune Pharmacol*, *6*(3), 389-398. doi:10.1007/s11481-010-9254-3

- Andrews, S. J., Das, D., Cherbuin, N., Anstey, K. J., & Eastal, S. (2016). Association of genetic risk factors with cognitive decline: the PATH through life project. *Neurobiol Aging*, *41*, 150-158. doi:10.1016/j.neurobiolaging.2016.02.016
- Ariza, M., Matarin, M. D., Junque, C., Mataro, M., Clemente, I., Moral, P., . . . Sahuquillo, J. (2006). Influence of Angiotensin-converting enzyme polymorphism on neuropsychological subacute performance in moderate and severe traumatic brain injury. *J Neuropsychiatry Clin Neurosci*, *18*(1), 39-44. doi:10.1176/jnp.18.1.39
- Assaraf, M. I., Diaz, Z., Liberman, A., Miller, W. H., Jr., Arvanitakis, Z., Li, Y., . . . Schipper, H. M. (2007). Brain erythropoietin receptor expression in Alzheimer disease and mild cognitive impairment. *J Neuropathol Exp Neurol*, *66*(5), 389-398. doi:10.1097/nen.0b013e3180517b28
- Bakanidze, G., Brandl, E. J., Hutzler, C., Aurass, F., Onken, S., Rapp, M. A., & Puls, I. (2016). Association of Dystrobrevin-Binding Protein 1 Polymorphisms with Sustained Attention and Set-Shifting in Schizophrenia Patients. *Neuropsychobiology*, *74*(1), 41-47. doi:10.1159/000450550
- Ballard, C. G., Morris, C. M., Rao, H., O'Brien, J. T., Barber, R., Stephens, S., . . . Kenny, R. A. (2004). APOE epsilon4 and cognitive decline in older stroke patients with early cognitive impairment. *Neurology*, *63*(8), 1399-1402.
- Barabash, A., Marcos, A., Ancin, I., Vazquez-Alvarez, B., de Ugarte, C., Gil, P., . . . Cabranes, J. A. (2009). APOE, ACT and CHRNA7 genes in the conversion from amnesic mild cognitive impairment to Alzheimer's disease. *Neurobiol Aging*, *30*(8), 1254-1264. doi:10.1016/j.neurobiolaging.2007.11.003
- Barahmani, N., Carpentieri, S., Li, X. N., Wang, T., Cao, Y., Howe, L., . . . Okcu, M. F. (2009). Glutathione S-transferase M1 and T1 polymorphisms may predict adverse effects after therapy in children with medulloblastoma. *Neuro Oncol*, *11*(3), 292-300. doi:10.1215/15228517-2008-089
- Bardoni, A., Felisari, G., Sironi, M., Comi, G., Lai, M., Robotti, M., & Bresolin, N. (2000). Loss of Dp140 regulatory sequences is associated with cognitive impairment in dystrophinopathies. *Neuromuscul Disord*, *10*(3), 194-199.
- Barratt, D. T., Klepstad, P., Dale, O., Kaasa, S., & Somogyi, A. A. (2015). Innate Immune Signalling Genetics of Pain, Cognitive Dysfunction and Sickness Symptoms in Cancer Pain Patients Treated with Transdermal Fentanyl. *PLoS One*, *10*(9), e0137179. doi:10.1371/journal.pone.0137179
- Barrett, M. J., Koeppl, A. F., Flanigan, J. L., Turner, S. D., & Worrall, B. B. (2016). Investigation of Genetic Variants Associated with Alzheimer Disease in Parkinson Disease Cognition. *J Parkinsons Dis*, *6*(1), 119-124. doi:10.3233/jpd-150706
- Bartres-Faz, D., Clemente, I. C., Junque, C., Valveny, N., Lopez-Alomar, A., Sanchez-Aldeguer, J., . . . Moral, P. (2001). APOE and APOC1 genetic polymorphisms in age-associated memory impairment. *Neurogenetics*, *3*(4), 215-219.
- Bartres-Faz, D., Clemente, I. C., Monras, M., Munoz, M., Lopez-Alomar, A., Valveny, N., . . . Junque, C. (2002). Relation of Apo E and ACE genes to cognitive performance in chronic alcoholic patients. *Addict Biol*, *7*(2), 227-233. doi:10.1080/135562102200120451

- Bartres-Faz, D., Junque, C., Clemente, I. C., Lopez-Alomar, A., Valveny, N., Lopez-Guillen, A., . . . Moral, P. (2000). Angiotensin I converting enzyme polymorphism in humans with age-associated memory impairment: relationship with cognitive performance. *Neurosci Lett*, *290*(3), 177-180.
- Bartres-Faz, D., Junque, C., Lopez, A., Valveny, N., Moral, P., Galvez, E., . . . Clemente, I. (1999). Apo E influences declarative and procedural learning in age-associated memory impairment. *Neuroreport*, *10*(14), 2923-2927.
- Bartres-Faz, D., Junque, C., Moral, P., Lopez-Alomar, A., Sanchez-Aldeguer, J., & Clemente, I. C. (2002). Apolipoprotein E gender effects on cognitive performance in age-associated memory impairment. *J Neuropsychiatry Clin Neurosci*, *14*(1), 80-83. doi:10.1176/jnp.14.1.80
- Barzilai, N., Atzmon, G., Derby, C. A., Bauman, J. M., & Lipton, R. B. (2006). A genotype of exceptional longevity is associated with preservation of cognitive function. *Neurology*, *67*(12), 2170-2175. doi:10.1212/01.wnl.0000249116.50854.65
- Bearden, C. E., Jawad, A. F., Lynch, D. R., Sokol, S., Kanes, S. J., McDonald-McGinn, D. M., . . . Simon, T. J. (2004). Effects of a functional COMT polymorphism on prefrontal cognitive function in patients with 22q11.2 deletion syndrome. *Am J Psychiatry*, *161*(9), 1700-1702. doi:10.1176/appi.ajp.161.9.1700
- Begemann, M., Grube, S., Papiol, S., Malzahn, D., Krampe, H., Ribbe, K., . . . Ehrenreich, H. (2010). Modification of cognitive performance in schizophrenia by complexin 2 gene polymorphisms. *Arch Gen Psychiatry*, *67*(9), 879-888. doi:10.1001/archgenpsychiatry.2010.107
- Benedict, C., Jacobsson, J. A., Ronnema, E., Sallman-Almen, M., Brooks, S., Schultes, B., . . . Schioth, H. B. (2011). The fat mass and obesity gene is linked to reduced verbal fluency in overweight and obese elderly men. *Neurobiol Aging*, *32*(6), 1159 e1151-1155. doi:10.1016/j.neurobiolaging.2011.02.006
- Benzerouk, F., Gierski, F., Gorwood, P., Ramoz, N., Stefaniak, N., Hubsch, B., . . . Limosin, F. (2013). Brain-derived neurotrophic factor (BDNF) Val66Met polymorphism and its implication in executive functions in adult offspring of alcohol-dependent probands. *Alcohol*, *47*(4), 271-274. doi:10.1016/j.alcohol.2013.03.001
- Berr, C., Richard, F., Dufouil, C., Amant, C., Alperovitch, A., & Amouyel, P. (1998). Polymorphism of the prion protein is associated with cognitive impairment in the elderly: the EVA study. *Neurology*, *51*(3), 734-737.
- Berry, A. S., Demeter, E., Sabhapathy, S., English, B. A., Blakely, R. D., Sarter, M., & Lustig, C. (2014). Disposed to distraction: genetic variation in the cholinergic system influences distractibility but not time-on-task effects. *J Cogn Neurosci*, *26*(9), 1981-1991. doi:10.1162/jocn_a_00607
- Beydoun, M. A., Boueiz, A., Abougergi, M. S., Kitner-Triolo, M. H., Beydoun, H. A., Resnick, S. M., . . . Zonderman, A. B. (2012). Sex differences in the association of the apolipoprotein E epsilon 4 allele with incidence of dementia, cognitive impairment, and decline. *Neurobiol Aging*, *33*(4), 720-731 e724. doi:10.1016/j.neurobiolaging.2010.05.017
- Biundo, R., Gardini, S., Caffarra, P., Concaro, L., Martorana, D., Neri, T. M., . . . Venneri, A. (2011). Influence of APOE status on lexical-semantic skills in mild cognitive impairment. *J Int Neuropsychol Soc*, *17*(3), 423-430. doi:10.1017/S135561771100021X

- Bobinska, K., Galecka, E., Szemraj, J., Galecki, P., & Talarowska, M. (2017). Is there a link between TNF gene expression and cognitive deficits in depression? *Acta Biochim Pol*, *64*(1), 65-73. doi:10.18388/abp.2016_1276
- Bonner-Jackson, A., Okonkwo, O., Tremont, G., & Alzheimer's Disease Neuroimaging, I. (2012). Apolipoprotein E epsilon2 and functional decline in amnesic mild cognitive impairment and Alzheimer disease. *Am J Geriatr Psychiatry*, *20*(7), 584-593. doi:10.1097/JGP.0b013e3182203c32
- Bosia, M., Buonocore, M., Guglielmino, C., Pirovano, A., Lorenzi, C., Marcone, A., . . . Cavallaro, R. (2012). Saitohin polymorphism and executive dysfunction in schizophrenia. *Neurol Sci*, *33*(5), 1051-1056. doi:10.1007/s10072-011-0893-9
- Bosia, M., Pigoni, A., Zagato, L., Merlino, L., Casamassima, N., Lorenzi, C., . . . Cavallaro, R. (2016). ADDing a piece to the puzzle of cognition in schizophrenia. *Eur J Med Genet*, *59*(1), 26-31. doi:10.1016/j.ejmg.2015.12.012
- Bour, A. M., Rasquin, S. M., Baars, L., van Boxtel, M. P., Visser, P. J., Limburg, M., & Verhey, F. R. (2010). The effect of the APOE-epsilon4 allele and ACE-I/D polymorphism on cognition during a two-year follow-up in first-ever stroke patients. *Dement Geriatr Cogn Disord*, *29*(6), 534-542. doi:10.1159/000314678
- Bretsky, P., Guralnik, J. M., Launer, L., Albert, M., Seeman, T. E., & MacArthur Studies of Successful, A. (2003). The role of APOE-epsilon4 in longitudinal cognitive decline: MacArthur Studies of Successful Aging. *Neurology*, *60*(7), 1077-1081.
- Bruno, A. M., Huang, J. Y., Bennett, D. A., Marr, R. A., Hastings, M. L., & Stutzmann, G. E. (2012). Altered ryanodine receptor expression in mild cognitive impairment and Alzheimer's disease. *Neurobiol Aging*, *33*(5), 1001 e1001-1006. doi:10.1016/j.neurobiolaging.2011.03.011
- Buchman, A. S., Yu, L., Boyle, P. A., Schneider, J. A., De Jager, P. L., & Bennett, D. A. (2016). Higher brain BDNF gene expression is associated with slower cognitive decline in older adults. *Neurology*, *86*(8), 735-741. doi:10.1212/WNL.0000000000002387
- Bufill, E., Roura-Poch, P., Sala-Matavera, I., Anton, S., Lleo, A., Sanchez-Saudinos, B., . . . Blesa, R. (2015). Reelin signaling pathway genotypes and Alzheimer disease in a Spanish population. *Alzheimer Dis Assoc Disord*, *29*(2), 169-172. doi:10.1097/WAD.0000000000000002
- Bungenberg, J., Surano, N., Grote, A., Surges, R., Pernhorst, K., Hofmann, A., . . . Becker, A. J. (2016). Gene expression variance in hippocampal tissue of temporal lobe epilepsy patients corresponds to differential memory performance. *Neurobiol Dis*, *86*, 121-130. doi:10.1016/j.nbd.2015.11.011
- Burdick, K. E., Funke, B., Goldberg, J. F., Bates, J. A., Jaeger, J., Kucherlapati, R., & Malhotra, A. K. (2007). COMT genotype increases risk for bipolar I disorder and influences neurocognitive performance. *Bipolar Disord*, *9*(4), 370-376. doi:10.1111/j.1399-5618.2007.00384.x
- Burdick, K. E., Lencz, T., Funke, B., Finn, C. T., Szeszko, P. R., Kane, J. M., . . . Malhotra, A. K. (2006). Genetic variation in DTNBP1 influences general cognitive ability. *Hum Mol Genet*, *15*(10), 1563-1568. doi:10.1093/hmg/ddi481
- Butcher, L. M., Meaburn, E., Dale, P. S., Sham, P., Schalkwyk, L. C., Craig, I. W., & Plomin, R. (2005). Association analysis of mild mental impairment using DNA pooling to screen 432 brain-expressed single-nucleotide polymorphisms. *Mol Psychiatry*, *10*(4), 384-392. doi:10.1038/sj.mp.4001589

- Byrne, P. C., Mc Monagle, P., Webb, S., Fitzgerald, B., Parfrey, N. A., & Hutchinson, M. (2000). Age-related cognitive decline in hereditary spastic paraparesis linked to chromosome 2p. *Neurology*, *54*(7), 1510-1517.
- Cai, Y., Hu, H., Liu, P., Feng, G., Dong, W., Yu, B., . . . Zhao, M. (2012). Association between the apolipoprotein E4 and postoperative cognitive dysfunction in elderly patients undergoing intravenous anesthesia and inhalation anesthesia. *Anesthesiology*, *116*(1), 84-93. doi:10.1097/ALN.0b013e31823da7a2
- Carrion-Baralt, J. R., Melendez-Cabrero, J., Rodriguez-Ubinas, H., Schmeidler, J., Beeri, M. S., Angelo, G., . . . Silverman, J. M. (2009). Impact of APOE epsilon4 on the cognitive performance of a sample of non-demented Puerto Rican nonagenarians. *J Alzheimers Dis*, *18*(3), 533-540. doi:10.3233/JAD-2009-1160
- Caselli, R. J., Dueck, A. C., Locke, D. E., Hoffman-Snyder, C. R., Woodruff, B. K., Rapcsak, S. Z., & Reiman, E. M. (2011). Longitudinal modeling of frontal cognition in APOE epsilon4 homozygotes, heterozygotes, and noncarriers. *Neurology*, *76*(16), 1383-1388. doi:10.1212/WNL.0b013e3182167147
- Caselli, R. J., Reiman, E. M., Osborne, D., Hentz, J. G., Baxter, L. C., Hernandez, J. L., & Alexander, G. G. (2004). Longitudinal changes in cognition and behavior in asymptomatic carriers of the APOE e4 allele. *Neurology*, *62*(11), 1990-1995.
- Cassidy, C., Buchy, L., Bodnar, M., Dell'elce, J., Choudhry, Z., Fathalli, F., . . . Joober, R. (2014). Association of a risk allele of ANK3 with cognitive performance and cortical thickness in patients with first-episode psychosis. *J Psychiatry Neurosci*, *39*(1), 31-39. doi:10.1503/jpn.120242
- Chai, Y. L., Yeo, H. K., Wang, J., Hilal, S., Ikram, M. K., Venketasubramanian, N., . . . Chen, C. L. (2016). Apolipoprotein varepsilon4 is Associated with Dementia and Cognitive Impairment Predominantly Due to Alzheimer's Disease and Not with Vascular Cognitive Impairment: A Singapore-Based Cohort. *J Alzheimers Dis*, *51*(4), 1111-1118. doi:10.3233/JAD-150902
- Chang, M., Sun, L., Liu, X., Sun, W., & You, X. (2015). Association of common variants in H2AFZ gene with schizophrenia and cognitive function in patients with schizophrenia. *J Hum Genet*, *60*(10), 619-624. doi:10.1038/jhg.2015.89
- Chen, C. J., Chen, C. C., Wu, D., Chi, N. F., Chen, P. C., Liao, Y. P., . . . Hu, C. J. (2013). Effects of the apolipoprotein E epsilon4 allele on functional MRI during n-back working memory tasks in healthy middle-aged adults. *AJNR Am J Neuroradiol*, *34*(6), 1197-1202. doi:10.3174/ajnr.A3369
- Chen, K. D., Chang, P. T., Ping, Y. H., Lee, H. C., Yeh, C. W., & Wang, P. N. (2011). Gene expression profiling of peripheral blood leukocytes identifies and validates ABCB1 as a novel biomarker for Alzheimer's disease. *Neurobiol Dis*, *43*(3), 698-705. doi:10.1016/j.nbd.2011.05.023
- Chen, K. L., Sun, Y. M., Zhou, Y., Zhao, Q. H., Ding, D., & Guo, Q. H. (2016). Associations between APOE polymorphisms and seven diseases with cognitive impairment including Alzheimer's disease, frontotemporal dementia, and dementia with Lewy bodies in southeast China. *Psychiatr Genet*, *26*(3), 124-131. doi:10.1097/YPG.000000000000126
- Chu, C. S., Lu, T., Tsai, S. J., Hong, C. J., Yeh, H. L., Yang, A. C., & Liu, M. E. (2014). APOE varepsilon4 polymorphism and cognitive deficit among the very old Chinese veteran men without dementia. *Neurosci Lett*, *576*, 17-21. doi:10.1016/j.neulet.2014.05.046

- Chu, Y., Cochran, E. J., Bennett, D. A., Mufson, E. J., & Kordower, J. H. (2001). Down-regulation of trkA mRNA within nucleus basalis neurons in individuals with mild cognitive impairment and Alzheimer's disease. *J Comp Neurol*, *437*(3), 296-307.
- Chung, S. J., Kim, M. J., Kim, Y. J., Kim, J., You, S., Jang, E. H., . . . Lee, J. H. (2014). CR1, ABCA7, and APOE genes affect the features of cognitive impairment in Alzheimer's disease. *J Neurol Sci*, *339*(1-2), 91-96. doi:10.1016/j.jns.2014.01.029
- Cornish, K. M., Kogan, C. S., Li, L., Turk, J., Jacquemont, S., & Hagerman, R. J. (2009). Lifespan changes in working memory in fragile X premutation males. *Brain Cogn*, *69*(3), 551-558. doi:10.1016/j.bandc.2008.11.006
- Cornish, K. M., Manly, T., Savage, R., Swanson, J., Morisano, D., Butler, N., . . . Hollis, C. P. (2005). Association of the dopamine transporter (DAT1) 10/10-repeat genotype with ADHD symptoms and response inhibition in a general population sample. *Mol Psychiatry*, *10*(7), 686-698. doi:10.1038/sj.mp.4001641
- Correa, D. D., Satagopan, J., Baser, R. E., Cheung, K., Richards, E., Lin, M., . . . Orlow, I. (2014). APOE polymorphisms and cognitive functions in patients with brain tumors. *Neurology*, *83*(4), 320-327. doi:10.1212/WNL.0000000000000617
- Counts, S. E., He, B., Che, S., Ikonovic, M. D., DeKosky, S. T., Ginsberg, S. D., & Mufson, E. J. (2007). Alpha7 nicotinic receptor up-regulation in cholinergic basal forebrain neurons in Alzheimer disease. *Arch Neurol*, *64*(12), 1771-1776. doi:10.1001/archneur.64.12.1771
- D'Souza, S., Backhouse-Smith, A., Thompson, J. M., Slykerman, R., Marlow, G., Wall, C., . . . Waldie, K. E. (2016). Associations Between the KIAA0319 Dyslexia Susceptibility Gene Variants, Antenatal Maternal Stress, and Reading Ability in a Longitudinal Birth Cohort. *Dyslexia*, *22*(4), 379-393. doi:10.1002/dys.1534
- Daniele, A., & Albanese, A. (2012). Early visual memory deficits: a neuropsychological marker of GBA mutations in PD? *Neurology*, *78*(18), 1372-1373. doi:10.1212/WNL.0b013e318253d67b
- de Rivero Vaccari, J. P., Brand, F. J., 3rd, Sedaghat, C., Mash, D. C., Dietrich, W. D., & Keane, R. W. (2014). RIG-1 receptor expression in the pathology of Alzheimer's disease. *J Neuroinflammation*, *11*, 67. doi:10.1186/1742-2094-11-67
- Degen, C., Zschocke, J., Toro, P., Sattler, C., Wahl, H. W., Schonknecht, P., & Schroder, J. (2016). The COMT Val158Met Polymorphism and Cognitive Performance in Adult Development, Healthy Aging and Mild Cognitive Impairment. *Dement Geriatr Cogn Disord*, *41*(1-2), 27-34. doi:10.1159/000439585
- Del Bo, R., Comi, G. P., Giorda, R., Crimi, M., Locatelli, F., Martinelli-Boneschi, F., . . . Scarlato, G. (2003). The 129 codon polymorphism of the prion protein gene influences earlier cognitive performance in Down syndrome subjects. *J Neurol*, *250*(6), 688-692. doi:10.1007/s00415-003-1057-5
- Di Maria, E., Cammarata, S., Parodi, M. I., Borghi, R., Benussi, L., Galli, M., . . . Tabaton, M. (2010). The H1 haplotype of the tau gene (MAPT) is associated with mild cognitive impairment. *J Alzheimers Dis*, *19*(3), 909-914. doi:10.3233/JAD-2010-1285
- Diaz De Leon Gonzalez, E., Gutierrez Hermsillo, H., Cedillo Rodriguez, J. A., Reyes Romero, M. A., Camacho Luis, A., Palacios Corona, R., . . . Tamez Perez, H. E. (2014). Association between polymorphism c.1-765G>C of the COX2 gene and cognitive impairment in individuals 65 years or more with diabetes from a Geriatric Service in Monterrey, Mexico. *Med Clin (Barc)*, *143*(9), 381-385. doi:10.1016/j.medcli.2013.07.031

- Dickerson, F., Boronow, J., Stallings, C., Origoni, A., & Yolken, R. (2007). The lymphotoxin Cys13Arg polymorphism and cognitive functioning in individuals with schizophrenia. *Schizophr Res*, *89*(1-3), 173-176. doi:10.1016/j.schres.2006.08.015
- Dickerson, F., Stallings, C., Origoni, A., Boronow, J., & Yolken, R. (2007). C-reactive protein is associated with the severity of cognitive impairment but not of psychiatric symptoms in individuals with schizophrenia. *Schizophr Res*, *93*(1-3), 261-265. doi:10.1016/j.schres.2007.03.022
- Dickerson, F., Stallings, C., Sullens, A., Origoni, A., Leister, F., Krivogorsky, B., & Yolken, R. (2008). Association between cognitive functioning, exposure to Herpes Simplex Virus type 1, and the COMT Val158Met genetic polymorphism in adults without a psychiatric disorder. *Brain Behav Immun*, *22*(7), 1103-1107. doi:10.1016/j.bbi.2008.04.156
- Dickerson, F. B., Boronow, J. J., Stallings, C., Origoni, A. E., Cole, S., Leister, F., . . . Yolken, R. H. (2006). The catechol O-methyltransferase Val158Met polymorphism and herpes simplex virus type 1 infection are risk factors for cognitive impairment in bipolar disorder: additive gene-environmental effects in a complex human psychiatric disorder. *Bipolar Disord*, *8*(2), 124-132. doi:10.1111/j.1399-5618.2006.00288.x
- Dik, M. G., Jonker, C., Bouter, L. M., Geerlings, M. I., van Kamp, G. J., & Deeg, D. J. (2000). APOE-epsilon4 is associated with memory decline in cognitively impaired elderly. *Neurology*, *54*(7), 1492-1497.
- Dresler, T., Ehlis, A. C., Heinzl, S., Renner, T. J., Reif, A., Baehne, C. G., . . . Fallgatter, A. J. (2010). Dopamine transporter (SLC6A3) genotype impacts neurophysiological correlates of cognitive response control in an adult sample of patients with ADHD. *Neuropsychopharmacology*, *35*(11), 2193-2202. doi:10.1038/npp.2010.91
- Dube, J. B., Johansen, C. T., Robinson, J. F., Lindsay, J., Hachinski, V., & Hegele, R. A. (2013). Genetic determinants of "cognitive impairment, no dementia". *J Alzheimers Dis*, *33*(3), 831-840. doi:10.3233/JAD-2012-121477
- Dufouil, C., Tzourio, C., Brayne, C., Berr, C., Amouyel, P., & Alperovitch, A. (2000). Influence of apolipoprotein E genotype on the risk of cognitive deterioration in moderate drinkers and smokers. *Epidemiology*, *11*(3), 280-284.
- Eicher, J. D., Stein, C. M., Deng, F., Ciesla, A. A., Powers, N. R., Boada, R., . . . Gruen, J. R. (2015). The DYX2 locus and neurochemical signaling genes contribute to speech sound disorder and related neurocognitive domains. *Genes Brain Behav*, *14*(4), 377-385. doi:10.1111/gbb.12214
- Elias-Sonnenschein, L. S., Viechtbauer, W., Ramakers, I. H., Verhey, F. R., & Visser, P. J. (2011). Predictive value of APOE-epsilon4 allele for progression from MCI to AD-type dementia: a meta-analysis. *J Neurol Neurosurg Psychiatry*, *82*(10), 1149-1156. doi:10.1136/jnnp.2010.231555
- Elwan, O., Madkour, O., Elwan, F., Mostafa, M., Abbas Helmy, A., Abdel-Naseer, M., . . . El Faiuomy, N. (2003). Brain aging in normal Egyptians: cognition, education, personality, genetic and immunological study. *J Neurol Sci*, *211*(1-2), 15-22.
- Fallon, S. J., Smulders, K., Esselink, R. A., van de Warrenburg, B. P., Bloem, B. R., & Cools, R. (2015). Differential optimal dopamine levels for set-shifting and working memory in Parkinson's disease. *Neuropsychologia*, *77*, 42-51. doi:10.1016/j.neuropsychologia.2015.07.031

- Ferris, S., Nordberg, A., Soininen, H., Darreh-Shori, T., & Lane, R. (2009). Progression from mild cognitive impairment to Alzheimer's disease: effects of sex, butyrylcholinesterase genotype, and rivastigmine treatment. *Pharmacogenet Genomics*, *19*(8), 635-646. doi:10.1097/FPC.0b013e32832f8c17
- Ford, A. H., Flicker, L., Hankey, G. J., Norman, P., van Bockxmeer, F. M., & Almeida, O. P. (2012). Homocysteine, methylenetetrahydrofolate reductase C677T polymorphism and cognitive impairment: the health in men study. *Mol Psychiatry*, *17*(5), 559-566. doi:10.1038/mp.2011.18
- Forlenza, O. V., Diniz, B. S., Teixeira, A. L., Ojopi, E. B., Talib, L. L., Mendonca, V. A., . . . Gattaz, W. F. (2010). Effect of brain-derived neurotrophic factor Val66Met polymorphism and serum levels on the progression of mild cognitive impairment. *World J Biol Psychiatry*, *11*(6), 774-780. doi:10.3109/15622971003797241
- Fraga, V. G., Guimaraes, H. C., Teixeira, A. L., Barbosa, M. T., Mateo, E. C., Carvalho, M. G., . . . Gomes, K. B. (2015). Genetic predisposition to higher production of interleukin-6 through -174 G > C polymorphism predicts global cognitive decline in oldest-old with cognitive impairment no dementia. *Arq Neuropsiquiatr*, *73*(11), 899-902. doi:10.1590/0004-282X20150137
- Frydecka, D., Misiak, B., Pawlak-Adamska, E., Karabon, L., Tomkiewicz, A., Sedlaczek, P., . . . Beszlej, J. A. (2015). Interleukin-6: the missing element of the neurocognitive deterioration in schizophrenia? The focus on genetic underpinnings, cognitive impairment and clinical manifestation. *Eur Arch Psychiatry Clin Neurosci*, *265*(6), 449-459. doi:10.1007/s00406-014-0533-5
- Fu, B. Y., Ma, S. L., Tang, N. L., Tam, C. W., Lui, V. W., Chiu, H. F., & Lam, L. C. (2009). Cholesterol 24-hydroxylase (CYP46A1) polymorphisms are associated with faster cognitive deterioration in Chinese older persons: a two-year follow up study. *Int J Geriatr Psychiatry*, *24*(9), 921-926. doi:10.1002/gps.2196
- Fu, Y., He, F., Tang, N. L., Tam, C. W., Lui, V. W., Chiu, H. F., & Lam, L. C. (2012). NEDD9 gene polymorphism influences the risk of Alzheimer disease and cognitive function in Chinese older persons. *Alzheimer Dis Assoc Disord*, *26*(1), 88-90. doi:10.1097/WAD.0b013e3182135ef3
- Gahete, M. D., Rubio, A., Cordoba-Chacon, J., Gracia-Navarro, F., Kineman, R. D., Avila, J., . . . Castano, J. P. (2010). Expression of the ghrelin and neurotensin systems is altered in the temporal lobe of Alzheimer's disease patients. *J Alzheimers Dis*, *22*(3), 819-828. doi:10.3233/JAD-2010-100873
- Galderisi, S., Maj, M., Kirkpatrick, B., Piccardi, P., Mucci, A., Invernizzi, G., . . . Del Zompo, M. (2005). Catechol-O-methyltransferase Val158Met polymorphism in schizophrenia: associations with cognitive and motor impairment. *Neuropsychobiology*, *52*(2), 83-89. doi:10.1159/000087096
- Gambardella, A., Aguglia, U., Chifari, R., Labate, A., Manna, I., Serra, P., . . . Quattrone, A. (2005). ApoE epsilon4 allele and disease duration affect verbal learning in mild temporal lobe epilepsy. *Epilepsia*, *46*(1), 110-117. doi:10.1111/j.0013-9580.2005.15804.x
- Gatta, L., Cardinale, A., Wannenes, F., Consoli, C., Armani, A., Molinari, F., . . . Fini, M. (2009). Peripheral blood mononuclear cells from mild cognitive impairment patients show deregulation of Bax and Sod1 mRNAs. *Neurosci Lett*, *453*(1), 36-40. doi:10.1016/j.neulet.2009.02.003

- Gill, C. J., Mwananyanda, L., MacLeod, W., Kwenda, G., Mwale, M., Williams, A. L., . . . Thea, D. M. (2016). Incidence of Severe and Nonsevere Pertussis Among HIV-Exposed and -Unexposed Zambian Infants Through 14 Weeks of Age: Results From the Southern Africa Mother Infant Pertussis Study (SAMIPS), a Longitudinal Birth Cohort Study. *Clin Infect Dis*, *63*(suppl 4), S154-S164. doi:10.1093/cid/ciw526
- Ginsberg, S. D., Alldred, M. J., Counts, S. E., Cataldo, A. M., Neve, R. L., Jiang, Y., . . . Che, S. (2010). Microarray analysis of hippocampal CA1 neurons implicates early endosomal dysfunction during Alzheimer's disease progression. *Biol Psychiatry*, *68*(10), 885-893. doi:10.1016/j.biopsych.2010.05.030
- Ginsberg, S. D., Che, S., Counts, S. E., & Mufson, E. J. (2006). Shift in the ratio of three-repeat tau and four-repeat tau mRNAs in individual cholinergic basal forebrain neurons in mild cognitive impairment and Alzheimer's disease. *J Neurochem*, *96*(5), 1401-1408. doi:10.1111/j.1471-4159.2005.03641.x
- Ginsberg, S. D., Che, S., Wu, J., Counts, S. E., & Mufson, E. J. (2006). Down regulation of trk but not p75NTR gene expression in single cholinergic basal forebrain neurons mark the progression of Alzheimer's disease. *J Neurochem*, *97*(2), 475-487. doi:10.1111/j.1471-4159.2006.03764.x
- Giunta, M., Rigamonti, A. E., Scarpini, E., Galimberti, D., Bonomo, S. M., Venturelli, E., . . . Cella, S. G. (2007). The leukocyte expression of CD36 is low in patients with Alzheimer's disease and mild cognitive impairment. *Neurobiol Aging*, *28*(4), 515-518. doi:10.1016/j.neurobiolaging.2006.02.002
- Godler, D. E., Slater, H. R., Bui, Q. M., Storey, E., Ono, M. Y., Gehling, F., . . . Loesch, D. Z. (2012). Fragile X mental retardation 1 (FMR1) intron 1 methylation in blood predicts verbal cognitive impairment in female carriers of expanded FMR1 alleles: evidence from a pilot study. *Clin Chem*, *58*(3), 590-598. doi:10.1373/clinchem.2011.177626
- Golanska, E., Sieruta, M., Gresner, S. M., Pfeffer, A., Chodakowska-Zebrowska, M., Sobow, T. M., . . . Liberski, P. P. (2013). APBB2 genetic polymorphisms are associated with severe cognitive impairment in centenarians. *Exp Gerontol*, *48*(4), 391-394. doi:10.1016/j.exger.2013.01.013
- Gomar, J. J., Conejero-Goldberg, C., Huey, E. D., Davies, P., Goldberg, T. E., & Alzheimer's Disease Neuroimaging, I. (2016). Lack of neural compensatory mechanisms of BDNF val66met met carriers and APOE E4 carriers in healthy aging, mild cognitive impairment, and Alzheimer's disease. *Neurobiol Aging*, *39*, 165-173. doi:10.1016/j.neurobiolaging.2015.12.004
- Gomperts, S. N., Locascio, J. J., Rentz, D., Santarlasci, A., Marquie, M., Johnson, K. A., & Growdon, J. H. (2013). Amyloid is linked to cognitive decline in patients with Parkinson disease without dementia. *Neurology*, *80*(1), 85-91. doi:10.1212/WNL.0b013e31827b1a07
- Goris, A., Williams-Gray, C. H., Clark, G. R., Foltynie, T., Lewis, S. J., Brown, J., . . . Sawcer, S. J. (2007). Tau and alpha-synuclein in susceptibility to, and dementia in, Parkinson's disease. *Ann Neurol*, *62*(2), 145-153. doi:10.1002/ana.21192
- Gozal, D., Khalyfa, A., Capdevila, O. S., Kheirandish-Gozal, L., Khalyfa, A. A., & Kim, J. (2012). Cognitive function in prepubertal children with obstructive sleep apnea: a modifying role for NADPH oxidase p22 subunit gene polymorphisms? *Antioxid Redox Signal*, *16*(2), 171-177. doi:10.1089/ars.2011.4189

- Grant, J. E., Leppink, E. W., Redden, S. A., Odlaug, B. L., & Chamberlain, S. R. (2015). COMT genotype, gambling activity, and cognition. *J Psychiatr Res*, *68*, 371-376. doi:10.1016/j.jpsychires.2015.04.029
- Greenbaum, L., Springer, R. R., Lutz, M. W., Heymann, A., Lubitz, I., Cooper, I., . . . Beeri, M. S. (2014). The TOMM40 poly-T rs10524523 variant is associated with cognitive performance among non-demented elderly with type 2 diabetes. *Eur Neuropsychopharmacol*, *24*(9), 1492-1499. doi:10.1016/j.euroneuro.2014.06.002
- Grigsby, J., Brega, A. G., Leehey, M. A., Goodrich, G. K., Jacquemont, S., Loesch, D. Z., . . . Hagerman, R. J. (2007). Impairment of executive cognitive functioning in males with fragile X-associated tremor/ataxia syndrome. *Mov Disord*, *22*(5), 645-650. doi:10.1002/mds.21359
- Grimm, S., Gartner, M., Fuge, P., Fan, Y., Weigand, A., Feeser, M., . . . Bajbouj, M. (2015). Variation in the corticotropin-releasing hormone receptor 1 (CRHR1) gene modulates age effects on working memory. *J Psychiatr Res*, *61*, 57-63. doi:10.1016/j.jpsychires.2014.12.001
- Guerini, F. R., Agliardi, C., Sironi, M., Arosio, B., Calabrese, E., Zanzottera, M., . . . Clerici, M. (2014). Possible association between SNAP-25 single nucleotide polymorphisms and alterations of categorical fluency and functional MRI parameters in Alzheimer's disease. *J Alzheimers Dis*, *42*(3), 1015-1028. doi:10.3233/JAD-140057
- Guerini, F. R., Beghi, E., Riboldazzi, G., Zangaglia, R., Pianezzola, C., Bono, G., . . . Martignoni, E. (2009). BDNF Val66Met polymorphism is associated with cognitive impairment in Italian patients with Parkinson's disease. *Eur J Neurol*, *16*(11), 1240-1245. doi:10.1111/j.1468-1331.2009.02706.x
- Gunstad, J., Benitez, A., Hoth, K. F., Spitznagel, M. B., McCaffery, J., McGeary, J., . . . Cohen, R. A. (2009). P-selectin 1087G/A polymorphism is associated with neuropsychological test performance in older adults with cardiovascular disease. *Stroke*, *40*(9), 2969-2972. doi:10.1161/STROKEAHA.109.553339
- Guo, J., Liu, Z., Dai, H., Zhu, Z., Wang, H., Yang, C., . . . Wang, G. (2014). Preliminary investigation of the influence of CREB1 gene polymorphisms on cognitive dysfunction in Chinese patients with major depression. *Int J Neurosci*, *124*(1), 22-29. doi:10.3109/00207454.2013.816956
- Hallam, B. J., Jacova, C., Hsiung, G. Y., Wittenberg, D., Sengdy, P., Bouchard-Kerr, P., . . . Mackenzie, I. R. (2014). Early neuropsychological characteristics of progranulin mutation carriers. *J Int Neuropsychol Soc*, *20*(7), 694-703. doi:10.1017/S1355617714000551
- Hao, Q., Ding, X., Gao, L., Yang, M., & Dong, B. (2016). G-395A polymorphism in the promoter region of the KLOTHO gene associates with reduced cognitive impairment among the oldest old. *Age (Dordr)*, *38*(1), 7. doi:10.1007/s11357-015-9869-7
- Hargreaves, A., Anney, R., O'Dushlaine, C., Nicodemus, K. K., Schizophrenia Psychiatric Genome-Wide Association Study, C., Wellcome Trust Case Control, C., . . . Donohoe, G. (2014). The one and the many: effects of the cell adhesion molecule pathway on neuropsychological function in psychosis. *Psychol Med*, *44*(10), 2177-2187. doi:10.1017/S0033291713002663

- Harries, L. W., Bradley-Smith, R. M., Llewellyn, D. J., Pilling, L. C., Fellows, A., Henley, W., . . . Melzer, D. (2012). Leukocyte CCR2 expression is associated with mini-mental state examination score in older adults. *Rejuvenation Res*, *15*(4), 395-404. doi:10.1089/rej.2011.1302
- Harwood, D. G., Barker, W. W., Ownby, R. L., Mullan, M., & Duara, R. (2002). Apolipoprotein E polymorphism and cognitive impairment in a bi-ethnic community-dwelling elderly sample. *Alzheimer Dis Assoc Disord*, *16*(1), 8-14.
- Hashimoto, R., Ohi, K., Yasuda, Y., Fukumoto, M., Iwase, M., Iike, N., . . . Takeda, M. (2010). The impact of a genome-wide supported psychosis variant in the ZNF804A gene on memory function in schizophrenia. *Am J Med Genet B Neuropsychiatr Genet*, *153B*(8), 1459-1464. doi:10.1002/ajmg.b.31123
- Hausner, L., Tschape, J. A., Schmitt, H. P., Hentschel, F., Hartmann, T., & Frolich, L. (2014). Clinical characterization of a presenilin 1 mutation (F177S) in a family with very early-onset Alzheimer's disease in the third decade of life. *Alzheimers Dement*, *10*(2), e27-39. doi:10.1016/j.jalz.2013.02.006
- Helbecque, N., Codron, V., Cottel, D., & Amouyel, P. (2008). An apolipoprotein A-I gene promoter polymorphism associated with cognitive decline, but not with Alzheimer's disease. *Dement Geriatr Cogn Disord*, *25*(2), 97-102. doi:10.1159/000112176
- Henderson, A. S., Easteal, S., Jorm, A. F., Mackinnon, A. J., Korten, A. E., Christensen, H., . . . Jacomb, P. A. (1995). Apolipoprotein E allele epsilon 4, dementia, and cognitive decline in a population sample. *Lancet*, *346*(8987), 1387-1390.
- Heyer, E. J., Mergeche, J. L., Stern, Y., Malone, H. R., Bruce, S. S., Ward, J. T., & Sander Connolly, E. (2014). Apolipoprotein E-epsilon4 polymorphism and cognitive dysfunction after carotid endarterectomy. *J Clin Neurosci*, *21*(2), 236-240. doi:10.1016/j.jocn.2013.04.009
- Heyer, E. J., Mergeche, J. L., Ward, J. T., Malone, H. R., Kellner, C., Bruce, S. S., & Connolly, E. S. (2013). Phosphodiesterase 4D single-nucleotide polymorphism 83 and cognitive dysfunction in carotid endarterectomy patients. *Neurosurgery*, *73*(5), 791-796; discussion 796. doi:10.1227/NEU.00000000000000085
- Hill, S. K., Bjorkquist, O., Carrathers, T., Roseberry, J. E., Hochberger, W. C., & Bishop, J. R. (2013). Sequential processing deficits in schizophrenia: relationship to neuropsychology and genetics. *Schizophr Res*, *151*(1-3), 91-96. doi:10.1016/j.schres.2013.09.012
- Ho, B. C., Milev, P., O'Leary, D. S., Librant, A., Andreasen, N. C., & Wassink, T. H. (2006). Cognitive and magnetic resonance imaging brain morphometric correlates of brain-derived neurotrophic factor Val66Met gene polymorphism in patients with schizophrenia and healthy volunteers. *Arch Gen Psychiatry*, *63*(7), 731-740. doi:10.1001/archpsyc.63.7.731
- Ho, B. C., Wassink, T. H., Ziebell, S., & Andreasen, N. C. (2011). Cannabinoid receptor 1 gene polymorphisms and marijuana misuse interactions on white matter and cognitive deficits in schizophrenia. *Schizophr Res*, *128*(1-3), 66-75. doi:10.1016/j.schres.2011.02.021
- Ho, L., Zhao, W., Dams-O'Connor, K., Tang, C. Y., Gordon, W., Peskind, E. R., . . . Pasinetti, G. M. (2012). Elevated plasma MCP-1 concentration following traumatic brain injury as a potential "predisposition" factor associated with an increased risk for subsequent development of Alzheimer's disease. *J Alzheimers Dis*, *31*(2), 301-313. doi:10.3233/JAD-2012-120598

- Holland, D., Desikan, R. S., Dale, A. M., McEvoy, L. K., & Alzheimer's Disease Neuroimaging, I. (2013). Higher rates of decline for women and apolipoprotein E epsilon4 carriers. *AJNR Am J Neuroradiol*, *34*(12), 2287-2293. doi:10.3174/ajnr.A3601
- Hong, Y. J., Yoon, B., Shim, Y. S., Kim, S. O., Kim, H. J., Choi, S. H., . . . Lee, J. H. (2015). Predictors of Clinical Progression of Subjective Memory Impairment in Elderly Subjects: Data from the Clinical Research Centers for Dementia of South Korea (CREDOS). *Dement Geriatr Cogn Disord*, *40*(3-4), 158-165. doi:10.1159/000430807
- Hou, Z., Yuan, Y., Zhang, Z., Hou, G., You, J., & Bai, F. (2010). The D-allele of ACE insertion/deletion polymorphism is associated with regional white matter volume changes and cognitive impairment in remitted geriatric depression. *Neurosci Lett*, *479*(3), 262-266. doi:10.1016/j.neulet.2010.05.076
- Howieson, D. B., Camicioli, R., Quinn, J., Silbert, L. C., Care, B., Moore, M. M., . . . Kaye, J. A. (2003). Natural history of cognitive decline in the old old. *Neurology*, *60*(9), 1489-1494.
- Hu, X., Pickering, E. H., Hall, S. K., Naik, S., Liu, Y. C., Soares, H., . . . John, S. L. (2011). Genome-wide association study identifies multiple novel loci associated with disease progression in subjects with mild cognitive impairment. *Transl Psychiatry*, *1*, e54. doi:10.1038/tp.2011.50
- Huang, Y., Zheng, L., Halliday, G., Dobson-Stone, C., Wang, Y., Tang, H. D., . . . Chen, S. D. (2011). Genetic polymorphisms in sigma-1 receptor and apolipoprotein E interact to influence the severity of Alzheimer's disease. *Curr Alzheimer Res*, *8*(7), 765-770.
- Huntington Study Group, P. I., Biglan, K. M., Shoulson, I., Kieburtz, K., Oakes, D., Kayson, E., . . . Shults, C. (2016). Clinical-Genetic Associations in the Prospective Huntington at Risk Observational Study (PHAROS): Implications for Clinical Trials. *JAMA Neurol*, *73*(1), 102-110. doi:10.1001/jamaneurol.2015.2736
- Iacono, D., Zandi, P., Gross, M., Markesbery, W. R., Pletnikova, O., Rudow, G., & Troncoso, J. C. (2015). APOepsilon2 and education in cognitively normal older subjects with high levels of AD pathology at autopsy: findings from the Nun Study. *Oncotarget*, *6*(16), 14082-14091. doi:10.18632/oncotarget.4118
- Iakoubov, L., Mossakowska, M., Szwed, M., & Puzianowska-Kuznicka, M. (2015). A common copy number variation polymorphism in the CNTNAP2 gene: sexual dimorphism in association with healthy aging and disease. *Gerontology*, *61*(1), 24-31. doi:10.1159/000363320
- Ikemoto, Y., Yoshida, A., & Oda, M. (1992). Blockade by trifluoperazine of a Ca(2+)-activated K+ channel in rat hippocampal pyramidal neurons. *Eur J Pharmacol*, *216*(2), 191-198.
- Jason, G. W., Suchowersky, O., Pajurkova, E. M., Graham, L., Klimek, M. L., Garber, A. T., & Poirier-Heine, D. (1997). Cognitive manifestations of Huntington disease in relation to genetic structure and clinical onset. *Arch Neurol*, *54*(9), 1081-1088.
- Katsel, P., Tan, W., Fam, P., Purohit, D. P., & Haroutunian, V. (2013). Cell cycle checkpoint abnormalities during dementia: A plausible association with the loss of protection against oxidative stress in Alzheimer's disease [corrected]. *PLoS One*, *8*(7), e68361. doi:10.1371/journal.pone.0068361

- Kelley, B. J., Haidar, W., Boeve, B. F., Baker, M., Shiung, M., Knopman, D. S., . . . Petersen, R. C. (2010). Alzheimer disease-like phenotype associated with the c.154delA mutation in progranulin. *Arch Neurol*, *67*(2), 171-177. doi:10.1001/archneurol.2010.113
- Kerchner, G. A., Berdnik, D., Shen, J. C., Bernstein, J. D., Fenesy, M. C., Deutsch, G. K., . . . Rutt, B. K. (2014). APOE epsilon4 worsens hippocampal CA1 apical neuropil atrophy and episodic memory. *Neurology*, *82*(8), 691-697. doi:10.1212/WNL.0000000000000154
- Kim, E., Lee, S. H., Lee, K. S., Cheong, H. K., Namkoong, K., Hong, C. H., & Oh, B. H. (2012). AMPK gamma2 subunit gene PRKAG2 polymorphism associated with cognitive impairment as well as diabetes in old age. *Psychoneuroendocrinology*, *37*(3), 358-365. doi:10.1016/j.psyneuen.2011.07.005
- Kircher, T., Krug, A., Markov, V., Whitney, C., Krach, S., Zerres, K., . . . Rietschel, M. (2009). Genetic variation in the schizophrenia-risk gene neuregulin 1 correlates with brain activation and impaired speech production in a verbal fluency task in healthy individuals. *Hum Brain Mapp*, *30*(10), 3406-3416. doi:10.1002/hbm.20761
- Klages, J., & Fisk, J. D. (2002). The relation between APOE status and neuropsychological memory test performance: an analysis of the Canadian Study of Health and Aging. *Brain Cogn*, *49*(2), 201-204.
- Klarner, B., Klunemann, H. H., Lurding, R., Aslanidis, C., & Rupprecht, R. (2007). Neuropsychological profile of adult patients with Niemann-Pick C1 (NPC1) mutations. *J Inherit Metab Dis*, *30*(1), 60-67. doi:10.1007/s10545-006-0417-6
- Kobayashi, N., Nagata, T., Shinagawa, S., Nakayama, R., Kondo, K., Nakayama, K., & Yamada, H. (2012). Association between neurotrophin-3 polymorphisms and executive function in Japanese patients with amnesic mild cognitive impairment and mild Alzheimer disease. *Dement Geriatr Cogn Disord*, *34*(3-4), 190-197. doi:10.1159/000343075
- Kobayashi, N., Shinagawa, S., Nagata, T., Shimada, K., Shibata, N., Ohnuma, T., . . . Kondo, K. (2016). Development of Biomarkers Based on DNA Methylation in the NCAPH2/LMF2 Promoter Region for Diagnosis of Alzheimer's Disease and Amnesic Mild Cognitive Impairment. *PLoS One*, *11*(1), e0146449. doi:10.1371/journal.pone.0146449
- Kontis, D., Theochari, E., Fryssira, H., Kleisas, S., Sofocleous, C., Andreopoulou, A., . . . Tsaltas, E. (2013). COMT and MTHFR polymorphisms interaction on cognition in schizophrenia: an exploratory study. *Neurosci Lett*, *537*, 17-22. doi:10.1016/j.neulet.2013.01.012
- Kos, M. Z., Carless, M. A., Peralta, J., Blackburn, A., Almeida, M., Roalf, D., . . . Almasy, L. (2016). Exome Sequence Data From Multigenerational Families Implicate AMPA Receptor Trafficking in Neurocognitive Impairment and Schizophrenia Risk. *Schizophr Bull*, *42*(2), 288-300. doi:10.1093/schbul/sbv135
- Koutroumani, M., Daniilidou, M., Giannakouros, T., Proitsi, P., Liapi, D., Germanou, A., . . . Tsolaki, M. (2013). The deletion variant of alpha2b-adrenergic receptor is associated with decreased risk in Alzheimer's disease and mild cognitive impairment. *J Neurol Sci*, *328*(1-2), 19-23. doi:10.1016/j.jns.2013.02.003

- Koutsis, G., Panas, M., Giogkaraki, E., Karadima, G., Sfagos, C., & Vassilopoulos, D. (2009). An APOA1 promoter polymorphism is associated with cognitive performance in patients with multiple sclerosis. *Mult Scler*, *15*(2), 174-179. doi:10.1177/1352458508097217
- Koutsis, G., Panas, M., Giogkaraki, E., Potagas, C., Karadima, G., Sfagos, C., & Vassilopoulos, D. (2007). APOE epsilon4 is associated with impaired verbal learning in patients with MS. *Neurology*, *68*(8), 546-549. doi:10.1212/01.wnl.0000254468.51973.44
- Kukulja, J., Thiel, C. M., Eggermann, T., Zerres, K., & Fink, G. R. (2010). Medial temporal lobe dysfunction during encoding and retrieval of episodic memory in non-demented APOE epsilon4 carriers. *Neuroscience*, *168*(2), 487-497. doi:10.1016/j.neuroscience.2010.03.044
- Kutner, K. C., Erlanger, D. M., Tsai, J., Jordan, B., & Relkin, N. R. (2000). Lower cognitive performance of older football players possessing apolipoprotein E epsilon4. *Neurosurgery*, *47*(3), 651-657; discussion 657-658.
- Laczo, J., Andel, R., Vyhnalek, M., Vlcek, K., Nedelska, Z., Matoska, V., . . . Hort, J. (2014). APOE and spatial navigation in amnesic MCI: results from a computer-based test. *Neuropsychology*, *28*(5), 676-684. doi:10.1037/neu0000072
- Lai, C. L., Liou, L. M., Liu, C. K., Yang, Y. H., & Lin, R. T. (2014). Effects of metabolic syndrome, apolipoprotein E, and CYP46 on cognition among Taiwanese Chinese. *Kaohsiung J Med Sci*, *30*(7), 343-349. doi:10.1016/j.kjms.2014.03.005
- Lane, R., Feldman, H. H., Meyer, J., He, Y., Ferris, S. H., Nordberg, A., . . . Greig, N. H. (2008). Synergistic effect of apolipoprotein E epsilon4 and butyrylcholinesterase K-variant on progression from mild cognitive impairment to Alzheimer's disease. *Pharmacogenet Genomics*, *18*(4), 289-298. doi:10.1097/FPC.0b013e3282f63f29
- Lara, V. P., Caramelli, P., Teixeira, A. L., Barbosa, M. T., Carmona, K. C., Guimaraes, H. C., . . . Gomes, K. B. (2016). Cortisol, HDL-c, VLDL-c, and APOE Polymorphisms as Laboratorial Parameters Associated to Cognitive Impairment No Dementia (CIND) and Dementia. *J Clin Lab Anal*, *30*(5), 374-380. doi:10.1002/jcla.21865
- Laws, S. M., Clarnette, R. M., Taddei, K., Martins, G., Paton, A., Almeida, O. P., . . . Martins, R. N. (2002). Association between the presenilin-1 mutation Glu318Gly and complaints of memory impairment. *Neurobiol Aging*, *23*(1), 55-58.
- Leblond, C. S., Nava, C., Polge, A., Gauthier, J., Huguet, G., Lumbroso, S., . . . Bourgeron, T. (2014). Meta-analysis of SHANK Mutations in Autism Spectrum Disorders: a gradient of severity in cognitive impairments. *PLoS Genet*, *10*(9), e1004580. doi:10.1371/journal.pgen.1004580
- Lehmann, D. J., Refsum, H., Nurk, E., Warden, D. R., Tell, G. S., Vollset, S. E., . . . Smith, A. D. (2006). Apolipoprotein E epsilon4 and impaired episodic memory in community-dwelling elderly people: a marked sex difference. The Hordaland Health Study. *J Neurol Neurosurg Psychiatry*, *77*(8), 902-908. doi:10.1136/jnnp.2005.077818
- Leroi, I., Barraclough, M., McKie, S., Hinvest, N., Evans, J., Elliott, R., & McDonald, K. (2013). Dopaminergic influences on executive function and impulsive behaviour in impulse control disorders in Parkinson's disease. *J Neuropsychol*, *7*(2), 306-325. doi:10.1111/jnp.12026

- Liao, Y. C., Hsiao, C. T., Fuh, J. L., Chern, C. M., Lee, W. J., Guo, Y. C., . . . Lee, Y. C. (2015). Characterization of CADASIL among the Han Chinese in Taiwan: Distinct Genotypic and Phenotypic Profiles. *PLoS One*, *10*(8), e0136501. doi:10.1371/journal.pone.0136501
- Lim, Y. Y., Villemagne, V. L., Laws, S. M., Ames, D., Pietrzak, R. H., Ellis, K. A., . . . Group, A. R. (2014). Effect of BDNF Val66Met on memory decline and hippocampal atrophy in prodromal Alzheimer's disease: a preliminary study. *PLoS One*, *9*(1), e86498. doi:10.1371/journal.pone.0086498
- Lim, Y. Y., Villemagne, V. L., Laws, S. M., Ames, D., Pietrzak, R. H., Ellis, K. A., . . . Lifestyle Research, G. (2013). BDNF Val66Met, Abeta amyloid, and cognitive decline in preclinical Alzheimer's disease. *Neurobiol Aging*, *34*(11), 2457-2464. doi:10.1016/j.neurobiolaging.2013.05.006
- Lim, Y. Y., Villemagne, V. L., Laws, S. M., Pietrzak, R. H., Snyder, P. J., Ames, D., . . . Maruff, P. (2015). APOE and BDNF polymorphisms moderate amyloid beta-related cognitive decline in preclinical Alzheimer's disease. *Mol Psychiatry*, *20*(11), 1322-1328. doi:10.1038/mp.2014.123
- Liu, C. G., Song, J., Zhang, Y. Q., & Wang, P. C. (2014). MicroRNA-193b is a regulator of amyloid precursor protein in the blood and cerebrospinal fluid derived exosomal microRNA-193b is a biomarker of Alzheimer's disease. *Mol Med Rep*, *10*(5), 2395-2400. doi:10.3892/mmr.2014.2484
- Liu, J. J., Lavebratt, C., Lou, F., & Forsell, Y. (2015). KIBRA genetic polymorphism and cognitive dysfunction in depression. *Psychiatry Res*, *226*(1), 405-406. doi:10.1016/j.psychres.2015.01.012
- Liu, X., Shi, Y., Niu, B., Shi, Z., Li, J., Ma, Z., . . . Zhang, K. (2016). Polymorphic variation in CHAT gene modulates general cognitive ability: An association study with random student cohort. *Neurosci Lett*, *617*, 122-126. doi:10.1016/j.neulet.2016.02.002
- Liu, X., Yue, C., Xu, Z., Shu, H., Pu, M., Yu, H., . . . Zhang, Z. (2012). Association study of candidate gene polymorphisms with amnesic mild cognitive impairment in a Chinese population. *PLoS One*, *7*(7), e41198. doi:10.1371/journal.pone.0041198
- Louko, A. M., Vilkki, J., & Niskakangas, T. (2006). ApoE genotype and cognition after subarachnoid haemorrhage: a longitudinal study. *Acta Neurol Scand*, *114*(5), 315-319. doi:10.1111/j.1600-0404.2006.00676.x
- Lovell, M. A., Soman, S., & Bradley, M. A. (2011). Oxidatively modified nucleic acids in preclinical Alzheimer's disease (PCAD) brain. *Mech Ageing Dev*, *132*(8-9), 443-448. doi:10.1016/j.mad.2011.08.003
- Luczywek, E., Nowicka, A., Pfeffer, A., Czyzewski, K., Styczynska, M., Lalowski, M., & Barcikowska, M. (2002). Cognitive deficits and polymorphism of apolipoprotein E in Alzheimer's disease. *Dement Geriatr Cogn Disord*, *13*(3), 171-177. doi:48649
- Luo, M., Ji, H., Zhou, X., Liang, J., & Zou, T. (2015). Correlation of homocysteine metabolic enzymes gene polymorphism and mild cognitive impairment in the Xinjiang Uygur population. *Med Sci Monit*, *21*, 326-332. doi:10.12659/MSM.893226
- Luo, M., Zhou, X., Ji, H., Ma, W., Liu, G., Dai, D., . . . Wang, Q. (2015). Population Difference in the Associations of KLOTH Promoter Methylation with Mild Cognitive Impairment in Xinjiang Uygur and Han Populations. *PLoS One*, *10*(7), e0132156. doi:10.1371/journal.pone.0132156

- Ma, C., Zhang, Y., Li, X., Chen, Y., Zhang, J., Liu, Z., . . . Zhang, Z. (2016). The TT allele of rs405509 synergizes with APOE epsilon4 in the impairment of cognition and its underlying default mode network in non-demented elderly. *Curr Alzheimer Res*, *13*(6), 708-717.
- Ma, Z., Niu, B., Shi, Z., Li, J., Wang, J., Zhang, F., . . . Zhang, K. (2017). Genetic Polymorphism of GABRR2 Modulates Individuals' General Cognitive Ability in Healthy Chinese Han People. *Cell Mol Neurobiol*, *37*(1), 93-100. doi:10.1007/s10571-016-0347-2
- MacPherson, S. E., Parra, M. A., Moreno, S., Lopera, F., & Della Sala, S. (2015). Dual memory task impairment in E280A presenilin-1 mutation carriers. *J Alzheimers Dis*, *44*(2), 481-492. doi:10.3233/JAD-140990
- Malec-Litwinowicz, M., Rudzinska, M., Szubiga, M., Michalski, M., Tomaszewski, T., & Szczudlik, A. (2014). Cognitive impairment in carriers of glucocerebrosidase gene mutation in Parkinson disease patients. *Neurol Neurochir Pol*, *48*(4), 258-261. doi:10.1016/j.pjnns.2014.07.005
- Marques, S. C., Lemos, R., Ferreira, E., Martins, M., de Mendonca, A., Santana, I., . . . Pereira, C. M. (2012). Epigenetic regulation of BACE1 in Alzheimer's disease patients and in transgenic mice. *Neuroscience*, *220*, 256-266. doi:10.1016/j.neuroscience.2012.06.029
- Martikainen, M. H., Ellfolk, U., & Majamaa, K. (2013). Impaired information-processing speed and working memory in leukoencephalopathy with brainstem and spinal cord involvement and elevated lactate (LBSL) and DARS2 mutations: a report of three adult patients. *J Neurol*, *260*(8), 2078-2083. doi:10.1007/s00415-013-6940-0
- Mata, I. F., Leverenz, J. B., Weintraub, D., Trojanowski, J. Q., Chen-Plotkin, A., Van Deerlin, V. M., . . . Zabetian, C. P. (2016). GBA Variants are associated with a distinct pattern of cognitive deficits in Parkinson's disease. *Mov Disord*, *31*(1), 95-102. doi:10.1002/mds.26359
- Mata, I. F., Leverenz, J. B., Weintraub, D., Trojanowski, J. Q., Hurtig, H. I., Van Deerlin, V. M., . . . Zabetian, C. P. (2014). APOE, MAPT, and SNCA genes and cognitive performance in Parkinson disease. *JAMA Neurol*, *71*(11), 1405-1412. doi:10.1001/jamaneurol.2014.1455
- McGuinness, B., Carson, R., Barrett, S. L., Craig, D., & Passmore, A. P. (2010). Apolipoprotein epsilon4 and neuropsychological performance in Alzheimer's disease and vascular dementia. *Neurosci Lett*, *483*(1), 62-66. doi:10.1016/j.neulet.2010.07.063
- Mikos, A. E., Piryatinsky, I., Tremont, G., & Malloy, P. F. (2013). The APOE epsilon4 allele is associated with increased frontally mediated neurobehavioral symptoms in amnesic MCI. *Alzheimer Dis Assoc Disord*, *27*(2), 109-115. doi:10.1097/WAD.0b013e318266c6c3
- Miller, L. A., Gunstad, J., Spitznagel, M. B., McCaffery, J., McGeary, J., Poppas, A., . . . Cohen, R. A. (2011). CAMTA1 T polymorphism is associated with neuropsychological test performance in older adults with cardiovascular disease. *Psychogeriatrics*, *11*(3), 135-140. doi:10.1111/j.1479-8301.2011.00357.x
- Moizard, M. P., Billard, C., Toutain, A., Berret, F., Marmin, N., & Moraine, C. (1998). Are Dp71 and Dp140 brain dystrophin isoforms related to cognitive impairment in Duchenne muscular dystrophy? *Am J Med Genet*, *80*(1), 32-41.

- Mora, M., Mansego, M. L., Serra-Prat, M., Palomera, E., Boquet, X., Chaves, J. F., . . . Mataro Ageing Study, G. (2014). Glucose impairment and ghrelin gene variants are associated to cognitive dysfunction. *Aging Clin Exp Res*, 26(2), 161-169. doi:10.1007/s40520-014-0203-5
- Morales, D., Hechavarria, R., Wojna, V., & Acevedo, S. F. (2013). YWHAЕ/14-3-3epsilon: a potential novel genetic risk factor and CSF biomarker for HIV neurocognitive impairment. *J Neurovirol*, 19(5), 471-478. doi:10.1007/s13365-013-0200-z
- Morgen, K., Ramirez, A., Frolich, L., Tost, H., Plichta, M. M., Kolsch, H., . . . Meyer-Lindenberg, A. (2014). Genetic interaction of PICALM and APOE is associated with brain atrophy and cognitive impairment in Alzheimer's disease. *Alzheimers Dement*, 10(5 Suppl), S269-276. doi:10.1016/j.jalz.2013.11.001
- Mukherjee, S., Kim, S., Ramanan, V. K., Gibbons, L. E., Nho, K., Glymour, M. M., . . . Alzheimer's Disease Neuroimaging, I. (2014). Gene-based GWAS and biological pathway analysis of the resilience of executive functioning. *Brain Imaging Behav*, 8(1), 110-118. doi:10.1007/s11682-013-9259-7
- Murphy, S., Gorman, G., Beetz, C., Byrne, P., Dytko, M., McMonagle, P., . . . Hutchinson, M. (2009). Dementia in SPG4 hereditary spastic paraplegia: clinical, genetic, and neuropathologic evidence. *Neurology*, 73(5), 378-384. doi:10.1212/WNL.0b013e3181b04c6c
- Nacmias, B., Piccini, C., Bagnoli, S., Tedde, A., Cellini, E., Bracco, L., & Sorbi, S. (2004). Brain-derived neurotrophic factor, apolipoprotein E genetic variants and cognitive performance in Alzheimer's disease. *Neurosci Lett*, 367(3), 379-383. doi:10.1016/j.neulet.2004.06.039
- Nagata, T., Shinagawa, S., Nukariya, K., Nakayama, R., Nakayama, K., & Yamada, H. (2011). Association between nerve growth factor gene polymorphism and executive dysfunction in Japanese patients with early-stage Alzheimer's disease and amnesic mild cognitive impairment. *Dement Geriatr Cogn Disord*, 32(6), 379-386. doi:10.1159/000335355
- Nagata, T., Shinagawa, S., Nukariya, K., Ochiai, Y., Kawamura, S., Agawa-Ohta, M., . . . Yamada, H. (2011). Association between brain-derived neurotrophic factor (BDNF) gene polymorphisms and executive function in Japanese patients with Alzheimer's disease. *Psychogeriatrics*, 11(3), 141-149. doi:10.1111/j.1479-8301.2011.00364.x
- Nagata, T., Shinagawa, S., Nukariya, K., Yamada, H., & Nakayama, K. (2012). Association between BDNF polymorphism (Val66Met) and executive function in patients with amnesic mild cognitive impairment or mild Alzheimer disease. *Dement Geriatr Cogn Disord*, 33(4), 266-272. doi:10.1159/000339358
- Nedic, G., Borovecki, F., Klepac, N., Mubrin, Z., Hajnsek, S., Nikolac, M., . . . Pivac, N. (2011). Association study of a functional catechol-o-methyltransferase polymorphism and cognitive function in patients with dementia. *Coll Antropol*, 35 Suppl 1, 79-84.
- Negash, S., Petersen, L. E., Geda, Y. E., Knopman, D. S., Boeve, B. F., Smith, G. E., . . . Petersen, R. C. (2007). Effects of ApoE genotype and mild cognitive impairment on implicit learning. *Neurobiol Aging*, 28(6), 885-893. doi:10.1016/j.neurobiolaging.2006.04.004

- Ng, T., Teo, S. M., Yeo, H. L., Shwe, M., Gan, Y. X., Cheung, Y. T., . . . Chan, A. (2016). Brain-derived neurotrophic factor genetic polymorphism (rs6265) is protective against chemotherapy-associated cognitive impairment in patients with early-stage breast cancer. *Neuro Oncol*, *18*(2), 244-251. doi:10.1093/neuonc/nov162
- Ni, P., Ma, X., Lin, Y., Lao, G., Hao, X., Guan, L., . . . Li, T. (2015). Methionine sulfoxide reductase A (MsrA) associated with bipolar I disorder and executive functions in A Han Chinese population. *J Affect Disord*, *184*, 235-238. doi:10.1016/j.jad.2015.06.004
- Nicodemus, K. K., Elvevag, B., Foltz, P. W., Rosenstein, M., Diaz-Asper, C., & Weinberger, D. R. (2014). Category fluency, latent semantic analysis and schizophrenia: a candidate gene approach. *Cortex*, *55*, 182-191. doi:10.1016/j.cortex.2013.12.004
- Nie, K., Zhang, Y., Gan, R., Wang, L., Zhao, J., Huang, Z., . . . Wang, L. (2013). Polymorphisms in immune/inflammatory cytokine genes are related to Parkinson's disease with cognitive impairment in the Han Chinese population. *Neurosci Lett*, *541*, 111-115. doi:10.1016/j.neulet.2013.02.024
- Norberg, J., Graff, C., Almkvist, O., Ewers, M., Frisoni, G. B., Frolich, L., . . . Visser, P. J. (2011). Regional differences in effects of APOE epsilon4 on cognitive impairment in non-demented subjects. *Dement Geriatr Cogn Disord*, *32*(2), 135-142. doi:10.1159/000330492
- O'Hara, R., Sommer, B., Way, N., Kraemer, H. C., Taylor, J., & Murphy, G. (2008). Slower speed-of-processing of cognitive tasks is associated with presence of the apolipoprotein epsilon4 allele. *J Psychiatr Res*, *42*(3), 199-204. doi:10.1016/j.jpsychires.2006.12.001
- Oliveri, R. L., Cittadella, R., Sibilia, G., Manna, I., Valentino, P., Gambardella, A., . . . Quattrone, A. (1999). APOE and risk of cognitive impairment in multiple sclerosis. *Acta Neurol Scand*, *100*(5), 290-295.
- Omoumi, A., Fok, A., Greenwood, T., Sadovnick, A. D., Feldman, H. H., & Hsiung, G. Y. (2014). Evaluation of late-onset Alzheimer disease genetic susceptibility risks in a Canadian population. *Neurobiol Aging*, *35*(4), 936 e935-912. doi:10.1016/j.neurobiolaging.2013.09.025
- Oroszi, G., Lapteva, L., Davis, E., Yarboro, C. H., Weickert, T., Roebuck-Spencer, T., . . . Illei, G. G. (2006). The Met66 allele of the functional Val66Met polymorphism in the brain-derived neurotrophic factor gene confers protection against neurocognitive dysfunction in systemic lupus erythematosus. *Ann Rheum Dis*, *65*(10), 1330-1335. doi:10.1136/ard.2006.051623
- Parachikova, A., Agadjanyan, M. G., Cribbs, D. H., Blurton-Jones, M., Perreau, V., Rogers, J., . . . Cotman, C. W. (2007). Inflammatory changes parallel the early stages of Alzheimer disease. *Neurobiol Aging*, *28*(12), 1821-1833. doi:10.1016/j.neurobiolaging.2006.08.014
- Park, Y., & Waldman, I. D. (2014). Influence of the COMT val(108/158)met polymorphism on continuous performance task indices. *Neuropsychologia*, *61*, 45-55. doi:10.1016/j.neuropsychologia.2014.06.008
- Payton, A., Dawes, P., Platt, H., Morton, C. C., Moore, D. R., Massey, J., . . . Pendleton, N. (2016). A role for HLA-DRB1*1101 and DRB1*0801 in cognitive ability and its decline with age. *Am J Med Genet B Neuropsychiatr Genet*, *171B*(2), 209-214. doi:10.1002/ajmg.b.32393

- Payton, A., Gibbons, L., Davidson, Y., Ollier, W., Rabbitt, P., Worthington, J., . . . Horan, M. (2005). Influence of serotonin transporter gene polymorphisms on cognitive decline and cognitive abilities in a nondemented elderly population. *Mol Psychiatry*, *10*(12), 1133-1139. doi:10.1038/sj.mp.4001733
- Peters, N., Opherk, C., Danek, A., Ballard, C., Herzog, J., & Dichgans, M. (2005). The pattern of cognitive performance in CADASIL: a monogenic condition leading to subcortical ischemic vascular dementia. *Am J Psychiatry*, *162*(11), 2078-2085. doi:10.1176/appi.ajp.162.11.2078
- Petersen, R. C., Smith, G. E., Ivnik, R. J., Tangalos, E. G., Schaid, D. J., Thibodeau, S. N., . . . Kurland, L. T. (1995). Apolipoprotein E status as a predictor of the development of Alzheimer's disease in memory-impaired individuals. *JAMA*, *273*(16), 1274-1278.
- Piscopo, P., Talarico, G., Crestini, A., Gasparini, M., Malvezzi-Campeggi, L., Piacentini, E., . . . Confaloni, A. (2010). A novel mutation in the predicted TMIII domain of the PSEN2 gene in an Italian pedigree with atypical Alzheimer's disease. *J Alzheimers Dis*, *20*(1), 43-47. doi:10.3233/JAD-2010-1369
- Polito, L., Poloni, T. E., Vaccaro, R., Abbondanza, S., Mangieri, M., Davin, A., . . . Guaita, A. (2016). High homocysteine and epistasis between MTHFR and APOE: association with cognitive performance in the elderly. *Exp Gerontol*, *76*, 9-16. doi:10.1016/j.exger.2016.01.005
- Porter, M. A., Dobson-Stone, C., Kwok, J. B., Schofield, P. R., Beckett, W., & Tassabehji, M. (2012). A role for transcription factor GTF2IRD2 in executive function in Williams-Beuren syndrome. *PLoS One*, *7*(10), e47457. doi:10.1371/journal.pone.0047457
- Powers, N. R., Eicher, J. D., Butter, F., Kong, Y., Miller, L. L., Ring, S. M., . . . Gruen, J. R. (2013). Alleles of a polymorphic ETV6 binding site in DCDC2 confer risk of reading and language impairment. *Am J Hum Genet*, *93*(1), 19-28. doi:10.1016/j.ajhg.2013.05.008
- Pozueta, A., Vazquez-Higuera, J. L., Sanchez-Juan, P., Rodriguez-Rodriguez, E., Sanchez-Quintana, C., Mateo, I., . . . Combarros, O. (2011). Genetic variation in caspase-1 as predictor of accelerated progression from mild cognitive impairment to Alzheimer's disease. *J Neurol*, *258*(8), 1538-1539. doi:10.1007/s00415-011-5935-y
- Quintino-Santos, S., Diniz, B. S., Firmo, J. O., Moriguchi, E. H., Lima-Costa, M. F., & Castro-Costa, E. (2015). APOE epsilon4 allele is associated with worse performance in memory dimensions of the mini-mental state examination: the Bambui Cohort Study of Aging. *Int J Geriatr Psychiatry*, *30*(6), 573-579. doi:10.1002/gps.4186
- Quintino-Santos, S. R., Lima-Costa, M. F., Uchoa, E., Firmo, J. O., Moriguchi, E. H., & Castro-Costa, E. (2012). Homozygosity for the APOE E4 allele is solely associated with lower cognitive performance in Brazilian community-dwelling older adults: the Bambui Study. *Rev Bras Psiquiatr*, *34*(4), 440-445.
- Ragnarsson, O., Glad, C. A., Berglund, P., Bergthorsdottir, R., Eder, D. N., & Johannsson, G. (2014). Common genetic variants in the glucocorticoid receptor and the 11beta-hydroxysteroid dehydrogenase type 1 genes influence long-term cognitive impairments in patients with Cushing's syndrome in remission. *J Clin Endocrinol Metab*, *99*(9), E1803-1807. doi:10.1210/jc.2014-1906
- Ramanan, V. K., Nho, K., Shen, L., Risacher, S. L., Kim, S., McDonald, B. C., . . . Saykin, A. J. (2015). FASTKD2 is associated with memory and hippocampal structure in older adults. *Mol Psychiatry*, *20*(10), 1197-1204. doi:10.1038/mp.2014.142

- Ramanan, V. K., Risacher, S. L., Nho, K., Kim, S., Shen, L., McDonald, B. C., . . . Alzheimer's Disease Neuroimaging, I. (2015). GWAS of longitudinal amyloid accumulation on 18F-florbetapir PET in Alzheimer's disease implicates microglial activation gene IL1RAP. *Brain*, *138*(Pt 10), 3076-3088. doi:10.1093/brain/awv231
- Rao, S. M., Bonner-Jackson, A., Nielson, K. A., Seidenberg, M., Smith, J. C., Woodard, J. L., & Durgerian, S. (2015). Genetic risk for Alzheimer's disease alters the five-year trajectory of semantic memory activation in cognitively intact elders. *Neuroimage*, *111*, 136-146. doi:10.1016/j.neuroimage.2015.02.011
- Redel, P., Bublak, P., Sorg, C., Kurz, A., Forstl, H., Muller, H. J., . . . Finke, K. (2012). Deficits of spatial and task-related attentional selection in mild cognitive impairment and Alzheimer's disease. *Neurobiol Aging*, *33*(1), 195 e127-142. doi:10.1016/j.neurobiolaging.2010.05.014
- Regal, P., Nair, B., & Hetherington, E. (2013). Apolipoprotein E epsilon4 is superior to apolipoprotein E epsilon2 in predicting cognitive scores over 30 months. *Clin Interv Aging*, *8*, 1461-1465. doi:10.2147/CIA.S47485
- Robins Wahlin, T. B., Lundin, A., & Dear, K. (2007). Early cognitive deficits in Swedish gene carriers of Huntington's disease. *Neuropsychology*, *21*(1), 31-44. doi:10.1037/0894-4105.21.1.31
- Roffman, J. L., Weiss, A. P., Deckersbach, T., Freudenreich, O., Henderson, D. C., Purcell, S., . . . Goff, D. C. (2007). Effects of the methylenetetrahydrofolate reductase (MTHFR) C677T polymorphism on executive function in schizophrenia. *Schizophr Res*, *92*(1-3), 181-188. doi:10.1016/j.schres.2007.01.003
- Rosa, E. C., Dickinson, D., Apud, J., Weinberger, D. R., & Elvevag, B. (2010). COMT Val158Met polymorphism, cognitive stability and cognitive flexibility: an experimental examination. *Behav Brain Funct*, *6*, 53. doi:10.1186/1744-9081-6-53
- Roussotte, F. F., Gutman, B. A., Hibar, D. P., Madsen, S. K., Narr, K. L., Thompson, P. M., & Alzheimer's Disease Neuroimaging, I. (2015). Carriers of a common variant in the dopamine transporter gene have greater dementia risk, cognitive decline, and faster ventricular expansion. *Alzheimers Dement*, *11*(10), 1153-1162. doi:10.1016/j.jalz.2014.10.011
- Ruiz-Martinez, J., Krebs, C. E., Makarov, V., Gorostidi, A., Marti-Masso, J. F., & Paisan-Ruiz, C. (2015). GIGYF2 mutation in late-onset Parkinson's disease with cognitive impairment. *J Hum Genet*, *60*(10), 637-640. doi:10.1038/jhg.2015.69
- Ryan, J., Carriere, I., Amieva, H., Rouaud, O., Berr, C., Ritchie, K., . . . Ancelin, M. L. (2013). Prospective analysis of the association between estrogen receptor gene variants and the risk of cognitive decline in elderly women. *Eur Neuropsychopharmacol*, *23*(12), 1763-1768. doi:10.1016/j.euroneuro.2013.06.003
- Sager, K. L., Wu, J., Leurgans, S. E., Rees, H. D., Gearing, M., Mufson, E. J., . . . Lah, J. J. (2007). Neuronal LR11/sorLA expression is reduced in mild cognitive impairment. *Ann Neurol*, *62*(6), 640-647. doi:10.1002/ana.21190
- Sapkota, S., Wiebe, S. A., Small, B. J., & Dixon, R. A. (2016). Apolipoprotein E and Clusterin can magnify effects of personality vulnerability on declarative memory performance in non-demented older adults. *Int J Geriatr Psychiatry*, *31*(5), 502-509. doi:10.1002/gps.4355

- Sarosi, A., Gonda, X., Balogh, G., Domotor, E., Szekely, A., Hejjas, K., . . . Faludi, G. (2008). Association of the STin2 polymorphism of the serotonin transporter gene with a neurocognitive endophenotype in major depressive disorder. *Prog Neuropsychopharmacol Biol Psychiatry*, *32*(7), 1667-1672. doi:10.1016/j.pnpbp.2008.06.014
- Scerri, T. S., Darki, F., Newbury, D. F., Whitehouse, A. J., Peyrard-Janvid, M., Matsson, H., . . . Paracchini, S. (2012). The dyslexia candidate locus on 2p12 is associated with general cognitive ability and white matter structure. *PLoS One*, *7*(11), e50321. doi:10.1371/journal.pone.0050321
- Schipper, H. M., Bennett, D. A., Liberman, A., Bienias, J. L., Schneider, J. A., Kelly, J., & Arvanitakis, Z. (2006). Glial heme oxygenase-1 expression in Alzheimer disease and mild cognitive impairment. *Neurobiol Aging*, *27*(2), 252-261. doi:10.1016/j.neurobiolaging.2005.01.016
- Schutte, D. L., Reed, D., Decrane, S., & Ersig, A. L. (2011). Saitohin and APOE polymorphisms influence cognition and function in persons with advanced Alzheimer Disease. *Dement Geriatr Cogn Disord*, *32*(2), 94-102. doi:10.1159/000329542
- Seo, E. H., Kim, S. H., Park, S. H., Kang, S. H., Choo, I. H., & Alzheimer's Disease Neuroimaging, I. (2016). Independent and Interactive Influences of the APOE Genotype and Beta-Amyloid Burden on Cognitive Function in Mild Cognitive Impairment. *J Korean Med Sci*, *31*(2), 286-295. doi:10.3346/jkms.2016.31.2.286
- Seshadri, S., DeStefano, A. L., Au, R., Massaro, J. M., Beiser, A. S., Kelly-Hayes, M., . . . Wolf, P. A. (2007). Genetic correlates of brain aging on MRI and cognitive test measures: a genome-wide association and linkage analysis in the Framingham Study. *BMC Med Genet*, *8 Suppl 1*, S15. doi:10.1186/1471-2350-8-S1-S15
- Sevin, M., Kutalik, Z., Bergman, S., Vercelletto, M., Renou, P., Lamy, E., . . . Jacquemont, S. (2009). Penetrance of marked cognitive impairment in older male carriers of the FMR1 gene premutation. *J Med Genet*, *46*(12), 818-824. doi:10.1136/jmg.2008.065953
- Shang, Z., Lv, H., Zhang, M., Duan, L., Wang, S., Li, J., . . . Jiang, Y. (2015). Genome-wide haplotype association study identify TNFRSF1A, CASP7, LRP1B, CDH1 and TG genes associated with Alzheimer's disease in Caribbean Hispanic individuals. *Oncotarget*, *6*(40), 42504-42514. doi:10.18632/oncotarget.6391
- Shi, J., Zhao, C. B., Vollmer, T. L., Tyry, T. M., & Kuniyoshi, S. M. (2008). APOE epsilon 4 allele is associated with cognitive impairment in patients with multiple sclerosis. *Neurology*, *70*(3), 185-190. doi:10.1212/01.wnl.0000264004.62612.44
- Shi, Y. M., Zhou, H., Zhang, Z. J., Yu, H., Bai, F., Yuan, Y. G., . . . Jia, J. P. (2009). Association of the LRP1 gene and cognitive performance with amnesic mild cognitive impairment in elderly Chinese. *Int Psychogeriatr*, *21*(6), 1072-1080. doi:10.1017/S104161020999072X
- Shin, M. H., Kweon, S. S., Choi, J. S., Lee, Y. H., Nam, H. S., Park, K. S., . . . Jeong, S. K. (2014). A disease modification effect of APOE E4 on the association between urinary albumin excretion and cognition in Korean adults. *Dis Markers*, *2014*, 724281. doi:10.1155/2014/724281
- Silver, H., Mandiuk, N., Enoch, R., Susser, E., Danovich, L., Bilker, W., . . . Weinreb, O. (2015). Improvement in verbal memory following SSRI augmentation of antipsychotic treatment is associated with changes in the expression of mRNA encoding for

- the GABA-A receptor and BDNF in PMC of schizophrenic patients. *Int Clin Psychopharmacol*, 30(3), 158-166. doi:10.1097/YIC.000000000000070
- Smith, G. E., Bohac, D. L., Waring, S. C., Kokmen, E., Tangalos, E. G., Ivnik, R. J., & Petersen, R. C. (1998). Apolipoprotein E genotype influences cognitive 'phenotype' in patients with Alzheimer's disease but not in healthy control subjects. *Neurology*, 50(2), 355-362.
- Soeira-de-Souza, M. G., Bio, D. S., Dias, V. V., Martins do Prado, C., Campos, R. N., Costa, L. F., . . . Moreno, R. A. (2010). SHORT COMMUNICATION: Apolipoprotein E genotype and cognition in bipolar disorder. *CNS Neurosci Ther*, 16(5), 316-321. doi:10.1111/j.1755-5949.2010.00153.x
- Soeiro-de-Souza, M. G., Bio, D. S., Dias, V. V., Vieta, E., Machado-Vieira, R., & Moreno, R. A. (2013). The CACNA1C risk allele selectively impacts on executive function in bipolar type I disorder. *Acta Psychiatr Scand*, 128(5), 362-369. doi:10.1111/acps.12073
- Soeiro-de-Souza, M. G., Machado-Vieira, R., Soares Bio, D., Do Prado, C. M., & Moreno, R. A. (2012). COMT polymorphisms as predictors of cognitive dysfunction during manic and mixed episodes in bipolar I disorder. *Bipolar Disord*, 14(5), 554-564. doi:10.1111/j.1399-5618.2012.01030.x
- Sole-Padulles, C., Bartres-Faz, D., Junque, C., Via, M., Matarin, M., Gonzalez-Perez, E., . . . Clemente, I. C. (2004). Poorer cognitive performance in humans with mild cognitive impairment carrying the T variant of the Glu/Asp NOS3 polymorphism. *Neurosci Lett*, 358(1), 5-8. doi:10.1016/j.neulet.2003.12.044
- Soler, J., Miret, S., Lazaro, L., Parellada, M., Martin, M., Lera-Miguel, S., . . . Fatjo-Vilas, M. (2016). Influence of DAOA and RGS4 genes on the risk for psychotic disorders and their associated executive dysfunctions: A family-based study. *Eur Psychiatry*, 32, 42-47. doi:10.1016/j.eurpsy.2015.11.002
- Somme, J. H., Molano Salazar, A., Gonzalez, A., Tijero, B., Berganzo, K., Lezcano, E., . . . Gomez-Esteban, J. C. (2015). Cognitive and behavioral symptoms in Parkinson's disease patients with the G2019S and R1441G mutations of the LRRK2 gene. *Parkinsonism Relat Disord*, 21(5), 494-499. doi:10.1016/j.parkreldis.2015.02.019
- Son, S. J., Lee, K. S., Lee, Y., Baek, J. H., Choi, S. H., Na, D. L., . . . Hong, C. H. (2012). Association between white matter hyperintensity severity and cognitive impairment according to the presence of the apolipoprotein E (APOE) epsilon4 allele in the elderly: retrospective analysis of data from the CREDOS study. *J Clin Psychiatry*, 73(12), 1555-1562. doi:10.4088/JCP.12m07702
- Spangaro, M., Bosia, M., Zanoletti, A., Bechi, M., Mariachiara, B., Pirovano, A., . . . Cavallaro, R. (2014). Exploring effects of EAAT polymorphisms on cognitive functions in schizophrenia. *Pharmacogenomics*, 15(7), 925-932. doi:10.2217/pgs.14.42
- Spector, S. A., Singh, K. K., Gupta, S., Cystique, L. A., Jin, H., Letendre, S., . . . Group, H. (2010). APOE epsilon4 and MBL-2 O/O genotypes are associated with neurocognitive impairment in HIV-infected plasma donors. *AIDS*, 24(10), 1471-1479. doi:10.1097/QAD.0b013e328339e25c

- Spellmann, I., Muller, N., Musil, R., Zill, P., Douhet, A., Dehning, S., . . . Riedel, M. (2008). Associations of SNAP-25 polymorphisms with cognitive dysfunctions in Caucasian patients with schizophrenia during a brief trial of treatment with atypical antipsychotics. *Eur Arch Psychiatry Clin Neurosci*, 258(6), 335-344. doi:10.1007/s00406-007-0800-9
- Stevanin, G., Azzedine, H., Denora, P., Boukhris, A., Tazir, M., Lossos, A., . . . consortium, S. (2008). Mutations in SPG11 are frequent in autosomal recessive spastic paraplegia with thin corpus callosum, cognitive decline and lower motor neuron degeneration. *Brain*, 131(Pt 3), 772-784. doi:10.1093/brain/awm293
- Stewart, A., Katznelson, R., Kraeva, N., Carroll, J., Pickworth, T., Rao, V., & Djaiani, G. (2013). Genetic variation and cognitive dysfunction one year after cardiac surgery. *Anaesthesia*, 68(6), 571-575. doi:10.1111/anae.12170
- Stewart, R., Russ, C., Richards, M., Brayne, C., Lovestone, S., & Mann, A. (2001). Apolipoprotein E genotype, vascular risk and early cognitive impairment in an African Caribbean population. *Dement Geriatr Cogn Disord*, 12(4), 251-256. doi:51267
- Striepens, N., Scheef, L., Wind, A., Meiberth, D., Popp, J., Spottke, A., . . . Jessen, F. (2011). Interaction effects of subjective memory impairment and ApoE4 genotype on episodic memory and hippocampal volume. *Psychol Med*, 41(9), 1997-2006. doi:10.1017/S0033291711000067
- Su, H., Tao, J., Zhang, J., Xie, Y., Wang, Y., Zhang, Y., . . . He, J. (2015). The Effects of BDNF Val66Met Gene Polymorphism on Serum BDNF and Cognitive Function in Methamphetamine-Dependent Patients and Normal Controls: A Case-Control Study. *J Clin Psychopharmacol*, 35(5), 517-524. doi:10.1097/JCP.0000000000000390
- Suarez, V. M., Fernandez, Y., Lopez Edel, C., Clarke, D. H., Bobes, M. A., Riveron, A. M., & Lopez-Canovas, L. (2014). Apolipoprotein E alleles in Cuban patients with mild cognitive impairment. *Am J Alzheimers Dis Other Demen*, 29(3), 236-241. doi:10.1177/1533317513517037
- Sung, H. Y., Choi, B. O., Jeong, J. H., Kong, K. A., Hwang, J., & Ahn, J. H. (2016). Amyloid Beta-Mediated Hypomethylation of Heme Oxygenase 1 Correlates with Cognitive Impairment in Alzheimer's Disease. *PLoS One*, 11(4), e0153156. doi:10.1371/journal.pone.0153156
- Swaminathan, S., Huentelman, M. J., Corneveaux, J. J., Myers, A. J., Faber, K. M., Foroud, T., . . . Group, N.-L. N. F. S. (2012). Analysis of copy number variation in Alzheimer's disease in a cohort of clinically characterized and neuropathologically verified individuals. *PLoS One*, 7(12), e50640. doi:10.1371/journal.pone.0050640
- Talarowska, M., Szemraj, J., Zajackowska, M., & Galecki, P. (2014). ASMT gene expression correlates with cognitive impairment in patients with recurrent depressive disorder. *Med Sci Monit*, 20, 905-912. doi:10.12659/MSM.890160
- Tallaksen, C. M., Guichart-Gomez, E., Verpillat, P., Hahn-Barma, V., Ruberg, M., Fontaine, B., . . . Durr, A. (2003). Subtle cognitive impairment but no dementia in patients with spastin mutations. *Arch Neurol*, 60(8), 1113-1118. doi:10.1001/archneur.60.8.1113
- Tan, H. Y., Chen, A. G., Kolachana, B., Apud, J. A., Mattay, V. S., Callicott, J. H., . . . Weinberger, D. R. (2012). Effective connectivity of AKT1-mediated dopaminergic working memory networks and pharmacogenetics of anti-dopaminergic treatment. *Brain*, 135(Pt 5), 1436-1445. doi:10.1093/brain/aws068

- Tang, M., Rao, D., Ma, C., Guo, Y., Han, H., Ling, K., & Ling, Y. (2008). Evaluation of choline acetyltransferase gene polymorphism (2384 G/A) in Alzheimer's disease and mild cognitive impairment. *Dement Geriatr Cogn Disord*, *26*(1), 9-14. doi:10.1159/000140612
- Tardiff, B. E., Newman, M. F., Saunders, A. M., Strittmatter, W. J., Blumenthal, J. A., White, W. D., . . . Reves, J. G. (1997). Preliminary report of a genetic basis for cognitive decline after cardiac operations. The Neurologic Outcome Research Group of the Duke Heart Center. *Ann Thorac Surg*, *64*(3), 715-720.
- Tassone, F., Hagerman, R. J., Taylor, A. K., Mills, J. B., Harris, S. W., Gane, L. W., & Hagerman, P. J. (2000). Clinical involvement and protein expression in individuals with the FMR1 premutation. *Am J Med Genet*, *91*(2), 144-152.
- Thai, C., Lim, Y. Y., Villemagne, V. L., Laws, S. M., Ames, D., Ellis, K. A., . . . Lifestyle Research, G. (2015). Amyloid-Related Memory Decline in Preclinical Alzheimer's Disease Is Dependent on APOE epsilon4 and Is Detectable over 18-Months. *PLoS One*, *10*(10), e0139082. doi:10.1371/journal.pone.0139082
- Thaler, A., Helmich, R. C., Or-Borichev, A., van Nuenen, B. F., Shapira-Lichter, I., Gurevich, T., . . . consortium, L. A. J. (2016). Intact working memory in non-manifesting LRRK2 carriers--an fMRI study. *Eur J Neurosci*, *43*(1), 106-112. doi:10.1111/ejn.13120
- Thambisetty, M., Beason-Held, L. L., An, Y., Kraut, M., Nalls, M., Hernandez, D. G., . . . Resnick, S. M. (2013). Alzheimer risk variant CLU and brain function during aging. *Biol Psychiatry*, *73*(5), 399-405. doi:10.1016/j.biopsych.2012.05.026
- Togsverd, M., Werge, T. M., Tanko, L. B., Bagger, Y. Z., Qin, G. G., Hansen, T., . . . Rasmussen, H. B. (2007). Cognitive performance in elderly women: significance of the 19bp insertion/deletion polymorphism in the 5' flank of the dopamine beta-hydroxylase gene, educational level, body fat measures, serum triglyceride, alcohol consumption and age. *Int J Geriatr Psychiatry*, *22*(9), 883-889. doi:10.1002/gps.1756
- Tranah, G. J., Nalls, M. A., Katzman, S. M., Yokoyama, J. S., Lam, E. T., Zhao, Y., . . . Yaffe, K. (2012). Mitochondrial DNA sequence variation associated with dementia and cognitive function in the elderly. *J Alzheimers Dis*, *32*(2), 357-372. doi:10.3233/JAD-2012-120466
- Traykov, L., Rigaud, A. S., Caputo, L., Couderc, R., Coste, J., Michot, J. L., . . . Boller, F. (1999). Apolipoprotein E phenotypes in demented and cognitively impaired patients with and without cerebrovascular disease. *Eur J Neurol*, *6*(4), 415-421.
- Trompet, S., de Craen, A. J., Jukema, J. W., Pons, D., Slagboom, P. E., Kremer, D., . . . Westendorp, R. G. (2011). Variation in the CBP gene involved in epigenetic control associates with cognitive function. *Neurobiol Aging*, *32*(3), 549 e541-548. doi:10.1016/j.neurobiolaging.2009.12.019
- Troster, A. I., Fields, J. A., Paolo, A. M., & Koller, W. C. (2006). Absence of the apolipoprotein E epsilon4 allele is associated with working memory impairment in Parkinson's disease. *J Neurol Sci*, *248*(1-2), 62-67. doi:10.1016/j.jns.2006.05.032
- Tupler, L. A., Krishnan, K. R., Greenberg, D. L., Marcovina, S. M., Payne, M. E., MacFall, J. R., . . . Doraiswamy, P. M. (2007). Predicting memory decline in normal elderly: genetics, MRI, and cognitive reserve. *Neurobiol Aging*, *28*(11), 1644-1656. doi:10.1016/j.neurobiolaging.2006.07.001

- Unmack Larsen, I., Vinther-Jensen, T., Gade, A., Nielsen, J. E., & Vogel, A. (2015). Assessing impairment of executive function and psychomotor speed in premanifest and manifest Huntington's disease gene-expansion carriers. *J Int Neuropsychol Soc*, *21*(3), 193-202. doi:10.1017/S1355617715000090
- van Munster, B. C., Korevaar, J. C., Zwinderman, A. H., Leeftang, M. M., & de Rooij, S. E. (2009). The association between delirium and the apolipoprotein E epsilon 4 allele: new study results and a meta-analysis. *Am J Geriatr Psychiatry*, *17*(10), 856-862. doi:10.1097/JGP.0b013e3181ab8c84
- Vazquez-Bourgon, J., Ayesa-Arriola, R., Fatjo-Vilas, M., Roiz-Santianez, R., Fananas, L., & Crespo-Facorro, B. (2015). Effect of DISC1 polymorphisms on the long-term course of neurocognitive deficits in non-affective psychosis. *Eur Psychiatry*, *30*(7), 861-867. doi:10.1016/j.eurpsy.2015.07.007
- Verbrugge, P., Bouwer, S., Wiltshire, S., Carter, K., Chandler, D., Cooper, M., . . . Kalaydjieva, L. (2012). Impact of the Reelin signaling cascade (ligands-receptors-adaptor complex) on cognition in schizophrenia. *Am J Med Genet B Neuropsychiatr Genet*, *159B*(4), 392-404. doi:10.1002/ajmg.b.32042
- Vignini, A., Morganti, S., Salvolini, E., Sartini, D., Luzzi, S., Fiorini, R., . . . Emanuelli, M. (2013). Amyloid precursor protein expression is enhanced in human platelets from subjects with Alzheimer's disease and frontotemporal lobar degeneration: a real-time PCR study. *Exp Gerontol*, *48*(12), 1505-1508.
- Villalba, K., Devieux, J. G., Rosenberg, R., & Cadet, J. L. (2015). DRD2 and DRD4 genes related to cognitive deficits in HIV-infected adults who abuse alcohol. *Behav Brain Funct*, *11*, 25. doi:10.1186/s12993-015-0072-x
- Voineskos, A. N., Felsky, D., Kovacevic, N., Tiwari, A. K., Zai, C., Chakravarty, M. M., . . . Kennedy, J. L. (2013). Oligodendrocyte genes, white matter tract integrity, and cognition in schizophrenia. *Cereb Cortex*, *23*(9), 2044-2057. doi:10.1093/cercor/bhs188
- Vyas, N. S., Ahn, K., Stahl, D. R., Caviston, P., Simic, M., Netherwood, S., . . . Aitchison, K. J. (2014). Association of KIBRA rs17070145 polymorphism with episodic memory in the early stages of a human neurodevelopmental disorder. *Psychiatry Res*, *220*(1-2), 37-43. doi:10.1016/j.psychres.2014.07.024
- Wagle, J., Farner, L., Flekkoy, K., Wyller, T. B., Sandvik, L., Eiklid, K. L., . . . Engedal, K. (2009). Association between ApoE epsilon4 and cognitive impairment after stroke. *Dement Geriatr Cogn Disord*, *27*(6), 525-533. doi:10.1159/000223230
- Wagle, J., Farner, L., Flekkoy, K., Wyller, T. B., Sandvik, L., Eiklid, K. L., . . . Engedal, K. (2010). Cognitive impairment and the role of the ApoE epsilon4-allele after stroke--a 13 months follow-up study. *Int J Geriatr Psychiatry*, *25*(8), 833-842. doi:10.1002/gps.2425
- Wang, S., Wang, R., Chen, L., Bennett, D. A., Dickson, D. W., & Wang, D. S. (2010). Expression and functional profiling of neprilysin, insulin-degrading enzyme, and endothelin-converting enzyme in prospectively studied elderly and Alzheimer's brain. *J Neurochem*, *115*(1), 47-57. doi:10.1111/j.1471-4159.2010.06899.x
- Wang, T., Chen, K., Li, H., Dong, S., Su, N., Liu, Y., . . . Xiao, S. (2015). The feasibility of utilizing plasma MiRNA107 and BACE1 messenger RNA gene expression for clinical diagnosis of amnesic mild cognitive impairment. *J Clin Psychiatry*, *76*(2), 135-141. doi:10.4088/JCP.13m08812

- Wang, W., Yang, L., Tan, L., Wu, X., Jiang, B., & Shen, X. (2014). Arg972 insulin receptor substrate-1 polymorphism and risk and severity of Alzheimer's disease. *J Clin Neurosci*, *21*(7), 1233-1237. doi:10.1016/j.jocn.2013.09.028
- Wang, W. X., Rajeev, B. W., Stromberg, A. J., Ren, N., Tang, G., Huang, Q., . . . Nelson, P. T. (2008). The expression of microRNA miR-107 decreases early in Alzheimer's disease and may accelerate disease progression through regulation of beta-site amyloid precursor protein-cleaving enzyme 1. *J Neurosci*, *28*(5), 1213-1223. doi:10.1523/JNEUROSCI.5065-07.2008
- Wang, X., Wang, H., Li, H., Li, T., & Yu, X. (2014). Frequency of the apolipoprotein E epsilon4 allele in a memory clinic cohort in Beijing: a naturalistic descriptive study. *PLoS One*, *9*(6), e99130. doi:10.1371/journal.pone.0099130
- Warburton, A., Miyajima, F., Shazadi, K., Crossley, J., Johnson, M. R., Marson, A. G., . . . Sills, G. J. (2016). NRSF and BDNF polymorphisms as biomarkers of cognitive dysfunction in adults with newly diagnosed epilepsy. *Epilepsy Behav*, *54*, 117-127. doi:10.1016/j.yebeh.2015.11.013
- Weiss, E. M., Schuler, G., Fink, A., Reiser, E. M., Mittenecker, E., Niederstatter, H., . . . Papousek, I. (2014). Influences of COMT and 5-HTTLPR polymorphisms on cognitive flexibility in healthy women: inhibition of prepotent responses and memory updating. *PLoS One*, *9*(1), e85506. doi:10.1371/journal.pone.0085506
- West, N. A., Haan, M. N., & Morgenstern, H. (2010). The PPAR-gamma Pro12Ala polymorphism and risk of cognitive impairment in a longitudinal study. *Neurobiol Aging*, *31*(5), 741-746. doi:10.1016/j.neurobiolaging.2008.06.005
- Wildemann, B., Haas, J., Stingele, K., Storch-Hagenlocher, B., McArthur, J. C., Dawson, T. M., & Dawson, V. L. (2001). Identification by mRNA differential display of two up-regulated genes as candidate mediators of AIDS dementia. *Mol Med*, *7*(3), 193-199.
- Williams-Gray, C. H., Evans, J. R., Goris, A., Foltynie, T., Ban, M., Robbins, T. W., . . . Barker, R. A. (2009). The distinct cognitive syndromes of Parkinson's disease: 5 year follow-up of the CamPaIGN cohort. *Brain*, *132*(Pt 11), 2958-2969. doi:10.1093/brain/awp245
- Williams-Gray, C. H., Hampshire, A., Barker, R. A., & Owen, A. M. (2008). Attentional control in Parkinson's disease is dependent on COMT val 158 met genotype. *Brain*, *131*(Pt 2), 397-408. doi:10.1093/brain/awm313
- Williams-Gray, C. H., Hampshire, A., Robbins, T. W., Owen, A. M., & Barker, R. A. (2007). Catechol O-methyltransferase Val158Met genotype influences frontoparietal activity during planning in patients with Parkinson's disease. *J Neurosci*, *27*(18), 4832-4838. doi:10.1523/JNEUROSCI.0774-07.2007
- Wilson, R. S., Schneider, J. A., Barnes, L. L., Beckett, L. A., Aggarwal, N. T., Cochran, E. J., . . . Bennett, D. A. (2002). The apolipoprotein E epsilon 4 allele and decline in different cognitive systems during a 6-year period. *Arch Neurol*, *59*(7), 1154-1160.
- Winder-Rhodes, S. E., Hampshire, A., Rowe, J. B., Peelle, J. E., Robbins, T. W., Owen, A. M., & Barker, R. A. (2015). Association between MAPT haplotype and memory function in patients with Parkinson's disease and healthy aging individuals. *Neurobiol Aging*, *36*(3), 1519-1528. doi:10.1016/j.neurobiolaging.2014.12.006

- Wozniak, M. A., Lugo Iparraguirre, L. M., Dirks, M., Deb-Chatterji, M., Pflugrad, H., Goldbecker, A., . . . Weissenborn, K. (2016). Apolipoprotein E-epsilon4 deficiency and cognitive function in hepatitis C virus-infected patients. *J Viral Hepat*, *23*(1), 39-46. doi:10.1111/jvh.12443
- Xu, Z. P., Yang, S. L., Zhao, S., Zheng, C. H., Li, H. H., Zhang, Y., . . . Wang, J. Z. (2016). Biomarkers for Early Diagnostic of Mild Cognitive Impairment in Type-2 Diabetes Patients: A Multicentre, Retrospective, Nested Case-Control Study. *EBioMedicine*, *5*, 105-113. doi:10.1016/j.ebiom.2016.02.014
- Yaffe, K., Edwards, E. R., Lui, L. Y., Zmuda, J. M., Ferrell, R. E., & Cauley, J. A. (2003). Androgen receptor CAG repeat polymorphism is associated with cognitive function in older men. *Biol Psychiatry*, *54*(9), 943-946.
- Yaffe, K., Kanaya, A. M., Lindquist, K., Hsueh, W. C., Cummings, S. R., Beamer, B., . . . Health, A. B. C. S. (2008). PPAR-gamma Pro12Ala genotype and risk of cognitive decline in elders. *Neurobiol Aging*, *29*(1), 78-83. doi:10.1016/j.neurobiolaging.2006.09.010
- Yaffe, K., Lindquist, K., Sen, S., Cauley, J., Ferrell, R., Penninx, B., . . . Cummings, S. R. (2009). Estrogen receptor genotype and risk of cognitive impairment in elders: findings from the Health ABC study. *Neurobiol Aging*, *30*(4), 607-614. doi:10.1016/j.neurobiolaging.2007.08.003
- Yaffe, K., Lui, L. Y., Grady, D., Stone, K., & Morin, P. (2002). Estrogen receptor 1 polymorphisms and risk of cognitive impairment in older women. *Biol Psychiatry*, *51*(8), 677-682.
- Yang, G., Song, Y., Zhou, X., Deng, Y., Liu, T., Weng, G., . . . Pan, S. (2015). DNA methyltransferase 3, a target of microRNA-29c, contributes to neuronal proliferation by regulating the expression of brain-derived neurotrophic factor. *Mol Med Rep*, *12*(1), 1435-1442. doi:10.3892/mmr.2015.3531
- Yang, S. T., Hsiao, I. T., Hsieh, C. J., Chiang, Y. H., Yen, T. C., Chiu, W. T., . . . Hu, C. J. (2015). Accumulation of amyloid in cognitive impairment after mild traumatic brain injury. *J Neurol Sci*, *349*(1-2), 99-104. doi:10.1016/j.jns.2014.12.032
- Yang, Y. H., Chiu, C. C., Teng, H. W., Chu, C. P., Chang, C. J., Chiu, W. C., . . . Sun, I. W. (2017). Methionine synthase 2756AA polymorphism is associated with the risk of cognitive impairment in patients with late-life depression. *Asia Pac Psychiatry*, *9*(1). doi:10.1111/appy.12242
- Yocum, G. T., Gaudet, J. G., Lee, S. S., Stern, Y., Teverbaugh, L. A., Sciacca, R. R., . . . Heyer, E. J. (2009). Inducible nitric oxide synthase promoter polymorphism affords protection against cognitive dysfunction after carotid endarterectomy. *Stroke*, *40*(5), 1597-1603. doi:10.1161/STROKEAHA.108.541177
- Yu, Y., Mingjiao, W., Yang, X., Sui, M., Zhang, T., Liang, J., . . . Wang, X. (2016). Association between DNA methylation of SORL1 5'-flanking region and mild cognitive impairment in type 2 diabetes mellitus. *Ann Endocrinol (Paris)*, *77*(6), 625-632. doi:10.1016/j.ando.2016.02.008
- Yuferov, V., Ho, A., Morgello, S., Yang, Y., Ott, J., & Kreek, M. J. (2013). Expression of ephrin receptors and ligands in postmortem brains of HIV-infected subjects with and without cognitive impairment. *J Neuroimmune Pharmacol*, *8*(1), 333-344. doi:10.1007/s11481-012-9429-1

- Zhang, B., Guan, F., Chen, G., Lin, H., Zhang, T., Feng, J., . . . Fu, D. (2015). Common variants in SLC1A2 and schizophrenia: Association and cognitive function in patients with schizophrenia and healthy individuals. *Schizophr Res*, *169*(1-3), 128-134. doi:10.1016/j.schres.2015.10.012
- Zhang, C., Cai, J., Zhang, J., Li, Z., Guo, Z., Zhang, X., . . . Fang, Y. (2014). Genetic modulation of working memory deficits by ankyrin 3 gene in schizophrenia. *Prog Neuropsychopharmacol Biol Psychiatry*, *50*, 110-115. doi:10.1016/j.pnpbp.2013.12.010
- Zhang, X. Y., Chen, D. C., Xiu, M. H., Haile, C. N., Luo, X., Xu, K., . . . Kosten, T. R. (2012). Cognitive and serum BDNF correlates of BDNF Val66Met gene polymorphism in patients with schizophrenia and normal controls. *Hum Genet*, *131*(7), 1187-1195. doi:10.1007/s00439-012-1150-x
- Zhang, Z., Deng, L., Bai, F., Shi, Y., Yu, H., Yuan, Y., . . . Zhang, Z. (2010). Alteration of resting brain function by genetic variation in angiotensin converting enzyme in amnesic-type mild cognitive impairment of Chinese Han. *Behav Brain Res*, *208*(2), 619-625. doi:10.1016/j.bbr.2010.01.008
- Zhang, Z., Deng, L., Yu, H., Shi, Y., Bai, F., Xie, C., . . . Zhang, Z. (2012). Association of angiotensin-converting enzyme functional gene I/D polymorphism with amnesic mild cognitive impairment. *Neurosci Lett*, *514*(1), 131-135. doi:10.1016/j.neulet.2012.02.074

Supplemental Table A3. Fatigue.

Significant Genes – Genomic Findings	Authors
<p>COMT (catechol-O-methyltransferase) Women with breast cancer and met/met reported higher fatigue scores</p>	(Fernandez-de-las-Penas et al., 2012)
<p>IL1B (interleukin 1 Beta) Among analyzed cytokine genes, polymorphisms in IL1B were associated with higher fatigue class among women after breast cancer surgery.</p> <p>IL1B rs1071676 and rs1143627 polymorphisms are two of five SNPs found to be associated with increased fatigue among patients with HIV/AIDS suggesting an association between inflammation and fatigue.</p>	(Kober et al., 2016) (Lee, Gay, Lerdal, Pullinger, & Aouizerat, 2014)
<p>TNF (tumor necrosis factor) Variant alleles in the TNFA and IL6 genes were more susceptible to fatigue after androgen deprivation therapy in prostate cancer patients.</p> <p>TNFA polymorphisms rs1800683 and rs1041981 are two of the five SNPs found to be associated with increased fatigue in patients with HIV/AIDS suggesting an association between inflammation and fatigue.</p> <p>Individual SNPs from promotor regions of cytokine genes TNF-308 G>A (rs1800629) and IL6-174 G>C (rs1800795) were independently associated with fatigue among patients with breast cancer.</p>	(Jim et al., 2012) (Lee et al., 2014) (Bower et al., 2013)
<p>IL6 (interleukin 6) Variant alleles in the TNFA and IL6 genes were more susceptible to fatigue after androgen deprivation therapy in prostate cancer patients.</p> <p>Individual SNPs from promotor regions of cytokine genes TNF-308 G>A (rs1800629) and IL6-174 G>C (rs1800795) were independently associated with fatigue among patients with breast cancer.</p>	(Jim et al., 2012) (Bower et al., 2013)
<p>IL4 (interleukin 4) IL4 rs2243274 polymorphism as one of five SNPs associated with high fatigue pattern in patients living with HIV/AIDS suggesting an association between inflammation and fatigue.</p>	(Lee et al., 2014)
<p>IL-10 (interleukin 10) Variations in IL-10 genotype was associated with lower risk of severe fatigue compared to other genotypes among women with early stage non-small cell lung cancer.</p> <p>Among analyzed cytokine genes, polymorphisms in IL1B were associated with higher fatigue class among women after breast cancer surgery.</p>	(Reyes-Gibby et al., 2013) (Kober et al., 2016)

IFN (interferon gamma) Of several SNPs in the cytokine genes thought to be associated with fatigue, IFN- γ +874 T/A SNP was associated with increased fatigue in the acute sickness response to infection.	(Piraino, Vollmer-Conna, & Lloyd, 2012)
IL-8 (interleukin 8) IL-8-T251A was associated with increased fatigue, as well as depressed mood, and pain, among patients with advanced stage lung cancer patients.	(Reyes-Gibby et al., 2013)
NTRK2 (neurotrophic receptor tyrosine kinase 2) NTRK2 SNP rs1212171 was associated with sleep disturbance and fatigue in breast cancer patients.	(Young et al., 2017)
Significant Genes – Epigenomic Findings	Authors
sTNFR2 (plasma soluble tumor necrosis factor receptor 2) Increases in sTNFR2, regardless of CpG methylation status, was associated with fatigue in breast cancer patients receiving chemotherapy.	(Smith et al., 2014)
Significant Genes – Transcriptomic Findings	Authors
IL-6 (interleukin 6) After controlling for age, smoking, BMI, treatment type, and antidepressant use, expression of IL6 and CRP was associated with fatigue after IMRT in head and neck cancer patients.	(Nishimura, 2015)
CRP (C-reactive protein) After controlling for age, smoking, BMI, treatment type, and antidepressant use, expression of IL6 and CRP was associated with fatigue after IMRT in head and neck cancer patients	(Nishimura, 2015)
IFI27 (interferon alpha-inducible protein 27) Correlation between increased IFI27 expression and fatigue scores among men undergoing external beam radiation for prostate cancer.	(Hsiao, Araneta, Wang, & Saligan, 2013)
NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells) Increased NF- κ B response elements in promoters of genes that are upregulated in persistently fatigued breast cancer survivors.	(Bower, Ganz, Irwin, Arevalo, & Cole, 2011)
GR (glucocorticoid receptor) Decreased glucocorticoid expression in the promoters of genes up-regulated in persistently fatigued breast cancer survivors regardless of cortisol output.	(Bower et al., 2011)
MS4A1 (membrane-spanning four domains, subfamily A, member) Downregulation of MS4A1 was associated with increased fatigue in men receiving external beam radiation for prostate cancer suggesting the possibility of an impaired B-cell immune response.	(Hsiao, Reddy, Chen, & Saligan, 2016)

References

- Bower, J. E., Ganz, P. A., Irwin, M. R., Arevalo, J. M., & Cole, S. W. (2011). Fatigue and gene expression in human leukocytes: increased NF-kappaB and decreased glucocorticoid signaling in breast cancer survivors with persistent fatigue. *Brain Behav Immun, 25*(1), 147-150. doi:10.1016/j.bbi.2010.09.010
- Bower, J. E., Ganz, P. A., Irwin, M. R., Castellon, S., Arevalo, J., & Cole, S. W. (2013). Cytokine genetic variations and fatigue among patients with breast cancer. *J Clin Oncol, 31*(13), 1656-1661. doi:10.1200/jco.2012.46.2143
- Fernandez-de-las-Penas, C., Fernandez-Lao, C., Cantarero-Villanueva, I., Ambite-Quesada, S., Rivas-Martinez, I., del Moral-Avila, R., & Arroyo-Morales, M. (2012). Catechol-O-methyltransferase genotype (Val158met) modulates cancer-related fatigue and pain sensitivity in breast cancer survivors. *Breast Cancer Res Treat, 133*(2), 405-412. doi:10.1007/s10549-011-1757-y
- Hsiao, C. P., Araneta, M., Wang, X. M., & Saligan, L. N. (2013). The association of IFI27 expression and fatigue intensification during localized radiation therapy: implication of a para-inflammatory bystander response. *Int J Mol Sci, 14*(8), 16943-16957. doi:10.3390/ijms140816943
- Hsiao, C. P., Reddy, S. Y., Chen, M. K., & Saligan, L. N. (2016). Genomic Profile of Fatigued Men Receiving Localized Radiation Therapy. *Biol Res Nurs, 18*(3), 281-289. doi:10.1177/1099800415618786
- Jim, H. S., Park, J. Y., Permuth-Wey, J., Rincon, M. A., Phillips, K. M., Small, B. J., & Jacobsen, P. B. (2012). Genetic predictors of fatigue in prostate cancer patients treated with androgen deprivation therapy: preliminary findings. *Brain Behav Immun, 26*(7), 1030-1036. doi:10.1016/j.bbi.2012.03.001

- Kober, K. M., Smoot, B., Paul, S. M., Cooper, B. A., Levine, J. D., & Miaskowski, C. (2016). Polymorphisms in Cytokine Genes Are Associated With Higher Levels of Fatigue and Lower Levels of Energy in Women After Breast Cancer Surgery. *Journal of Pain and Symptom Management*, *52*(5), 695-708.e694. doi:<https://doi.org/10.1016/j.jpainsymman.2016.04.014>
- Lee, K. A., Gay, C. L., Lerdal, A., Pullinger, C. R., & Aouizerat, B. E. (2014). Cytokine polymorphisms are associated with fatigue in adults living with HIV/AIDS. *Brain Behav Immun*, *40*, 95-103. doi:10.1016/j.bbi.2014.02.017
- Nishimura, Y. (2015). Adaptive Radiation Therapy in Intensity-Modulated Radiation Therapy for Head and Neck Cancer. In Y. Nishimura & R. Komaki (Eds.), *Intensity-Modulated Radiation Therapy: Clinical Evidence and Techniques* (pp. 113-127). Tokyo: Springer Japan.
- Piraino, B., Vollmer-Conna, U., & Lloyd, A. R. (2012). Genetic associations of fatigue and other symptom domains of the acute sickness response to infection. *Brain Behav Immun*, *26*(4), 552-558. doi:10.1016/j.bbi.2011.12.009
- Reyes-Gibby, C. C., Wang, J., Spitz, M., Wu, X., Yennurajalingam, S., & Shete, S. (2013). Genetic variations in interleukin-8 and interleukin-10 are associated with pain, depressed mood, and fatigue in lung cancer patients. *J Pain Symptom Manage*, *46*(2), 161-172. doi:10.1016/j.jpainsymman.2012.07.019
- Smith, A. K., Conneely, K. N., Pace, T. W., Mister, D., Felger, J. C., Kilaru, V., . . . Torres, M. A. (2014). Epigenetic changes associated with inflammation in breast cancer patients treated with chemotherapy. *Brain Behav Immun*, *38*, 227-236. doi:10.1016/j.bbi.2014.02.010
- Young, E. E., Kelly, D. L., Shim, I., Baumbauer, K. M., Starkweather, A., & Lyon, D. E. (2017). Variations in COMT and NTRK2 Influence Symptom Burden in Women Undergoing Breast Cancer Treatment. *Biol Res Nurs*, *19*(3), 318-328. doi:10.1177/1099800417692877

Supplemental Table A4. GI Distress.

Significant Genes – Genomic Findings	Authors
<p>HTR1A (5-hydroxytryptamine receptor 1A) HTR1A rs6295 was associated with increased diarrhea in patients treated with SSRI's for depression.</p>	(Garfield et al., 2014)
<p>HTR3A ((5-hydroxytryptamine receptor 3A) Genetic variations are associated with the individual risk of developing postoperative nausea and vomiting (PONV).</p> <p>rs33940208(C/T) and rs10160548 were found to be protective for PONV and rs1985242 was found to be associated with increased risk in surgical patients from Taiwan.</p> <p>Pregnant women who are carriers of a variant rs1062613 allele had significantly worse final Pregnancy Unique Quantification of Emesis (PUQE) scores.</p>	(Reuffert et al., 2009) (Joy Lin, Hsu, Hsieh, Tseng, & Sun, 2014) (Lehmann et al., 2013)
<p>HTR3B (5-hydroxytryptamine receptor 3B) Patients homozygous for the deletion c.-104.102delAGA reported higher scores of chemotherapy-induced nausea and vomiting (CINV)</p> <p>Large European study found <i>HTR3B</i> was associated with increased risk for (CINV).</p> <p>The -AAG deletion variant of this serotonin receptor gene may contribute to variability in response to antiemetic therapy (serotonin antagonists) for CINV regardless of dose escalation.</p> <p>Patients homozygous for the -100_-102delAAG deletion polymorphism of the promoter region experienced chemotherapy induced vomiting more frequently than did all the other patients.</p> <p>Genetic variations are associated with the individual risk of developing postoperative nausea and vomiting (PONV).</p> <p>Pregnant women with rs3782025 had significantly better initial and final emesis scores.</p> <p>Psychiatric patients with the rs11766744 and treated with paroxetine have significantly more nausea. Patients with an AA genotype present with a 4 fold increased risk.</p> <p>A significant association was found between the incidence of nausea and the -100_-102AAG insertion/deletion polymorphism of the 5-HT3B receptor gene.</p>	(Kaiser et al., 2002) (Laugsand et al., 2011) (Kang et al., 2017) (Tremblay et al., 2003) (Reuffert et al., 2009) (Lehmann et al., 2013) (Sugai et al., 2006) (Tanaka et al., 2008)

Response to ondansetron was reduced (Increased PONV) in those patients who were homozygous for the -100_-102AAG deletion polymorphism.	(Kim, Lee, Choi, Kim, & Choi, 2015)
Increased postoperative vomiting was significantly associated with the rs3758987 SNP in Chinese women following gynecological surgery.	(Ma, Chen, Wu, Hu, & Fang, 2013)
HTR3C (5-hydroxytryptamine receptor 3C) A variant (rs6766410) was strongly associated with vomiting in patients receiving chemotherapy.	(Fasching et al., 2008)
Rs6806362 and rs6807670 were found to be associated with pregnancy-induced nausea and vomiting.	(Goecke et al., 2010)
rs6766410 was associated with increased frequency of CIN	(Mukoyama et al., 2016)
HTR3D (5-hydroxytryptamine receptor 3D) A coding variant Gly36Ala (rs6443930) was moderately associated with vomiting in patients receiving chemotherapy.	(Hammer et al., 2010)
ABCB1 (ATP binding cassette, subfamily B, member 1) Compared with palonosetron, ramosetron may be superior for reducing PONV severity, especially in patients with ABCB1 3435TT or 2677TT genotype.	(Song et al., 2016)
Another study found that the ABCB1 (C1236T genotype) may be a good predictor of responsiveness to ondansetron.	(Farhat et al., 2015)
In the acute phase, patients (taking serotonin antagonists)with ABCB13435TT, 1236TT or 2677TT genotypes had a higher control rate of CINV than other genotype groups: Subjects carrying homozygous variant alleles together (TT-TT-TT) showed a significantly higher protection from nausea and vomiting	(Zoto et al., 2015)
ABCB1 genotype (2677G>T/A) has also been noted to be a clinical predictor of responsiveness for ondansetron	(Choi, Lee, Choi, & Choi, 2010)
ABCB1 was associated with the frequency of vomiting in Japanese cancer patients taking morphine for pain.	(Fujita et al., 2010)
Multivariate analysis identified that the ABCB1 GG-CC diplotype was a borderline-significant (P = .07) predictive factor of morphine induced nausea and vomiting in postoperative patients.	(Coulbault et al., 2006)
Carriers of the CTG haplotype of the ABCB1 gene experienced Grade 3 and 4 chemotherapy-induced nausea and vomiting more often than other haplotypes in the delayed phase (P< 0.05)	(Perwitasari et al., 2011)

<p>CHRM3 (cholinergic receptor muscarinic 3) Large European study found CHRM3 was associated with increased risk for chemotherapy-induced nausea and vomiting</p> <p>In the only GWAS study the association with PONV was confirmed for one SNP (rs2165870), which is located upstream of the promoter for the muscarinic acetylcholine receptor 3 subtype (CHRM3) gene.</p>	<p>(Laugsand, et al., 2011)</p> <p>(Janicki et al., 2011)</p>
<p>COMT (catechol-O-methyltransferase) Large European study found COMT (rs4680 and rs4633) was associated with increased risk for chemotherapy-induced nausea and vomiting.</p> <p>Nausea and sedation scores were significantly lower during all observed postoperative periods for heterozygous patients of rs4680 (Val158Met).</p> <p>rs4680 was associated with increased frequency of CIN</p> <p>Following surgery for breast cancer, subjects who were homozygous Val/Val and Met/Met reported higher levels of nausea than subjects who carried the Val/Met genotype.</p> <p>COMT 158Met was significantly more prevalent in the IBS group (P=0.040) and significantly more prevalent in Chinese patients with diarrhea (P=0.029). 158Met was also more prevalent in those patients who had experienced symptoms for over 5 years</p>	<p>(Laugsand, et al., 2011)</p> <p>(Kolesnikov et al., 2013)</p> <p>(Mukoyama et al., 2016)</p> <p>(Wesmiller, et al., 2017)</p> <p>(Wang, Wu, Qiao, & Zhang, 2014)</p>
<p>CD14 (NDUFA2 gene NADH:ubiquinone oxidoreductase subunit A2) Rs2569190 CT genotype was related to higher nausea burden scores in patients with functional dyspepsia.</p>	<p>(Triantafyllou, Kourikou, Gazouli, Karamanolis, & Dimitriadis, 2017)</p>
<p>CYP2D6 (cytochrome P450 family 2 subfamily D member 6) Postoperative patients who were CYP2D6 ultra-metabolizers experienced significantly more PONV than patients who fell in the other metabolic categories.</p> <p>Trauma surgical patients who were classified as poor metabolizers had less postoperative nausea and vomiting compared to extensive or intermediate metabolizers in this study.</p> <p>Approximately 30% of all patients receiving chemotherapy experienced nausea and vomiting. Genetically defined ultrarapid meta-bolizers of CYP2D6 substrates had higher frequency of vomiting within the first 4 hours (P <.001) and within the period 5 to 24 hours (P <.03) after treatment than all the other patients</p>	<p>(Candiotti et al., 2005)</p> <p>(S. Wesmiller et al., 2013)</p> <p>(Kaiser et al., 2002)</p>
<p>CYP2J2 (cytochrome P450 family 2, subfamily J, member 2) The CYP2J2 c.-76T allele was associated with increased risk for treatment-induced nausea and/or vomiting in kidney transplant patients. (OR: 5.30, 95% confidence interval 1.49-18.79, p<0.05).</p>	<p>(Genvigir et al., 2017)</p>

<p>DRD2 (Dopamine Receptor D2) /ANKK (Ankyrin Repeat And Kinase Domain Containing 1) The DRD2 Taq IA polymorphism was associated with increased frequency of early PONV (PONV occurring in the post anesthesia care unit (PACU)).</p> <p>In a white cohort, the TaqIA A2 allele was significantly associated with a history of PONV.</p> <p>Rs1076560 was associated with increased frequency of CINV</p> <p>The incidence of nausea was significantly higher in the DRD2 TaqIA A1A2+A1A1 group than in the A2A2 group</p>	<p>(Nakagawa et al., 2008)</p> <p>(Frey et al., 2016)</p> <p>(Mukoyama et al., 2016)</p> <p>(Tashiro, Naito, Ohnishi, Kagawa, & Kawakami, 2014)</p>
<p>DRD3 (Dopamine Receptor D3) Odds ratios demonstrated that alleles for the DRD3 gene were associated with decreased PONV.</p>	<p>(S. W. Wesmiller et al., 2017)</p>
<p>HNF-1α (HNF1 homeobox A) In patients receiving mycophenolic acid post renal transplant, HNF1α genotypes were significantly different at week 1 in the overall Gastrointestinal Symptom Rating Scale, and for acid reflux and constipation subscales.</p>	<p>(Vu et al., 2013)</p>
<p>IL-1A (interleukin 1 alpha) IL-1 haplotypes may be associated with susceptibility to gastroesophageal reflux</p>	<p>(Izakovicova Holla et al., 2013)</p>
<p>IL-1B (interleukin 1 beta) IL-1B haplotypes may be associated with susceptibility to gastroesophageal reflux</p>	<p>(Izakovicova Holla et al., 2013)</p>
<p>IL-1RN (Interleukin 1 Receptor Antagonist) IL-1RN haplotypes may be associated with susceptibility to gastroesophageal reflux</p>	<p>(Izakovicova Holla et al., 2013)</p>
<p>OCT1 (POU2F1 Gene POU Class 2 Homeobox 1) OCT1 polymorphism rs12208357 was associated with high incidences of PONV and PONV leading to prolonged post anesthesia care unit stay in children</p>	<p>(Balyan et al., 2017)</p>
<p>OPRM1 (Opioid Receptor Mu 1) The severity of PONV in carriers of the GGGAACGC haplotype was significantly lower than in the carriers of the other haplotypes</p> <p>OPRM1 splice variant SNP, rs540825 was significantly associated with fentanyl-induced emesis in women undergoing minor gynaecological surgery.</p> <p>The results showed that 118G allele variant carriers consumed more opioids for analgesia, but reported less nausea and vomiting than the homozygous 118AA patients during the first 24 hours following surgery.</p> <p>The patients who carried the homozygous GG alleles for the A118G polymorphism, consumed more morphine than the others yet experienced less nausea and vomiting following total knee surgery.</p>	<p>(Sugino et al., 2014)</p> <p>(Pang et al., 2012)</p> <p>(Ren et al., 2015)</p> <p>(Chou et al., 2006)</p>

The AA group at A118G was associated with the highest incidence of nausea (P=0.02; 9.6%) versus AG (5.6%) and GG (1.2%) groups	(Sia et al., 2008)
SLC6A4 (Solute Carrier Family 6 Member 4) Women who inherited the LA/LA genotypes were at greater risk for nausea and vomiting when compared to women who carried any other combination of genotype.	(S. Wesmiller et al., 2014)
Individuals with amyloidotic polyneuropathy who are LA carriers, are noted to have decreased diarrhea than the other genotype groups.	(Obayashi et al., 2008)
TACR1 (Tachykinin receptor 1) In patients following lower abdominal surgery, rs3755468 showed significant association with the incidence and severity of postoperative nausea and vomiting.	(Hayase, Sugino, Moriya, & Yamakage, 2015)
TPH1 (Tryptophan Hydroxylase 1) Among IBS patients, five TPH1 SNPs showed some association with diarrhea and loose type of stool consistency, However, no P-values were less than the conservative multiple-comparison-adjusted threshold of 0.001 and hence these results must be interpreted cautiously.	(Jun, Kohen, Cain, Jarrett, & Heitkemper, 2011)
Odds ratios demonstrated that alleles for the TPH gene were associated with decreased PONV.	(S. W. Wesmiller et al., 2017)
UGT1A9 (UDP Glucuronosyltransferase Family 1 Member A9) In patients receiving mycophenolic acid post renal transplant, the UGT1A9 alleles are associated with the severity of early GI side effects as measured by the Gastrointestinal Symptom Rating Scale.	(Vu et al., 2013)
UGT2B7 (UDP Glucuronosyltransferase Family 2 Member B7) Patient reported nausea was statistically significantly associated with UGT2B7 (-G840A)	(Xia, Persaud, & Birnbaum, 2015)
The frequency of nausea was higher in patients without UGT2B7*2 allele in Japanese cancer patients taking morphine.	(Fujita et al., 2010)
XPD (ERCC2 Gene ERCC Excision Repair 2, TFIIH Core Complex Helicase Subunit) c.934GA or AA genotypes were at decreased risk for CINV from cisplatin chemoradiation in patients treated for head and neck cancers.	(Lopes-Aguiar et al., 2017)
Significant Genes – Epigenomic Findings none	Authors
Significant Genes – Transcriptomic Findings	Authors

CCL-16 (C-C Motif Chemokine Ligand 16) Pro-inflammatory chemokine CCL-16 gene expression was over expressed by over 130 fold in IBS constipation patients compared to IBS diarrhea patients and healthy controls.	(Del Valle-Pinero et al., 2011)
TNF (tumor necrosis factor0) TNF was significantly elevated (2.05-fold, p = 0.025) in patients experiencing CINV for treatment of esophageal cancer.	(Bowen et al., 2015)

References

- Balyan, R., Zhang, X., Chidambaran, V., Martin, L. J., Mizuno, T., Fukuda, T., . . . Sadhasivam, S. (2017). OCT1 genetic variants are associated with postoperative morphine-related adverse effects in children. *Pharmacogenomics*, *18*(7), 621-629. doi:10.2217/pgs-2017-0002
- Bowen, J. M., White, I., Smith, L., Tsykin, A., Kristaly, K., Thompson, S. K., . . . Keefe, D. M. (2015). Pre-therapy mRNA expression of TNF is associated with regimen-related gastrointestinal toxicity in patients with esophageal cancer: a pilot study. *Support Care Cancer*, *23*(11), 3165-3172. doi:10.1007/s00520-015-2696-7
- Candiotti, K. A., Birnbach, D. J., Lubarsky, D. A., Nhuch, F., Kamat, A., Koch, W. H., . . . Andrews, D. (2005). The impact of pharmacogenomics on postoperative nausea and vomiting: Do CYP2D6 allele copy number and polymorphisms affect the success or failure of ondansetron prophylaxis? *Anesthesiology*, *102*(3), 543-549. doi:00000542-200503000-00011 [pii]
- Choi, E. M., Lee, M. G., Choi, K. W., & Choi, S. H. (2010). Association of ABCB1 polymorphisms with the efficacy of ondansetron for postoperative nausea and vomiting. *Anaesthesia*, *65*, 996-1000.
- Chou, W., Yang, L., Lu, H., Ko, J., Wang, C., Lin, S., . . . Hsu, C. (2006). Association of mu-opioid receptor gene polymorphism (A118G) with variations in morphine consumption for analgesia after total knee arthroplasty. *Acta Anaesthesiologica Scandinavica*, *50*(7), 787-792.
- Coulbault, L., Beaussier, M., Verstuyft, C., Weickmans, H., Dubert, L., Tregouet, D., . . . Becquemont, L. (2006). Environmental and genetic factors associated with morphine response in the postoperative period. *Clin Pharmacol Ther*, *79*(4), 316-324. doi:10.1016/j.clpt.2006.01.007
- Del Valle-Pinero, A. Y., Martino, A. C., Taylor, T. J., Majors, B. L., Patel, N. S., Heitkemper, M. M., & Henderson, W. A. (2011). Pro-inflammatory chemokine C-C motif ligand 16 (CCL-16) dysregulation in irritable bowel syndrome (IBS): a pilot study. *Neurogastroenterol Motil*, *23*(12), 1092-1097. doi:10.1111/j.1365-2982.2011.01792.x
- Farhat, K., Waheed, A., Hussain, A., Ismail, M., Mansoor, Q., Pasha, A. K., & Jafery, N. (2015). Influence of genetic variations in ABCB1 on the clinical efficacy of ondansetron - A pharmacogenetic analysis of Pakistani population. *J Pak Med Assoc*, *65*(9), 963-966.
- Fasching, P. A., Kollmannsberger, B., Strissel, P. L., Niesler, B., Engel, J., Kreis, H., . . . Strick, R. (2008). Polymorphisms in the novel serotonin receptor subunit gene HTR3C show different risks for acute chemotherapy-induced vomiting after anthracycline chemotherapy. *J Cancer Res Clin Oncol*, *134*(10), 1079-1086. doi:10.1007/s00432-008-0387-1
- Frey, U. H., Schnee, C., Achilles, M., Silvanus, M. T., Esser, J., & Peters, J. (2016). Postoperative nausea and vomiting: The role of the dopamine D2 receptor TaqIA polymorphism. *Eur J Anaesthesiol*, *33*(2), 84-89. doi:10.1097/eja.0000000000000320
- Fujita, K., Ando, Y., Yamamoto, W., Miya, T., Endo, H., Sunakawa, Y., . . . Sasaki, Y. (2010). Association of UGT2B7 and ABCB1 genotypes with morphine-induced adverse drug reactions in Japanese patients with cancer. *Cancer Chemother Pharmacol*, *65*(2), 251-258. doi:10.1007/s00280-009-1029-2
- Garfield, L. D., Dixon, D., Nowotny, P., Lotrich, F. E., Pollock, B. G., Kristjansson, S. D., . . . Lenze, E. J. (2014). Common selective serotonin reuptake inhibitor side effects in older adults associated with genetic polymorphisms in the serotonin transporter and receptors: data from a randomized controlled trial. *Am J Geriatr Psychiatry*, *22*(10), 971-979. doi:10.1016/j.jagp.2013.07.003
- Genvigir, F. D. V., Nishikawa, A. M., Felipe, C. R., Tedesco-Silva, H., Jr., Oliveira, N., Salazar, A. B. C., . . . Hirata, R. D. C. (2017). Influence of ABCC2, CYP2C8, and CYP2J2 Polymorphisms on Tacrolimus and Mycophenolate Sodium-Based Treatment in Brazilian Kidney Transplant Recipients. *Pharmacotherapy*, *37*(5), 535-545. doi:10.1002/phar.1928
- Goecke, T. W., Ekici, A. B., Niesler, B., Loehberg, C. R., Hammer, C., Rappold, G., . . . Fasching, P. A. (2010). Two naturally occurring variants of the serotonin receptor gene HTR3C are associated with nausea in pregnancy. *Acta Obstet Gynecol Scand*, *89*(1), 7-14. doi:10.3109/00016340903322727

- Hammer, C., Fasching, P. A., Loehberg, C. R., Rauh, C., Ekici, A. B., Jud, S. M., . . . Niesler, B. (2010). Polymorphism in HTR3D shows different risks for acute chemotherapy-induced vomiting after anthracycline chemotherapy. *Pharmacogenomics*, *11*(7), 943-950. doi:10.2217/pgs.10.67
- Hayase, T., Sugino, S., Moriya, H., & Yamakage, M. (2015). TACR1 gene polymorphism and sex differences in postoperative nausea and vomiting. *Anaesthesia*, *70*(10), 1148-1159. doi:10.1111/anae.13082
- Izakovicova Holla, L., Borilova Linhartova, P., Hrdlickova, B., Marek, F., Dolina, J., Rihak, V., & Kala, Z. (2013). Haplotypes of the IL-1 gene cluster are associated with gastroesophageal reflux disease and Barrett's esophagus. *Hum Immunol*, *74*(9), 1161-1169. doi:10.1016/j.humimm.2013.06.026
- Janicki, P., Vealey, R., Liu, J., Escajeda, J., Postula, M., & Welker, K. (2011). Genome-wide association study using pooled DNA to identify candidate markers mediating susceptibility to postoperative nausea and vomiting. *Anesthesiology*, *115*(1), 54-64. doi:10.1097/ALN.0b013e31821810c7
- Joy Lin, Y. M., Hsu, C. D., Hsieh, H. Y., Tseng, C. C., & Sun, H. S. (2014). Sequence variants of the HTR3A gene contribute to the genetic prediction of postoperative nausea in Taiwan. *J Hum Genet*, *59*(12), 655-660. doi:10.1038/jhg.2014.89
- Jun, S., Kohen, R., Cain, K. C., Jarrett, M. E., & Heitkemper, M. M. (2011). Associations of tryptophan hydroxylase gene polymorphisms with irritable bowel syndrome. *Neurogastroenterol Motil*, *23*(3), 233-239. doi:10.1111/j.1365-2982.2010.01623.x
- Kaiser, R., Sezer, O., Papias, A., Bauer, S., Schelenz, C., Tremblay, P., . . . Brockmüller, J. (2002). Patient-tailored anti-emetic treatment with 5HT3 receptor antagonists according to cytochrome P-450 2D6 genotypes. *Journal of Clinical Oncology*, *20*, 2805-2811.
- Kang, G., Kim, K. R., Shim, H. J., Hwang, J. E., Bae, W. K., Chung, I. J., . . . Cho, S. H. (2017). Effect of the allelic variants of ABCB1, CYP2D6 and HTR3B on response of ramosetron to prevent chemotherapy-induced nausea and vomiting in Korean cancer patients. *Asia Pac J Clin Oncol*, *13*(1), 53-60. doi:10.1111/ajco.12575
- Kim, M. S., Lee, J. R., Choi, E. M., Kim, E. H., & Choi, S. H. (2015). Association of 5-HT3B Receptor Gene Polymorphisms with the Efficacy of Ondansetron for Postoperative Nausea and Vomiting. *Yonsei Med J*, *56*(5), 1415-1420. doi:10.3349/ymj.2015.56.5.1415
- Kolesnikov, Y., Gabovits, B., Levin, A., Veske, A., Qin, L., Dai, F., & Belfer, I. (2013). Chronic pain after lower abdominal surgery: do catechol-O-methyl transferase/opioid receptor mu-1 polymorphisms contribute? *Mol Pain*, *9*, 19. doi:10.1186/1744-8069-9-19
- Laugsand, E. A., Fladvad, T., Skorpen, F., Maltoni, M., Kaasa, S., Fayers, P., & Klepstad, P. (2011). Clinical and genetic factors associated with nausea and vomiting in cancer patients receiving opioids. *Eur J Cancer*, *47*(11), 1682-1691. doi:10.1016/j.ejca.2011.04.014
- Lehmann, A. S., Renbarger, J. L., McCormick, C. L., Topletz, A. R., Rouse, C., & Haas, D. M. (2013). Pharmacogenetic predictors of nausea and vomiting of pregnancy severity and response to antiemetic therapy: a pilot study. *BMC Pregnancy Childbirth*, *13*, 132. doi:10.1186/1471-2393-13-132
- Lopes-Aguiar, L., Costa, E. F., Nogueira, G. A., Lima, T. R., Visacri, M. B., Pincinato, E. C., . . . Lima, C. S. (2017). XPD c.934G>A polymorphism of nucleotide excision repair pathway in outcome of head and neck squamous cell carcinoma patients treated with cisplatin chemoradiation. *Oncotarget*, *8*(10), 16190-16201. doi:10.18632/oncotarget.7668
- Ma, X. X., Chen, Q. X., Wu, S. J., Hu, Y., & Fang, X. M. (2013). Polymorphisms of the HTR3B gene are associated with post-surgery emesis in a Chinese Han population. *J Clin Pharm Ther*, *38*(2), 150-155. doi:10.1111/jcpt.12033
- Mukoyama, N., Yoshimi, A., Goto, A., Kotani, H., Ishikawa, K., Miyazaki, N., . . . Noda, Y. (2016). An Analysis of Behavioral and Genetic Risk Factors for Chemotherapy-Induced Nausea and Vomiting in Japanese Subjects. *Biol Pharm Bull*, *39*(11), 1852-1858. doi:10.1248/bpb.b16-00440
- Nakagawa, M., Kuri, M., Kambara, N., Tanigami, H., Tanaka, H., Kishi, Y., & Hamajima, N. (2008). Dopamine D2 receptor Taq IA polymorphism is associated with postoperative nausea and vomiting. *J Anesth*, *22*(4), 397-403. doi:10.1007/s00540-008-0661-z

- Obayashi, K., Olsson, M., Anan, I., Ueda, M., Nakamura, M., Okamoto, S., . . . Suhr, O. B. (2008). Impact of serotonin transporter and catechol-O-methyl transferase genes polymorphism on gastrointestinal dysfunction in Swedish and Japanese familial amyloidotic polyneuropathy patients. *Clin Chim Acta*, *398*(1-2), 10-14. doi:10.1016/j.cca.2008.07.033
- Pang, G. S., Ithnin, F., Wong, Y. Y., Wang, J. B., Lim, Y., Sia, A. T., & Lee, C. G. (2012). A non-synonymous single nucleotide polymorphism in an OPRM1 splice variant is associated with fentanyl-induced emesis in women undergoing minor gynaecological surgery. *PLoS One*, *7*(11), e48416. doi:10.1371/journal.pone.0048416
- Perwitasari, D. A., Wessels, J. A., van der Straaten, R. J., Baak-Pablo, R. F., Mustofa, M., Hakimi, M., . . . Guchelaar, H. J. (2011). Association of ABCB1, 5-HT_{3B} receptor and CYP2D6 genetic polymorphisms with ondansetron and metoclopramide antiemetic response in Indonesian cancer patients treated with highly emetogenic chemotherapy. *Jpn J Clin Oncol*, *41*(10), 1168-1176. doi:10.1093/jjco/hyr117
- Ren, Z. Y., Xu, X. Q., Bao, Y. P., He, J., Shi, L., Deng, J. H., . . . Lu, L. (2015). The impact of genetic variation on sensitivity to opioid analgesics in patients with postoperative pain: A systematic review and meta-analysis. *Pain Physician*, *18*(2), 131-152.
- Reuffert, H., Thieme, V., Wallenborn, J., Lemnitz, N., Bergmann, A., Rudolf, K., . . . Kaisers, U. (2009). Do variations in the 5-HT_{3A} and 5-HT_{3B} serotonin receptor genes (*HTR3A* and *HTR3B*) influence the occurrence of postoperative vomiting? *Ambulatory Anesthesiology*, *109*(5), 1442-1447.
- Sia, A. T., Lim, Y., Lim, E. C., Goh, R. W., Law, H. Y., Landau, R., . . . Tan, E. C. (2008). A118G single nucleotide polymorphism of human mu-opioid receptor gene influences pain perception and patient-controlled intravenous morphine consumption after intrathecal morphine for postcesarean analgesia. *Anesthesiology*, *109*(3), 520-526. doi:10.1097/ALN.0b013e318182af21
- Song, J. W., Shim, J. K., Choi, S. H., Soh, S., Jang, J., & Kwak, Y. L. (2016). Comparison of Ramosetron and Palonosetron for Preventing Nausea and Vomiting after Spinal Surgery: Association With ABCB1 Polymorphisms. *J Neurosurg Anesthesiol*. doi:10.1097/ana.0000000000000361
- Sugai, T., Suzuki, Y., Sawamura, K., Fukui, N., Inoue, Y., & Someya, T. (2006). The effect of 5-hydroxytryptamine 3A and 3B receptor genes on nausea induced by paroxetine. *Pharmacogenomics J*, *6*(5), 351-356. doi:10.1038/sj.tpj.6500382
- Sugino, S., Hayase, T., Higuchi, M., Saito, K., Moriya, H., Kumeta, Y., . . . Janicki, P. K. (2014). Association of mu-opioid receptor gene (OPRM1) haplotypes with postoperative nausea and vomiting. *Exp Brain Res*, *232*(8), 2627-2635. doi:10.1007/s00221-014-3987-9
- Tanaka, M., Kobayashi, D., Murakami, Y., Ozaki, N., Suzuki, T., Iwata, N., . . . Mine, K. (2008). Genetic polymorphisms in the 5-hydroxytryptamine type 3B receptor gene and paroxetine-induced nausea. *Int J Neuropsychopharmacol*, *11*(2), 261-267. doi:10.1017/s1461145707007985
- Tashiro, M., Naito, T., Ohnishi, K., Kagawa, Y., & Kawakami, J. (2014). Impact of genetic and non-genetic factors on clinical responses to prochlorperazine in oxycodone-treated cancer patients. *Clin Chim Acta*, *429*, 175-180. doi:10.1016/j.cca.2013.12.011
- Tremblay, P. B., Kaiser, R., Sezer, O., Rosler, N., Schelenz, C., Possinger, K., . . . Brockmoller, J. (2003). Variations in the 5-hydroxytryptamine type 3B receptor gene as predictors of the efficacy of antiemetic treatment in cancer patients. *J Clin Oncol*, *21*(11), 2147-2155. doi:10.1200/jco.2003.05.164
- Triantafyllou, K., Kourikou, A., Gazouli, M., Karamanolis, G. P., & Dimitriadis, G. D. (2017). Functional dyspepsia susceptibility is related to CD14, GNB3, MIF, and TRPV1 gene polymorphisms in the Greek population. *Neurogastroenterol Motil*, *29*(1). doi:10.1111/nmo.12913
- Vu, D., Tellez-Corrales, E., Yang, J., Qazi, Y., Shah, T., Naraghi, R., . . . Min, D. I. (2013). Genetic polymorphisms of UGT1A8, UGT1A9 and HNF-1alpha and gastrointestinal symptoms in renal transplant recipients taking mycophenolic acid. *Transpl Immunol*, *29*(1-4), 155-161. doi:10.1016/j.trim.2013.05.005
- Wang, Y., Wu, Z., Qiao, H., & Zhang, Y. (2014). A genetic association study of single nucleotide polymorphisms in GNBeta3 and COMT in elderly patients with irritable bowel syndrome. *Med Sci Monit*, *20*, 1246-1254. doi:10.12659/msm.890315

- Wesmler, S., Bender, C., Sereika, S., Ahrendt, G., Bonaventura, M., Bovbjerg, D., & Conley, Y. (2014). The association of the serotonin transport gene and post discharge nausea and vomiting in women following breast cancer surgery. *Oncology Nursing Forum*, *41*(2), 195-202. doi:10.1188/14.ONF.195-202
- Wesmler, S., Henker, R. A., Sereika, S. M., Donovan, H. S., Meng, L., Gruen, G. S., . . . Conley, Y. P. (2013). The association of CYP2D6 genotype and postoperative nausea and vomiting in orthopedic trauma patients. *Biol Res Nurs*, *15*(4), 382-389. doi:10.1177/1099800412449181
- Wesmler, S. W., Sereika, S. M., Bender, C. M., Bovbjerg, D., Ahrendt, G., Bonaventura, M., & Conley, Y. P. (2017). Exploring the multifactorial nature of postoperative nausea and vomiting in women following surgery for breast cancer. *Auton Neurosci*, *202*, 102-107. doi:10.1016/j.autneu.2016.09.017
- Xia, S., Persaud, S., & Birnbaum, A. (2015). Exploratory study on association of single-nucleotide polymorphisms with hydromorphone analgesia in ED. *Am J Emerg Med*, *33*(3), 444-447. doi:10.1016/j.ajem.2014.12.008
- Zoto, T., Kilickap, S., Yasar, U., Celik, I., Bozkurt, A., & Babaoglu, M. O. (2015). Improved anti-emetic efficacy of 5-HT3 receptor antagonists in cancer patients with genetic polymorphisms of ABCB1 (MDR1) drug transporter. *Basic Clin Pharmacol Toxicol*, *116*(4), 354-360. doi:10.1111/bcpt.12334

Supplemental Table A5. Pain.

Significant Genes – Genomic Findings	Authors
<p>ABCB1 (ATP binding cassette, subfamily B, member 1) C3435T Cancer patients with the wild-type (CC) are more sensitive to pain.</p> <p>Children who underwent surgery and who had CC alleles were more likely to have more severe pain episodes than CT or TT (using facial pain scale).</p>	<p>(Wang et al., 2015)</p> <p>(Mamie, Rebsamen, Morris, & Morabia, 2013)</p>
<p>ACTN3 (Actinin Alpha 3 Gene/Pseudogene) R577X Post marathon, runners with one or 2 X alleles reported more pain.</p>	<p>(Del Coso et al., 2017)</p>
<p>ADRB1 (Adrenoceptor Beta 1) Postoperative patients with Arg/Arg genotype experience more pain (visual analog scale) at 2 hours post-surgery.</p> <p>A145G patients with A alleles were more sensitive to cold induced pain, especially males.</p>	<p>(W. Wei et al., 2015)</p> <p>(Moriyama et al., 2013)</p>
<p>ADRB2 (Adrenoceptor Beta 2) rs12654778 and rs1042713 were associated chronic widespread pain or pain status. Researchers found common haplotypes associated with pain too.</p> <p>rs2053044 was associated with comorbid neck and back pain and pain in 3 to 4 pain areas in the past month.</p>	<p>(Hocking et al., 2010)</p> <p>(Skouen et al., 2012)</p>
<p>ADRA1A (Alpha1a-adrenoceptor) rs1048101 polymorphism is complex is associated with development of regional pain syndrome type I.</p>	<p>(Herlyn et al., 2010)</p>
<p>ApoE The epsilon4 allele is associated with headache (tension and migraine grouped together) in a meta-analysis.</p>	<p>(Miao, Wang, Zheng, & Zhuang, 2015)</p>
<p>BDNF (brain-derived neurotrophic factor) Val⁶⁶Met allele In presence of chronic pain, BDNF Met carriers experienced a greater pain response to Event Related Potentials compared with Val homozygotes. In absence of chronic pain, the Met response was weaker than Val.</p> <p>Met carriers indicated more pain (Chronic Pain Grade questionnaire) than the Val⁶⁶Val group. BDNF expression did not differ between the groups.</p> <p>Val⁶⁶Met is associated with reduced response to repeated evoked potentials in healthy participants, and may be related to plasticity.</p> <p>Those with Met/Met allele evoked potentials did not show a significant difference in response</p>	<p>(Vossen et al., 2010)</p> <p>(Generaal et al., 2016)</p> <p>(Di Lorenzo et al., 2012)</p> <p>(Hwang, Kim, Yoon, Uhm, & Chang,</p>

between sub- and supra-thresholds, possibly due to difference in plasticity.	2015)
In women with primary dysmenorrhea, those with Met/Met reported more pain.	(L. C. Lee et al., 2014)
Met/met report more pain (McGill Pain Inventory) in dysmenorrhea and demonstrated less neuroplasticity.	(S. Y. Wei et al., 2016)
CACNG2 (calcium voltage-gated channel auxiliary subunit gamma 2) This gene is associated with chronic pain in women post mastectomy.	(Nissenbaum et al., 2010)
CNR1 (cannabinoid receptor 1) Patients with irritable bowel syndrome who have >10/>10 AAT repeats report higher pain scores.	(Park et al., 2011)
COMT (catechol-O-methyltransferase) Val¹⁵⁸Met allele In participants with chronic pain, the COMT Met carriers experienced an increased the cortical pain response on Event Related Potentials compared with the Val homozygotes. In absence of chronic pain, the Met response was weaker than Val.	(Vossen et al., 2010)
Val¹⁵⁸Met allele (rs4680) In patients with temporomandibular disorder, this COMT was associated with pain (1 or 2 copies of met produce reduced activity), and the Val allele is protective.	(Smith et al., 2014)
Minor A allele of SNP rs165774. A meta-analysis on 2 separate cohorts (patients with temporomandibular disorder), this allele provided a protective effect and decreased pain sensitivity (quantitative sensory testing with heat and pressure pain).	(Meloto et al., 2015)
Cancer patients with Val/Val reported more pain (Brief Pain Inventory, numeric rating scale) than those with Val/Met.	(Wang et al., 2015)
Val¹⁵⁸Met allele Met/Met cardiac patients undergoing a painful procedure reported more pain (numeric rating scale) than Val/Met or Val/Val.	(Ahlers et al., 2013)
In patients 6 weeks after motor vehicle accident, less pain (numeric rating scale 0-10) was reported in those with CGGG haplotype plus TCG.	(Bortsov, Diatchenko, & McLean, 2014)
Patients with fibromyalgia and Met/Met alleles had lower nociocceptive flexion reflex threshold (quantitative sensory testing) than Val/Val. Met/Met tended to have higher pain scores (ns).	(Desmeules et al., 2014)
Participants homozygous for low pain sensitivity (Val/Val) had lower pain scores (visual analog scores) to stimuli.	(Diatchenko et al., 2006)
Met/met was associated with lower pain pressure thresholds in children with chronic tension headaches.	(Fernandez-de-las-Penas et al., 2011)

Women with depression and the low pain sensitivity haplotype SNPs rs6269, rs4633, rs4818, and rs4680 reported more overall pain and pain while awake. This haplotype result was not the same for men.

(Fijal, Perlis, Heinloth, & Houston, 2010)

Patients who had disc herniation and Met/Met reported more pain (visual analog scale).

(Jacobsen et al., 2012)

Healthy participants with met/met reported more pain (visual analog scale 0-100) to the painful stimuli for the experiment than Val/val.

(Jensen, Lonsdorf, Schalling, Kosek, & Ingvar, 2009)

Minor alleles were associated with less pain for rs165774 (heat pain intensity) and rs887200 (cold pain intensity).

(Kambur et al., 2013)

In children post-surgery, facial pain scores were higher for AA or GA alleles than for GG.

(Mamie et al., 2013)

In post-surgical trauma patients, those with rs4680 A/A alleles reported more pain at 45 minutes time point in PACU.

(Henker et al., 2013)

In women with carpal tunnel syndrome, Met/Met carriers reported more pain.

(Fernandez-de-las-Penas, Ambite-Quesada, Ortega-Santiago, et al., 2013)

rs4680 Met/Met genotype was more frequent in patients with multiple sclerosis with pain.

(Fernandez-de-las-Penas, Ambite-Quesada, Ortiz-Gutierrez, et al., 2013)

rs4818 and rs6269 rare alleles were associated with less pain at rest and on movement.

rs6267 the T allele is associated with pain in Parkinson's disease.

(P. J. Lee, Delaney, Keogh, Sleeman, & Shorten, 2011)
(W. Li, Chen, Yin, & Zhang, 2014)

rs6269, rs4633, rs4818, and rs4680. Patients with fibromyalgia and met/met for rs4680 or with haplotypes for high or average pain sensitivity had higher thermal pain and pressure sensitivity.

(Martinez-Jauand et al., 2013)

ACCG, a haplotype of high sensitivity to pain, showed an interaction with stress. Number of copies of the haplotype are associated with pain in nonstressed participants and in one cohort this was influenced by sex (occurred in males only).

(Meloto et al., 2016)

In healthy volunteers, rs4680 A allele carriers report a higher bone pain tolerance.

rs4633 and rs4680 were associated with less pain in patients with low back pain, but the two were perfectly correlated. In rs4680, the heterozygote had the most reduction in pain after

(Nielsen, Olesen, Sato, Christrup, & Drewes, 2016)
(Omair, Lie, Reikeras, Holden, & Brox,

<p>intervention.</p> <p>COMT “vulnerable genotype” is associated with higher pain ratings in patients with thermal burns.</p> <p>Those with rs6269 AA, rs4633 TT, rs4818 CC, and rs4680 AA reported lower preop pain intensity and 1 year postop.</p> <p>rs6269, rs4633, and rs4680 were associated with FLACC pain scores in children postop.</p> <p>As number of met alleles increases, heat pain sensation decreased (lower temperature causes pain) in healthy participants, but no effect was found in those with borderline personality disorder. fMRI measuring pain response differed between healthy and those with borderline personality disorder.</p> <p>Depressive symptoms moderate the relationship between COMT and temporomandibular pain: rs5993882 is associated with pain in those without depressive symptoms and rs1544325 is found in those with depressive symptoms and TMD pain.</p> <p>rs4818 is associated with time-averaged pain scores in women postop hysterectomy.</p> <p>Female carriers of Met allele were more likely to have osteoarthritic hip pain than Val/Val.</p> <p>Only one SNP, rs4633 was associated with pain in male Han Chinese during transcutaneous electrical acupoint stimulation.</p> <p>Val¹⁵⁸Met. In healthy men and women, the met/met allele showed less response in μ opioid receptor binding potentials in the brain to sustained pain and greater sensory and affective ratings. (McGill pain scale and visual analog scale, MRI) Val/Val was the opposite.</p>	<p>2012)</p> <p>(Orrey et al., 2012)</p> <p>(Rut et al., 2014)</p> <p>(Sadhasivam et al., 2014)</p> <p>(Schmahl et al., 2012)</p> <p>(Schwahn et al., 2012)</p> <p>(Tan et al., 2016)</p> <p>(van Meurs et al., 2009)</p> <p>(Xiang et al., 2012)</p> <p>(Zubieta et al., 2003)</p>
<p>DAT dopamine transporter gene (or SLC6A3)</p> <p>VNTR 10 allele was associated with a lower cold pain tolerance.</p>	<p>(Treister et al., 2009)</p>
<p>DRD3 (Dopamine Receptor D3)</p> <p>Ser9Gly predicts diffuse nociceptive inhibitory control in patients with fibromyalgia and controls and is associated with the thermal pain threshold in fibromyalgia.</p>	<p>(Potvin et al., 2009)</p>

<p>DRD4 (Dopamine Receptor D4) Alleles with less than 4 repeats were considered “short”. The Short/Short genotype was associated with more pain in patients undergoing cosmetic surgery.</p> <p>DRD4-521C/T modulates cold pain response and may influence opioid dependence.</p> <p>957C>T polymorphism TT exhibits lower thermal and pain sensitivity.</p>	<p>(Aoki et al., 2013)</p> <p>(Ho, Tang, Cheung, & Stadlin, 2008)</p> <p>(Jaaskelainen et al., 2014)</p>
<p>ESR1 (estrogen receptor 1) In women with TMJ osteoarthritis, those with the PX haplotype were more likely to report moderate/severe pain.</p> <p>Higher back pain scores (visual analog scale) were associated with GG genotype.</p>	<p>(Kang et al., 2007)</p> <p>(Roh et al., 2013)</p>
<p>FAAH (fatty acid amide hydrolase) P129T rs324420 is associated with cold pain sensitivity in women with breast cancer.</p> <p>rs324419 was associated with pain in Parkinson’s Disease patients.</p>	<p>(Cajanus et al., 2016)</p> <p>(Greenbaum et al., 2012)</p>
<p>FKBP5 (FK506 binding protein 5) rs3800373, rs9380526, rs9394314, rs2817032, and rs2817040 were associated with pain in 2 cohorts of patients with MVA trauma and victims of sexual assault.</p> <p>rs2817038 moderated the relationship between musculoskeletal pain after motor vehicle accident and neighborhood disadvantage.</p>	<p>(Bortsov et al., 2013)</p> <p>(Ulirsch et al., 2014)</p>
<p>GNB3 (G Protein Subunit Beta 3) 825 TT was associated with more epigastric pain in patients with dyspepsia.</p>	<p>(Oshima et al., 2010)</p>
<p>GCH1 (GTP Cyclohydrolase 1) rs4411417, rs3783641, and rs752688 uncommon alleles were associated with less capsaicin pain in healthy participants.</p> <p>A pain protective haplotype was associated with lower pain scores in outpatient pain centers.</p> <p>GCH1 CCTA haplotypes may protect against fibromyalgia pain.</p>	<p>(Campbell et al., 2009)</p> <p>(Doehring et al., 2009)</p> <p>(S. K. Kim et al., 2013)</p>
<p>HLA-DRB1 (Major Histocompatibility Complex, Class II, DR Beta 1) In Japanese patients with post herpetic neuralgia (visual analog scale) HLA-A*3303, HLA-B*4403, and HLA-DRB1*1320 were associated with pain.</p> <p>HLA-DRB1*04 – DQB1*03:02 haplotype increased risk of developing post-surgical pain in 2 cohorts.</p>	<p>(M. Sato et al., 2002)</p> <p>(Dominguez et al., 2013)</p>
<p>HTR1A (5-hydroxytryptamine receptor 1A) rs6295 minor G allele is associated with less sensitivity to thermal pain, but increased their response at high intensities.</p>	<p>(Lindstedt et al., 2012)</p>

<p>HTR2A (5-hydroxytryptamine receptor 2A) Localized temporomandibular disorder facial pain was associated with 6 serotonergic pathway SNPs to create a risk index: rs9316233 (HTR2A); rs4776783 (MAP2K1) rs12439516 (MAP2K1); rs2276008 (MAPK1); rs6928 (MAPK1); and rs3813928 (HTR2C).</p> <p>5-Ht2A receptor gene is associated with abdominal pain ratings (visual analog scale) in patients with irritable bowel syndrome with TT having higher scores.</p> <p>rs17289394 and rs12584920, T allele, were associated with more pain sites, and having chronic widespread pain (American College of Rheumatology criteria).</p>	<p>(Slade et al., 2013)</p> <p>(Pata et al., 2004)</p> <p>(Nicholl et al., 2011)</p>
<p>HTR2C (5-hydroxytryptamine receptor 2C) Localized temporomandibular disorder facial pain was associated with 6 serotonergic pathway SNPs to create a risk index: rs9316233 (HTR2A); rs4776783 (MAP2K1) rs12439516 (MAP2K1); rs2276008 (MAPK1); rs6928 (MAPK1); and rs3813928 (HTR2C).</p>	<p>(Slade et al., 2013)</p>
<p>HTR3B (5-hydroxytryptamine receptor 3B) In patients taking certain statins, myalgia was associated with rs2276307.</p>	<p>(Ruano et al., 2007)</p>
<p>HTR7 (5-Hydroxytryptamine Receptor 7) In patients taking certain statins, myalgia was associated with rs1935349.</p>	<p>(Ruano et al., 2007)</p>
<p>IL-10 (interleukin 10) Men with chronic pelvic pain syndrome (pain measured by the NIH-Chronic Prostatitis Symptom Index) were more likely to have the IL10 AA genotype, which is associated with lower IL-10 expression.</p> <p>IL-10 haplotype A8 was associated with persistent breast pain in women after breast cancer surgery.</p> <p>rs1800871 was associated with pain (less) in patients with lung cancer.</p>	<p>(Shoskes, Albakri, Thomas, & Cook, 2002)</p> <p>(Stephens et al., 2014)</p> <p>(Rausch et al., 2010)</p>
<p>IL13 (interleukin 13) Women with breast cancer and rs1295686 minor allele were more likely to report breast pain before surgery.</p>	<p>(McCann et al., 2012)</p>
<p>IL18RAP (Interleukin 18 Receptor Accessory Protein) T-C-C-A-T haplotype with IL1A, IL18R1 and IL18RAP are associated with improvement in pain in patients with low back pain.</p>	<p>(Omair, Holden, Lie, Reikeras, & Brox, 2013)</p>
<p>IL18R1 (Interleukin 18 Receptor 1) T-C-C-A-T haplotype with IL1A, IL18R1 and IL18RAP are associated with improvement in pain in patients with low back pain.</p>	<p>(Omair et al., 2013)</p>
<p>IL-1A (interleukin 1 alpha) Patients with low back pain who had CT/TT genotype reported more pain intensity and had a lower pain threshold versus CC.</p>	<p>(Schistad, Jacobsen, Roe, & Gjerstad, 2014)</p>

Patients with low back pain IL-1 α T889 (with IL-1RNA1812) reported a greater pain intensity.	(Solovieva et al., 2004)
T-C-C-A-T haplotype with IL1A, IL18R1 and IL18RAP are associated with improvement in pain in patients with low back pain.	(Omair et al., 2013)
In patients with back pain, IL1A T allele in combination with IL1RN A allele report more pain on follow-up.	(Moen, Schistad, Rygh, Roe, & Gjerstad, 2014)
IL-1B (interleukin 1 beta) rs1143634 This was associated with increased pain in a sample of veterans with low back pain.	(Loncar, Curic, Mestrovic, Mickovic, & Bilic, 2013)
IL1R1 (Interleukin 1 Receptor Type 1) rs2110726 minor allele was associated with less pain preop in women with breast cancer.	(McCann et al., 2012)
IL-1R2 (interleukin 1 receptor 2) rs11674595 was associated with persistent breast pain in women after breast cancer surgery.	(Stephens et al., 2014)
IL1RN (Interleukin 1 Receptor Antagonist) In patients with back pain, IL1A T allele in combination with IL1RN A allele report more pain on follow-up.	(Moen et al., 2014)
IL6 (interleukin 6) -147 G/G This cytokine genotype was associated with more pain in patients with juvenile rheumatoid arthritis.	(Oen et al., 2005)
-174 G/C Female cancer patients with the G/G allele reported more pain severity (numeric rating 0-10) than G/C or C/C. Males did not differ statistically.	(Reyes-Gibby et al., 2008)
IL8 (interleukin 8) -251 T/A This was significantly associated with more pain in a group of patients with pancreatic cancer, in AT and TT versus AA in Caucasians.	(Reyes-Gibby, Shete, et al., 2009)
In patients with non-small cell lung cancer, TA and AA reported more pain than TT in Caucasians.	(Reyes-Gibby et al., 2007)
IL8-T251T/A In patients with advanced stage non-small cell lung cancer, TT reported less pain severity (and less severe fatigue) than AT or AA.	(Reyes-Gibby et al., 2013)
KCNJ3 (Potassium Voltage-Gated Channel Subfamily J Member 3) rs7574878 Women with breast cancer who had preoperative pain in the breast and the TT allele were more likely to report this pain. One haplotype also increased likelihood of pain.	(Langford et al., 2014)

<p>KCNJ6 (Potassium Voltage-Gated Channel Subfamily J Member 6) Surgical patients with the A/A genotype required more analgesia post-op (clinical data and pain rating).</p> <p>rs2835859 C allele carriers are less sensitive to cold and mechanical pain stimuli.</p> <p>rs2835914 Women with breast cancer who had preoperative pain in the breast and the GG allele were more likely to report this pain. KCNJ6 rs8129919: Women with the A allele were more likely to report this pain in a dose-dependent manner. KCNJ6 rs2836050: women with TT were more likely to report this pain.</p>	<p>(Nishizawa et al., 2009)</p> <p>(Nishizawa et al., 2014)</p> <p>(Langford et al., 2014)</p>
<p>KCNK9 (Potassium Two Pore Domain Channel Subfamily K Member 9) rs3780039 Women with breast cancer who had preoperative pain in the breast and the G allele (hetero- or homozygous) were more likely to report this pain and for rs11166921 were more likely to report pain if they had the AA allele.</p>	<p>(Langford et al., 2014)</p>
<p>KCNS1 (Potassium Voltage-Gated Channel Modifier Subfamily S Member 1) Val allele rs734784 Participants across 5 cohorts were more likely to have higher pain scores if they have a Val allele, and this is increased more for 2 Val alleles.</p> <p>rs4499491 Women with breast cancer who had preoperative pain in the breast and the AA allele were more likely to report this pain.</p>	<p>(Costigan et al., 2010)</p> <p>(Langford et al., 2014)</p>
<p>LTA (lymphotoxin alpha) rs1799964 was associated with pain (SF-8) in >5-year lung cancer survivors. Those with one or 2 G alleles were associated with less pain.</p>	<p>(Rausch et al., 2012)</p>
<p>MAO-A (Monoamine Oxidase A) VNTR—carriers of the 4 allele have a lower cold tolerance.</p>	<p>(Treister et al., 2009)</p>
<p>MAO-B (Monoamine Oxidase B) In males the A/G polymorphism in intron 13 G allele experienced a more intense pain than those with A allele post tonsillectomy.</p>	<p>(Sery et al., 2006)</p>
<p>MAPK1 (Mitogen-Activated Protein Kinase 1) Localized temporomandibular disorder facial pain was associated with 6 serotonergic pathway SNPs to create a risk index: rs9316233 (HTR2A); rs4776783 (MAP2K1) rs12439516 (MAP2K1); rs2276008 (MAPK1); rs6928 (MAPK1); and rs3813928 (HTR2C).</p> <p>MAPK1/ERK2 rs8136867 was associated with severe pain in head and neck cancer patients.</p>	<p>(Slade et al., 2013)</p> <p>(Reyes-Gibby et al., 2016)</p>
<p>MAP2K1 (Mitogen-Activated Protein Kinase Kinase 1) Localized temporomandibular disorder facial pain was associated with 6 serotonergic pathway SNPs to create a risk index: rs9316233 (HTR2A); rs4776783 (MAP2K1) rs12439516 (MAP2K1); rs2276008 (MAPK1); rs6928 (MAPK1); and rs3813928 (HTR2C).</p>	<p>(Slade et al., 2013)</p>

<p>MMP1 (Matrix Metalloproteinase 1) rs1799750 2G/2G genotype reported more pain (visual analog scale, McGill Pain Questionnaire) in patients with low back and sciatic pain.</p>	(Jacobsen et al., 2013)
<p>MMP3 (Matrix Metalloproteinase 3) rs72520913 A/A is associated with less pain reduction versus other allele combinations in patients with low back pain.</p>	(Omair et al., 2013)
<p>NTRK1 (Neurotrophic Receptor Tyrosine Kinase 1_ Pain scores (facial pain score) in children post-surgery were higher during mobilization for CT or TT alleles than for CC allele.</p>	(Mamie et al., 2013)
<p>OPG (TNFRSF11B TNF Receptor Superfamily Member 11b) rs2073618 was associated with severity of pain in patients with breast cancer treated with aromatase inhibitors.</p>	(Lintermans et al., 2016)
<p>OPRK1 (Opioid Receptor Kappa 1) rs6473799 was associated with sensitivity to heat pain and rs7016778 and rs7824175 were associated with pressure pain in healthy participants.</p> <p>rs7016778 and rs7824175 was associated with baseline cuff pressure response in healthy participants.</p> <p>In healthy volunteers, rs6473799 C allele carriers report a higher mechanical visceral pain tolerance threshold.</p>	(H. Sato et al., 2013) (R. Olsen et al., 2016) (Nielsen et al., 2016)
<p>OPRM1 (Opioid Receptor Mu 1) (A118G) Postoperative patients with AG or GG alleles (versus AA) appear to experience more pain and need more pain medication in this study.</p> <p>Children who underwent surgery and had the GA allele were more likely to have severe pain than those with the AA allele (facial pain scale).</p> <p>The G allele was associated with more pain in breast cancer patients post-surgery.</p> <p>In patients with diabetic foot ulcers, AG and GG were more likely to be assigned to the painless group versus AA in painful group (by self-reported pain).</p> <p>Healthy participants with AG and GG alleles were associated with less pain sensitivity to pressure pain; for heat pain, males with those alleles were associated with less pain and females associated with more pain.</p> <p>Post-surgical trauma patients with A118G reported higher pain scores (numeric rating) at 15 minutes timepoint in the PACU.</p>	(Bartosova, Polanecky, Perlik, Adamek, & Slanar, 2015) (Mamie et al., 2013) (Cajanus, Kaunisto, Tallgren, Jokela, & Kalso, 2014) (Cheng, Lin, Chang, Wang, & Lai, 2010) (Fillingim et al., 2005) (Henker et al., 2013) (Ochroch, Vachani, Gottschalk, &

<p>In post-thoracotomy patients, rs634479, rs499796, rs548646, and rs679987 were associated with pain.</p> <p>In women post-op caesarean section, 118G/G reported higher pain scores than those with A alleles.</p> <p>In women with pain post sexual assault, the G allele is associated with less pain and a reduced extent of pain.</p> <p>Heterozygous and wild-type have different pain responses (surgical patients, visual analog scale).</p> <p>rs7824175 was associated with residual pain in cancer patients.</p> <p>In healthy Han Chinese women, those with the GA allele of the IVS2+31G>A polymorphism had a higher pressure pain threshold than GG.</p> <p>In patients with chronic postsurgical pain, rs1799971 carrying at least one copy of the G allele had more pain.</p> <p>In migraine sufferers, A118G G allele is associated with more pain than A allele.</p> <p>A118G women with G allele reported more pain at 1year post disc herniation than men and no difference between men and women with AA.</p> <p>rs563649 was associated with pain perception in healthy volunteers.</p> <p>A118G AA pain scores were lower and GG were the highest post cesarean surgery.</p> <p>Minor allele 118G was associated with higher pain scores in hysterectomy patients.</p> <p>A118G polymorphism. Pain tolerance threshold was measured (electrical stimulation) in preoperative women and the G allele had a dose dependent effect on pain (lessening the tolerance).</p>	<p>Kanetsky, 2012)</p> <p>(Tan et al., 2009)</p> <p>(Ballina et al., 2013)</p> <p>(De Capraris et al., 2011)</p> <p>(Droney et al., 2013)</p> <p>(Huang et al., 2008)</p> <p>(Kolesnikov et al., 2013)</p> <p>(Menon et al., 2012)</p> <p>(M. B. Olsen et al., 2012)</p> <p>(Shabalina et al., 2009)</p> <p>(Sia et al., 2008)</p> <p>(Sia et al., 2013)</p> <p>(Zhang et al., 2010)</p>
<p>P2RY12 (Purinergic Receptor P2Y12) Minor allele is associated with increased pain (numeric rating scale) in cancer and postoperative pain cohorts.</p>	<p>(Sumitani et al., 2017)</p>
<p>P2RX7 (Purinergic Receptor P2X 7) rs1718125 in those who did not have the A allele, pain score (visual analog) was lower.</p>	<p>(Ide et al., 2014)</p>

An association with low pain intensity and His270 rs7958311 in cohorts with pain after mastectomy and one with osteoarthritis.	(Sorge et al., 2012)
<p>PTGS2 (Prostaglandin-endoperoxide synthetase 2) rs5277 was associated with pain in 3-5 year lung cancer survivors, and those with one or 2 G alleles were associated with higher pain scores.</p> <p>COX-2 Endodontic patients post-operative with the haplotype rs2383515 G, rs5277 G, rs5275 T, and rs2206593 were associated with pain.</p> <p>rs5275 CC genotype was associated with less severe pain in non-small cell lung cancer (not alone, but if adding protective effects of TNF-alpha AA and NFKBIA TT, pain severity risk decreases substantially).</p>	<p>(Rausch et al., 2012)</p> <p>(Applebaum, Nackley, Bair, Maixner, & Khan, 2015)</p> <p>(Reyes-Gibby, Spitz, et al., 2009)</p>
<p>Chromosome 17 upstream of RHBDF2 rs12948783 Cancer patients with the GG genotype exhibited nearly complete pain relief with opioids when compared with AA or GA. Found 7 other SNPs associated with pain relief: on chromosomes 2, 6, 10 11, and 19.</p>	(Galvan et al., 2011)
<p>SCN9A (Sodium Voltage-Gated Channel Alpha Subunit 9) rs16851778 was associated with low mechanical pain sensitivity in healthy women of Chinese descent.</p> <p>rs4286289 and rs6746030 were associated with greater postoperative pain (numeric rating scale) in Chinese women.</p> <p>In patients with Parkinson's Disease, rs6746030 was associated with pain susceptibility.</p> <p>Val991Leu/Met932Leu was associated with pain (numeric pain rating) in patients with diabetic peripheral neuropathy.</p> <p>rs6746030 A allele was associated with more pain in osteoarthritis and held in additional cohorts.</p>	<p>(Duan et al., 2015)</p> <p>(Duan et al., 2016)</p> <p>(Greenbaum et al., 2012)</p> <p>(Q. S. Li et al., 2015)</p> <p>(Reimann et al., 2010)</p>
<p>SLC6A4 (Solute Carrier Family 6 Member 4) Serotonin Transporter 5-HTTLPR genotype Short/Short carriers report more pain in trigeminal neuralgia.</p> <p>5-HTT L_A/L_A changed their perception of pain based on their emotional state. If emotional state was negative, pain was rated worse; if positive, pain was rated less.</p> <p>Carriers of the S allele reported lower pain thresholds and increased pain catastrophizing.</p> <p>Those men with short allele 5-HTTLPR have a higher pain threshold and tolerance.</p>	<p>(Cui, Yu, & Zhang, 2014)</p> <p>(Horjales-Araujo et al., 2013)</p> <p>(Kunz, Hennig, Karmann, & Lautenbacher, 2016)</p> <p>(Palit et al., 2011)</p>

Those with 5HTTLPR short allele had a decreased pain inhibition.	(Treister et al., 2011)
Postoperative women with 5HTTLPR L_A/L_A and rs25331 G alleles reported more pain (brief pain inventory).	(Wesmler et al., 2014)
TAOK3 (TAO Kinase 3) rs795484 was associated with pain in pediatric patients postoperatively, European Caucasian and African American.	(Cook-Sather et al., 2014)
TCL1A Chromosome 14 near T-cell Leukemia 1A SNPs rs47158782, rs7159713, rs2369049, rs11849538 In an aromatase inhibitor (breast cancer) trial, GWAS was done to determine genes associated with musculoskeletal pain and 4 SNPs were found to be associated with greater pain. In a follow-up article, these SNPs were related to expression of several interleukins.	(Ingle et al., 2010) and (M. Liu et al., 2012)
rs13361160, rs2386592 upstream of CCT5 and downstream of FAM173B In a GWAS and meta-analysis of numerous studies, two SNPs were significantly associated with chronic widespread pain (Fibromyalgia Criteria American College Rheumatology).	(Peters et al., 2013)
TNF (tumor necrosis factor) -308G/A Men with cancer and the G/G allele reported less pain severity. There was not a statistical difference in women.	(Reyes-Gibby et al., 2008)
In black South African patients with HIV, rs28445017*A was associated with more pain.	(Hendry et al., 2016)
-308GA AA is associated with less severe pain in patients with non-small cell lung cancer.	(Reyes-Gibby, Spitz, et al., 2009)
TRPA1 (Transient Receptor Potential Cation Channel Subfamily A Member 1) Variations in heat pain sensitivity and gender were found.	(H. Kim, Mittal, Iadarola, & Dionne, 2006)
TRPV1 (transient receptor potential cation channel, subfamily V, member 1) 585 Ile-Ile genotype; rs8065080 This genotype was associated with less osteoarthritic knee pain in a meta-analysis of 7 large cohorts. Pain indicates “symptomatic” OA as radiologic examination is not a reliable indication of knee OA pain. This gene is also associated with less thermal pain sensitivity.	(Valdes et al., 2011)
Females with the Val (585) Val allele had longer cold withdrawal times.	(H. Kim et al., 2004)
Significant Genes – Epigenomic Findings	Authors
OPRM1 (Opioid Receptor Mu 1) CpG island 5' UTR In former heroin users on methadone (smoking as a covariate) DNA position +126 showed higher methylation (trend) and at global methylation site LINE-1. Patients with chronic pain on opioids for more than a year, showed a similar increase in methylation and LINE-	(Doehring, Oertel, Sittl, & Lotsch, 2013)

1 methylation was associated with increased pain. Methylation at CpG sites 13 and 22 were associated with chronic postsurgical pain (0-10) in adolescent scoliosis patients after controlling for preop pain and other variables.	(Chidambaran et al., 2017)
PRDM12 (PR/SET Domain 12) Polyalanine expansion (nociceptor) Studied congenital insensitivity to pain (CIP, autosomal recessive); expansion decreases bioavailability of PRDM12; think loss of histone modification d/t missense affects neurogenesis	(Chen et al., 2015)
SPARC (Secreted Protein, Acidic, Rich in Cysteine) Promoter methylation When comparing a small sample of preoperative patients with chronic low back pain with healthy controls, promoter methylation was shown to silence the SPARC gene and is associated with increased pain (pain scale 0-100).	(Tajerian et al., 2011)
TRPA1 (Transient Receptor Potential Cation Channel Subfamily A Member 1) Differentially methylated region showed more methylation in twins with a lower pain threshold, established by using quantitative sensory testing, in discordant monozygotic twins (50) and compared with healthy unrelated participants (50). Methylation in the promoter could cause downregulation in gene expression for this ion channel gene.	(Bell et al., 2014)
Significant Genes – Transcriptomic Findings	Authors
ADRB1 (Adrenoceptor Beta 1) Higher expression of this adrenergic receptor was associated with greater pain severity (0-100) in prostate cancer patients.	(Light et al., 2013)
ADRA2A (Alpha-2a adrenergic receptor) Higher expression of this adrenergic receptor was associated with greater pain severity (0-100) in prostate cancer patients.	(Light et al., 2013)
Higher expression correlated with post-exercise pain (visual analog scale) in patients with chronic fatigue syndrome and in MS patients with lower α -2a levels pre-exercise (compared with MS patients with higher levels), increased pain scores were associated with increased expression.	(White, Light, Hughen, Vanhaitsma, & Light, 2012)
ADRA2C (Adrenoceptor Alpha 2C) Higher expression of this adrenergic receptor was associated with greater pain severity (0-100) in prostate cancer patients.	(Light et al., 2013)
BATF2 (basic leucine zipper transcription factor, ATF-like) In patients with fibromyalgia, the high pain score (Brief Pain Inventory) group exhibited increased gene expression.	(Lukkahatai, Majors, Reddy, Walitt, & Saligan, 2013)
BDKRB1 (Bradykinin receptor B1) BDKRB1 expression correlated with pain intensity (visual analog scale) in patients with minor surgery taking ketorolac. TRPV1 was correlated with BDKRB1.	(Hamza et al., 2010)

BDKRB2 (Bradykinin receptor B2) BDKRB2 expression correlated with pain intensity (visual analog scale) in patients with minor surgery taking ketorolac.	(Hamza et al., 2010)
CASP5 (caspase 5, apoptosis-related cysteine peptidase) In patients with fibromyalgia, the high pain score (Brief Pain Inventory) group exhibited increased gene expression.	(Lukkahatai et al., 2013)
CCR1 (chemokine (C-C motif) receptor 1) In patients with fibromyalgia, the high pain score (Brief Pain Inventory) group exhibited increased gene expression.	(Lukkahatai et al., 2013)
CD26 macrophage (DPP4 Dipeptidyl Peptidase 4) Increased CD205 numbers were found in the pain group tendons versus pain-free.	(Dean et al., 2015)
CD45 pan-leucocyte (PTPRC Protein Tyrosine Phosphatase, Receptor Type C) Increased CD45 numbers were found in pain versus pain-free tendons.	(Dean et al., 2015)
CD69 Molecule CD69 molecule In patients with fibromyalgia, the high pain score (Brief Pain Inventory) group exhibited increased gene expression.	(Lukkahatai et al., 2013)
CEACAM1 (carcinoembryonic antigen-related cell adhesion molecule 1 biliary glycoprotein) In patients with fibromyalgia, the high pain score (Brief Pain Inventory) group exhibited increased gene expression.	(Lukkahatai et al., 2013)
FAK (PTK2 Protein Tyrosine Kinase 2) In women with endometriosis, elevated FAK protein and mRNA expression was associated with pelvic pain.	(Mu et al., 2008)
FLJ12541 (STRA6 stimulated by retinoic acid 6) MEF2C and FLJ12541 expression correlated with pain (0-5 scale) in patients with infectious mononucleosis and accounted for more than 80% of the variance in the regression analysis.	(Vernon et al., 2006)
GZMM (Granzyme M) Expression was associated with heat pain sensitivity in a twin study.	(Williams et al., 2012)
IL-1β (Interleukin 1 Beta) Three cohort of OA patients and controls were assessed for OA pain (visual analog, WOMAC, American College of Rheumatology criteria). Peripheral blood leukocytes were evaluated for potential diagnostic biomarkers. IL-1 β expression was elevated in the subgroup with more pain/symptomatic OA. Expression was elevated in surgical intervertebral disc samples in patients with pain (rated by patients during discography). Cadaver samples of persons without back pain history were also used (but some living patients were in the pain-free group). IL-6 and IL-8 expressions were not significant.	(Attur et al., 2011) (Kepler et al., 2013)
IL-10 (interleukin 10) Higher expression was found in sural nerve samples of patients with painful neuropathies (0-10	(Uceyler, Riediger, Kafke, & Sommer,

scale) compared with painless neuropathies and it was expressed more in both inflammatory and noninflammatory.	2015)
IL-33 (interleukin 33) Using skin biopsies, patients with psoriatic arthritis had a higher IL-33 expression than healthy controls and those patients reporting more pain (versus patients with no pain) had a greater expression as well.	(Patruno et al., 2015)
IL-6 (interleukin 6) Higher expression was found in sural nerve samples of patients with painful neuropathies (0-10 scale) compared with painless neuropathies and it was expressed more in both inflammatory and non-inflammatory. However, it did not correlate with current pain levels. IL-6 levels in peritoneal fluid correlated with pelvic pain (0-10 scale) in women with endometriosis.	(Uceyler et al., 2015) (Velasco, Acien, Campos, Acien, & Ruiz-Macia, 2010)
LTA (lymphotoxin alpha) Increased expression of this gene was associated with higher pain severity scores (0-100) in patients with chronic fatigue syndrome.	(Light et al., 2013)
LY6E (Lymphocyte Antigen 6 Complex, Locus E) Lymphocyte antigen 6 complex, locus E In patients with fibromyalgia, the high pain score (Brief Pain Inventory) group exhibited decreased gene expression.	(Lukkahatai et al., 2013)
MEF2C (Myocyte Enhancer Factor 2C) MEF2C and FLJ12541 expression correlated with pain (0-5 scale) in patients with infectious mononucleosis and accounted for more than 80% of the variance in the regression analysis.	(Vernon et al., 2006)
miR-145-5p (MicroRNA 145) In a small study, decreased expression of this microRNA in cerebrospinal fluid of fibromyalgia patients was found but increased levels were associated with greater pain, assessed with a visual analog scale in the fibromyalgia impact questionnaire.	(Bjersing, Lundborg, Bokarewa, & Mannerkorpi, 2013)
miR-199 a/b (MicroRNA 199 a1 a2) In IBS patients, decreased expression of miR-199 a and b were associated with increased visceral pain scores and increased TRPV1.	(Q. Zhou et al., 2016)
Fractalkine (CX3CR1 C-X3-C Motif Chemokine Receptor 1) Fractalkine mRNA, a chemokine, showed increased expression in chronic pancreatic pain (Likert scale, self-report).	(Ceyhan et al., 2009)
KA1 (kainate receptor 1) Using the Oxford Shoulder Score to measure pain in preoperative and postoperative patients and dividing them into pain and pain-free groups, respectively, KA1 was expressed more in the pain group tendons.	(Dean et al., 2015)
mGluR2 (metabotropic glutamate receptor 2) In pain versus pain-free groups of shoulder surgery patients, mGluR2 was expressed more in the pain group tendons.	(Dean et al., 2015)
mRNA ATP5E (ATP Synthase, H+ Transporting, Mitochondrial F1 Complex, Epsilon	

Subunit) Higher pain scores (0-100) correlated with greater expression of this mitochondrial mRNA in patients with prostate cancer.	(Light et al., 2013)
mRNA HSPA (HSPBP1 HSPA (Hsp70) Binding Protein 1) Higher pain scores (0-100) correlated with greater expression of this mitochondrial mRNA in patients with prostate cancer.	(Light et al., 2013)
mRNA NDUFS5 (NDUFS5 NADH:Ubiquinone Oxidoreductase Subunit S5) Higher pain scores (0-100) correlated with greater expression of this mitochondrial mRNA in patients with prostate cancer.	(Light et al., 2013)
Nav1.3 (SCN3A Sodium Voltage-Gated Channel Alpha Subunit 3) Patients with trigeminal neuralgia pain (visual analog scale) exhibited an upregulation of Nav1.3.	(Siqueira, Alves, Malpartida, Teixeira, & Siqueira, 2009)
Nav1.7 (SCN9A Sodium Voltage-Gated Channel Alpha Subunit 9) Patients with trigeminal neuralgia pain (visual analog scale) exhibited a downregulation of Nav1.7.	(Siqueira et al., 2009)
NK-1R (neurokinin 1 receptor) mRNA In patients with chronic pancreatitis, NK-1R levels were associated with increased pain (as well as frequency and duration). Pain severity and frequency was assessed using a 4 point Likert scale.	(Shrikhande et al., 2001)
NPY (neuropeptide Y) In healthy and patients with major depressive disorder (MDD), low expression of NPY was associated with negative affect during a pain stressor. The MDD patients were more likely to have this low expression. Authors think that this low expression may make people more sensitive to negative stimuli. Lower expression is associated with amygdala activation and less resiliency to pain/stress activation in opioid transmission regions of the brain. rs16147 appears to alter the expression.	(Mickey et al., 2011) (Z. Zhou et al., 2008)
PARP14 (poly (ADP-ribose) polymerase family, member 14) In patients with fibromyalgia, the high pain score (Brief Pain Inventory) group exhibited decreased gene expression.	(Lukkahatai et al., 2013)
P2RY1 (Purinergic Receptor P2Y1) Expression of this gene was correlated with higher pain severity scores (0-100) in patients with prostate cancer.	(Light et al., 2013)
P2X4 (Purinergic Receptor P2X 4) Using a visual analog scale to measure pain post-exercise, patients with chronic fatigue syndrome and MS who had higher expression of P2X4 reported higher levels of pain.	(White et al., 2012)
RANTES (CCL5 C-C Motif Chemokine Ligand 5) RANTES expression was 3.6 times more elevated in surgical intervertebral disc samples in patients with pain (rated by patients during discography). Cadaver samples of persons without back pain history were also used (but some living patients were in the pain-free group).	(Kepler et al., 2013)

<p>RPL23 (ribosomal protein L23) In patients with fibromyalgia, the high pain score (Brief Pain Inventory) group exhibited decreased gene expression.</p>	(Lukkahatai et al., 2013)
<p>RPL7 (ribosomal protein L7) In patients with fibromyalgia, the high pain score (Brief Pain Inventory) group exhibited decreased gene expression.</p>	(Lukkahatai et al., 2013)
<p>SCO2 (SCO2 cytochrome c oxidase assembly protein) In patients with fibromyalgia, the high pain score (Brief Pain Inventory) group exhibited decreased gene expression.</p>	(Lukkahatai et al., 2013)
<p>SERPING1 (serpin peptidase inhibitor, clade G (C1 inhibitor), member 1) In patients with fibromyalgia, the high pain score (Brief Pain Inventory) group exhibited decreased gene expression.</p>	(Lukkahatai et al., 2013)
<p>SH2D1B S(H2 domain containing 1B) In patients with fibromyalgia, the high pain score (Brief Pain Inventory) group exhibited decreased gene expression.</p>	(Lukkahatai et al., 2013)
<p>SIRT1 (sirtuin 1) Increased expression of this gene was associated with higher pain severity scores (0-100) in patients with chronic fatigue syndrome.</p>	(Light et al., 2013)
<p>SLC6A4 (Solute Carrier Family 6 Member 4) Serotonin Transporter 5-HTTLPR genotype Healthy participants with low expression, S_A/S_A and L_G/S_A (versus high expression group L_A/L_A) showed a higher state anxiety and reduced conditioned pain modulation mediated pain inhibition for both pressure pain thresholds and heat pain testing.</p>	(Lindstedt et al., 2011)
<p>Substance P (TAC1 Tachykinin Precursor 1) There was greater expression of substance P in dental pulp of patients with tooth pain versus those without tooth pain (self-reported pain history pre-op extraction).</p>	(Rodd & Boissonade, 2000)
<p>TNF-a (tumor necrosis factor-alpha) TNF-a was upregulated in the pain group shoulder tendons versus the pain-free group.</p> <p>TNF-a levels in plasma were negatively associated with oral pain intensity in stem cell transplant patients. However, buccal samples showed increase TNF-alpha RNA expression which correlated with pain when swallowing.</p>	(Dean et al., 2015) (Fall-Dickson, Ramsay, Castro, Woltz, & Sportes, 2007)
<p>TRPV1 (Transient Receptor Potential Cation Channel Subfamily V Member 1) TRPV1-immunoreactive nerve fiber density was associated with increased bladder pain (visual analog scale) in patients with interstitial cystitis and bladder pain syndrome.</p> <p>TRPV1 was expressed more in a family with known hyposensitivity to pain, capsaicin, and thermal stimuli when compared with healthy control subjects.</p>	(B. L. Liu et al., 2014) (Spinsanti et al., 2008)

References

Ahlers, S. J., Elens, L. L., van Gulik, L., van Schaik, R. H., van Dongen, E. P., Bruins, P., . . . Knibbe, C. A. (2013). The Val158Met polymorphism of the COMT gene is associated with increased pain sensitivity in morphine-treated patients undergoing a painful procedure after cardiac surgery. *Br J Clin Pharmacol*, 75(6), 1506-1515. doi:10.1111/bcp.12052

- Aoki, Y., Nishizawa, D., Kasai, S., Fukuda, K., Ichinohe, T., Yamashita, S., & Ikeda, K. (2013). Association between the variable number of tandem repeat polymorphism in the third exon of the dopamine D4 receptor gene and sensitivity to analgesics and pain in patients undergoing painful cosmetic surgery. *Neurosci Lett*, *542*, 1-4. doi:10.1016/j.neulet.2013.02.039
- Applebaum, E., Nackley, A. G., Bair, E., Maixner, W., & Khan, A. A. (2015). Genetic Variants in Cyclooxygenase-2 Contribute to Post-treatment Pain among Endodontic Patients. *J Endod*, *41*(8), 1214-1218. doi:10.1016/j.joen.2015.04.021
- Attur, M., Belitskaya-Levy, I., Oh, C., Krasnokutsky, S., Greenberg, J., Samuels, J., . . . Abramson, S. B. (2011). Increased interleukin-1beta gene expression in peripheral blood leukocytes is associated with increased pain and predicts risk for progression of symptomatic knee osteoarthritis. *Arthritis Rheum*, *63*(7), 1908-1917. doi:10.1002/art.30360
- Ballina, L. E., Ulirsch, J. C., Soward, A. C., Rossi, C., Rotolo, S., Linnstaedt, S. D., . . . McLean, S. A. (2013). mu-Opioid receptor gene A118G polymorphism predicts pain recovery after sexual assault. *J Pain*, *14*(2), 165-171. doi:10.1016/j.jpain.2012.10.013
- Bartosova, O., Polanecky, O., Perlik, F., Adamek, S., & Slanar, O. (2015). OPRM1 and ABCB1 polymorphisms and their effect on postoperative pain relief with piritramide. *Physiol Res*, *64 Suppl 4*, S521-527.
- Bell, J. T., Loomis, A. K., Butcher, L. M., Gao, F., Zhang, B., Hyde, C. L., . . . Spector, T. D. (2014). Differential methylation of the TRPA1 promoter in pain sensitivity. *Nat Commun*, *5*, 2978. doi:10.1038/ncomms3978
- Bjersing, J. L., Lundborg, C., Bokarewa, M. I., & Mannerkorpi, K. (2013). Profile of cerebrospinal microRNAs in fibromyalgia. *PLoS One*, *8*(10), e78762. doi:10.1371/journal.pone.0078762
- Bortsov, A. V., Diatchenko, L., & McLean, S. A. (2014). Complex multilocus effects of catechol-O-methyltransferase haplotypes predict pain and pain interference 6 weeks after motor vehicle collision. *Neuromolecular Med*, *16*(1), 83-93. doi:10.1007/s12017-013-8255-9
- Bortsov, A. V., Smith, J. E., Diatchenko, L., Soward, A. C., Ulirsch, J. C., Rossi, C., . . . McLean, S. A. (2013). Polymorphisms in the glucocorticoid receptor co-chaperone FKBP5 predict persistent musculoskeletal pain after traumatic stress exposure. *Pain*, *154*(8), 1419-1426. doi:10.1016/j.pain.2013.04.037
- Cajanus, K., Holmstrom, E. J., Wessman, M., Anttila, V., Kaunisto, M. A., & Kalso, E. (2016). Effect of endocannabinoid degradation on pain: role of FAAH polymorphisms in experimental and postoperative pain in women treated for breast cancer. *Pain*, *157*(2), 361-369. doi:10.1097/j.pain.0000000000000398
- Cajanus, K., Kaunisto, M. A., Tallgren, M., Jokela, R., & Kalso, E. (2014). How much oxycodone is needed for adequate analgesia after breast cancer surgery: effect of the OPRM1 118A>G polymorphism. *J Pain*, *15*(12), 1248-1256. doi:10.1016/j.jpain.2014.09.002
- Campbell, C. M., Edwards, R. R., Carmona, C., Uhart, M., Wand, G., Carteret, A., . . . Campbell, J. N. (2009). Polymorphisms in the GTP cyclohydrolase gene (GCH1) are associated with ratings of capsaicin pain. *Pain*, *141*(1-2), 114-118. doi:10.1016/j.pain.2008.10.023

- Ceyhan, G. O., Deucker, S., Demir, I. E., Erkan, M., Schmelz, M., Bergmann, F., . . . Friess, H. (2009). Neural fractalkine expression is closely linked to pain and pancreatic neuritis in human chronic pancreatitis. *Lab Invest*, *89*(3), 347-361. doi:10.1038/labinvest.2008.170
- Chen, Y. C., Auer-Grumbach, M., Matsukawa, S., Zitzelsberger, M., Themistocleous, A. C., Strom, T. M., . . . Senderek, J. (2015). Transcriptional regulator PRDM12 is essential for human pain perception. *Nat Genet*, *47*(7), 803-808. doi:10.1038/ng.3308
- Cheng, K. I., Lin, S. R., Chang, L. L., Wang, J. Y., & Lai, C. S. (2010). Association of the functional A118G polymorphism of OPRM1 in diabetic patients with foot ulcer pain. *J Diabetes Complications*, *24*(2), 102-108. doi:10.1016/j.jdiacomp.2009.02.003
- Chidambaran, V., Zhang, X., Martin, L. J., Ding, L., Weirauch, M. T., Geisler, K., . . . Ji, H. (2017). DNA methylation at the mu-1 opioid receptor gene (OPRM1) promoter predicts preoperative, acute, and chronic postsurgical pain after spine fusion. *Pharmgenomics Pers Med*, *10*, 157-168. doi:10.2147/pgpm.s132691
- Cook-Sather, S. D., Li, J., Goebel, T. K., Sussman, E. M., Rehman, M. A., & Hakonarson, H. (2014). TAOK3, a novel genome-wide association study locus associated with morphine requirement and postoperative pain in a retrospective pediatric day surgery population. *Pain*, *155*(9), 1773-1783. doi:10.1016/j.pain.2014.05.032
- Costigan, M., Belfer, I., Griffin, R. S., Dai, F., Barrett, L. B., Coppola, G., . . . Woolf, C. J. (2010). Multiple chronic pain states are associated with a common amino acid-changing allele in KCNS1. *Brain*, *133*(9), 2519-2527. doi:10.1093/brain/awq195
- Cui, W., Yu, X., & Zhang, H. (2014). The serotonin transporter gene polymorphism is associated with the susceptibility and the pain severity in idiopathic trigeminal neuralgia patients. *J Headache Pain*, *15*, 42. doi:10.1186/1129-2377-15-42
- De Capraris, A., Cinnella, G., Marolla, A., Salatto, P., Da Lima, S., Vetuschi, P., . . . Dambrosio, M. (2011). Micro opioid receptor A118G polymorphism and post-operative pain: opioids' effects on heterozygous patients. *Int J Immunopathol Pharmacol*, *24*(4), 993-1004. doi:10.1177/039463201102400417
- Dean, B. J., Snelling, S. J., Dakin, S. G., Murphy, R. J., Javaid, M. K., & Carr, A. J. (2015). Differences in glutamate receptors and inflammatory cell numbers are associated with the resolution of pain in human rotator cuff tendinopathy. *Arthritis Res Ther*, *17*, 176. doi:10.1186/s13075-015-0691-5
- Del Coso, J., Valero, M., Salinero, J. J., Lara, B., Diaz, G., Gallo-Salazar, C., . . . Cacabelos, R. (2017). ACTN3 genotype influences exercise-induced muscle damage during a marathon competition. *Eur J Appl Physiol*, *117*(3), 409-416. doi:10.1007/s00421-017-3542-z
- Desmeules, J., Chabert, J., Rebsamen, M., Rapiti, E., Piguët, V., Besson, M., . . . Cedraschi, C. (2014). Central pain sensitization, COMT Val158Met polymorphism, and emotional factors in fibromyalgia. *J Pain*, *15*(2), 129-135. doi:10.1016/j.jpain.2013.10.004
- Di Lorenzo, C., Di Lorenzo, G., Daverio, A., Pasqualetti, P., Coppola, G., Giannoudas, I., . . . Seri, S. (2012). The Val66Met polymorphism of the BDNF gene influences trigeminal pain-related evoked responses. *J Pain*, *13*(9), 866-873. doi:10.1016/j.jpain.2012.05.014

- Diatchenko, L., Nackley, A. G., Slade, G. D., Bhalang, K., Belfer, I., Max, M. B., . . . Maixner, W. (2006). Catechol-O-methyltransferase gene polymorphisms are associated with multiple pain-evoking stimuli. *Pain, 125*(3), 216-224. doi:10.1016/j.pain.2006.05.024
- Doehring, A., Freynhagen, R., Griessinger, N., Zimmermann, M., Sittl, R., Hentig, N., . . . Lotsch, J. (2009). Cross-sectional assessment of the consequences of a GTP cyclohydrolase 1 haplotype for specialized tertiary outpatient pain care. *Clin J Pain, 25*(9), 781-785. doi:10.1097/AJP.0b013e3181b43e12
- Doehring, A., Oertel, B. G., Sittl, R., & Lotsch, J. (2013). Chronic opioid use is associated with increased DNA methylation correlating with increased clinical pain. *Pain, 154*(1), 15-23. doi:10.1016/j.pain.2012.06.011
- Dominguez, C. A., Kalliomaki, M., Gunnarsson, U., Moen, A., Sandblom, G., Kockum, I., . . . Piehl, F. (2013). The DQB1 *03:02 HLA haplotype is associated with increased risk of chronic pain after inguinal hernia surgery and lumbar disc herniation. *Pain, 154*(3), 427-433. doi:10.1016/j.pain.2012.12.003
- Droney, J. M., Gretton, S. K., Sato, H., Ross, J. R., Branford, R., Welsh, K. I., . . . Riley, J. (2013). Analgesia and central side-effects: two separate dimensions of morphine response. *Br J Clin Pharmacol, 75*(5), 1340-1350. doi:10.1111/bcp.12008
- Duan, G., Guo, S., Zhang, Y., Ying, Y., Huang, P., Wang, Q., . . . Zhang, X. (2015). The Effect of SCN9A Variation on Basal Pain Sensitivity in the General Population: An Experimental Study in Young Women. *J Pain, 16*(10), 971-980. doi:10.1016/j.jpain.2015.06.011
- Duan, G., Xiang, G., Guo, S., Zhang, Y., Ying, Y., Huang, P., . . . Zhang, X. (2016). Genotypic Analysis of SCN9A for Prediction of Postoperative Pain in Female Patients Undergoing Gynecological Laparoscopic Surgery. *Pain Physician, 19*(1), E151-162.
- Fall-Dickson, J. M., Ramsay, E. S., Castro, K., Woltz, P., & Sportes, C. (2007). Oral mucositis-related oropharyngeal pain and correlative tumor necrosis factor-alpha expression in adult oncology patients undergoing hematopoietic stem cell transplantation. *Clin Ther, 29 Suppl*, 2547-2561. doi:10.1016/j.clinthera.2007.12.004
- Fernandez-de-las-Penas, C., Ambite-Quesada, S., Ortega-Santiago, R., Martinez-Perez, A., Diaz, H. F., Martinez-Martin, J., & Parejam, J. A. (2013). Catechol-O-methyltransferase Val158Met polymorphism is associated with pain and disability, but not widespread pressure pain sensitivity, in women with carpal Tunnel syndrome. *Pain Physician, 16*(5), E591-600.
- Fernandez-de-las-Penas, C., Ambite-Quesada, S., Ortiz-Gutierrez, R., Ortega-Santiago, R., Gil-Crujera, A., & Caminero, A. B. (2013). Catechol-O-methyltransferase Val158Met polymorphism (rs4680) is associated with pain in multiple sclerosis. *J Pain, 14*(12), 1719-1723. doi:10.1016/j.jpain.2013.09.007
- Fernandez-de-las-Penas, C., Ambite-Quesada, S., Rivas-Martinez, I., Ortega-Santiago, R., de-la-Llave-Rincon, A. I., Fernandez-Mayoralas, D. M., & Pareja, J. A. (2011). Genetic contribution of catechol-O-methyltransferase polymorphism (Val158Met) in children with chronic tension-type headache. *Pediatr Res, 70*(4), 395-399. doi:10.1203/PDR.0b013e318229448a
- Fijal, B., Perlis, R. H., Heinloth, A. N., & Houston, J. P. (2010). The association of single nucleotide polymorphisms in the catechol-O-methyltransferase gene and pain scores in female patients with major depressive disorder. *J Pain, 11*(9), 910-915, 915.e911-919. doi:10.1016/j.jpain.2009.12.016

- Fillingim, R. B., Kaplan, L., Staud, R., Ness, T. J., Glover, T. L., Campbell, C. M., . . . Wallace, M. R. (2005). The A118G single nucleotide polymorphism of the mu-opioid receptor gene (OPRM1) is associated with pressure pain sensitivity in humans. *J Pain*, *6*(3), 159-167. doi:10.1016/j.jpain.2004.11.008
- Galvan, A., Skorpén, F., Klepstad, P., Knudsen, A. K., Fladvad, T., Falvella, F. S., . . . Dragani, T. A. (2011). Multiple Loci modulate opioid therapy response for cancer pain. *Clin Cancer Res*, *17*(13), 4581-4587. doi:10.1158/1078-0432.ccr-10-3028
- Generaal, E., Milaneschi, Y., Jansen, R., Elzinga, B. M., Dekker, J., & Penninx, B. W. (2016). The brain-derived neurotrophic factor pathway, life stress, and chronic multi-site musculoskeletal pain. *Mol Pain*, *12*. doi:10.1177/1744806916646783
- Greenbaum, L., Tegeder, I., Barhum, Y., Melamed, E., Roditi, Y., & Djaldetti, R. (2012). Contribution of genetic variants to pain susceptibility in Parkinson disease. *Eur J Pain*, *16*(9), 1243-1250. doi:10.1002/j.1532-2149.2012.00134.x
- Hamza, M., Wang, X. M., Adam, A., Brahim, J. S., Rowan, J. S., Carmona, G. N., & Dionne, R. A. (2010). Kinin B1 receptors contributes to acute pain following minor surgery in humans. *Mol Pain*, *6*, 12. doi:10.1186/1744-8069-6-12
- Hendry, L. M., Wadley, A. L., Cherry, C. L., Price, P., Lombard, Z., & Kamerman, P. R. (2016). TNF Block Gene Variants Associate With Pain Intensity in Black Southern Africans With HIV-associated Sensory Neuropathy. *Clin J Pain*, *32*(1), 45-50. doi:10.1097/ajp.0000000000000224
- Henker, R. A., Lewis, A., Dai, F., Lariviere, W. R., Meng, L., Gruen, G. S., . . . Conley, Y. P. (2013). The associations between OPRM1 and COMT genotypes and postoperative pain, opioid use, and opioid-induced sedation. *Biol Res Nurs*, *15*(3), 309-317. doi:10.1177/1099800411436171
- Herlyn, P., Muller-Hilke, B., Wendt, M., Hecker, M., Mittlmeier, T., & Grادل, G. (2010). Frequencies of polymorphisms in cytokines, neurotransmitters and adrenergic receptors in patients with complex regional pain syndrome type I after distal radial fracture. *Clin J Pain*, *26*(3), 175-181. doi:10.1097/AJP.0b013e3181bff8b9
- Ho, A. M., Tang, N. L., Cheung, B. K., & Stadlin, A. (2008). Dopamine receptor D4 gene -521C/T polymorphism is associated with opioid dependence through cold-pain responses. *Ann NY Acad Sci*, *1139*, 20-26. doi:10.1196/annals.1432.054
- Hocking, L. J., Smith, B. H., Jones, G. T., Reid, D. M., Strachan, D. P., & Macfarlane, G. J. (2010). Genetic variation in the beta2-adrenergic receptor but not catecholamine-O-methyltransferase predisposes to chronic pain: results from the 1958 British Birth Cohort Study. *Pain*, *149*(1), 143-151. doi:10.1016/j.pain.2010.01.023
- Horjales-Araujo, E., Demontis, D., Lund, E. K., Vase, L., Finnerup, N. B., Borglum, A. D., . . . Svensson, P. (2013). Emotional modulation of muscle pain is associated with polymorphisms in the serotonin transporter gene. *Pain*, *154*(8), 1469-1476. doi:10.1016/j.pain.2013.05.011
- Huang, C. J., Liu, H. F., Su, N. Y., Hsu, Y. W., Yang, C. H., Chen, C. C., & Tsai, P. S. (2008). Association between human opioid receptor genes polymorphisms and pressure pain sensitivity in females*. *Anaesthesia*, *63*(12), 1288-1295. doi:10.1111/j.1365-2044.2008.05760.x
- Hwang, J. M., Kim, Y. H., Yoon, K. J., Uhm, K. E., & Chang, W. H. (2015). Different responses to facilitatory rTMS according to BDNF genotype. *Clin Neurophysiol*, *126*(7), 1348-1353. doi:10.1016/j.clinph.2014.09.028

- Ide, S., Nishizawa, D., Fukuda, K., Kasai, S., Hasegawa, J., Hayashida, M., . . . Ikeda, K. (2014). Haplotypes of P2RX7 gene polymorphisms are associated with both cold pain sensitivity and analgesic effect of fentanyl. *Mol Pain*, *10*, 75. doi:10.1186/1744-8069-10-75
- Ingle, J. N., Schaid, D. J., Goss, P. E., Liu, M., Mushiroda, T., Chapman, J. A., . . . Weinshilboum, R. M. (2010). Genome-wide associations and functional genomic studies of musculoskeletal adverse events in women receiving aromatase inhibitors. *J Clin Oncol*, *28*(31), 4674-4682. doi:10.1200/jco.2010.28.5064
- Jaaskelainen, S. K., Lindholm, P., Valmunen, T., Pesonen, U., Taiminen, T., Virtanen, A., . . . Pertovaara, A. (2014). Variation in the dopamine D2 receptor gene plays a key role in human pain and its modulation by transcranial magnetic stimulation. *Pain*, *155*(10), 2180-2187. doi:10.1016/j.pain.2014.08.029
- Jacobsen, L. M., Schistad, E. I., Storesund, A., Pedersen, L. M., Espeland, A., Rygh, L. J., . . . Gjerstad, J. (2013). The MMP1 rs1799750 2G allele is associated with increased low back pain, sciatica, and disability after lumbar disk herniation. *Clin J Pain*, *29*(11), 967-971. doi:10.1097/AJP.0b013e31827df7fd
- Jacobsen, L. M., Schistad, E. I., Storesund, A., Pedersen, L. M., Rygh, L. J., Roe, C., & Gjerstad, J. (2012). The COMT rs4680 Met allele contributes to long-lasting low back pain, sciatica and disability after lumbar disc herniation. *Eur J Pain*, *16*(7), 1064-1069. doi:10.1002/j.1532-2149.2011.00102.x
- Jensen, K. B., Lonsdorf, T. B., Schalling, M., Kosek, E., & Ingvar, M. (2009). Increased sensitivity to thermal pain following a single opiate dose is influenced by the COMT val(158)met polymorphism. *PLoS One*, *4*(6), e6016. doi:10.1371/journal.pone.0006016
- Kambur, O., Kaunisto, M. A., Tikkanen, E., Leal, S. M., Ripatti, S., & Kalso, E. A. (2013). Effect of catechol-o-methyltransferase-gene (COMT) variants on experimental and acute postoperative pain in 1,000 women undergoing surgery for breast cancer. *Anesthesiology*, *119*(6), 1422-1433. doi:10.1097/aln.0000000000000013
- Kang, S. C., Lee, D. G., Choi, J. H., Kim, S. T., Kim, Y. K., & Ahn, H. J. (2007). Association between estrogen receptor polymorphism and pain susceptibility in female temporomandibular joint osteoarthritis patients. *Int J Oral Maxillofac Surg*, *36*(5), 391-394. doi:10.1016/j.ijom.2006.12.004
- Kepler, C. K., Markova, D. Z., Dibra, F., Yadla, S., Vaccaro, A. R., Risbud, M. V., . . . Anderson, D. G. (2013). Expression and relationship of proinflammatory chemokine RANTES/CCL5 and cytokine IL-1beta in painful human intervertebral discs. *Spine (Phila Pa 1976)*, *38*(11), 873-880. doi:10.1097/BRS.0b013e318285ae08
- Kim, H., Mittal, D. P., Iadarola, M. J., & Dionne, R. A. (2006). Genetic predictors for acute experimental cold and heat pain sensitivity in humans. *J Med Genet*, *43*(8), e40. doi:10.1136/jmg.2005.036079
- Kim, H., Neubert, J. K., San Miguel, A., Xu, K., Krishnaraju, R. K., Iadarola, M. J., . . . Dionne, R. A. (2004). Genetic influence on variability in human acute experimental pain sensitivity associated with gender, ethnicity and psychological temperament. *Pain*, *109*(3), 488-496. doi:10.1016/j.pain.2004.02.027

- Kim, S. K., Kim, S. H., Nah, S. S., Lee, J. H., Hong, S. J., Kim, H. S., . . . Lee, S. S. (2013). Association of guanosine triphosphate cyclohydrolase 1 gene polymorphisms with fibromyalgia syndrome in a Korean population. *J Rheumatol*, *40*(3), 316-322. doi:10.3899/jrheum.120929
- Kolesnikov, Y., Gabovits, B., Levin, A., Veske, A., Qin, L., Dai, F., & Belfer, I. (2013). Chronic pain after lower abdominal surgery: do catechol-O-methyl transferase/opioid receptor mu-1 polymorphisms contribute? *Mol Pain*, *9*, 19. doi:10.1186/1744-8069-9-19
- Kunz, M., Hennig, J., Karmann, A. J., & Lautenbacher, S. (2016). Relationship of 5-HTTLPR Polymorphism with Various Factors of Pain Processing: Subjective Experience, Motor Responsiveness and Catastrophizing. *PLoS One*, *11*(4), e0153089. doi:10.1371/journal.pone.0153089
- Langford, D. J., West, C., Elboim, C., Cooper, B. A., Abrams, G., Paul, S. M., . . . Miaskowski, C. (2014). Variations in potassium channel genes are associated with breast pain in women prior to breast cancer surgery. *J Neurogenet*, *28*(1-2), 122-135. doi:10.3109/01677063.2013.856430
- Lee, L. C., Tu, C. H., Chen, L. F., Shen, H. D., Chao, H. T., Lin, M. W., & Hsieh, J. C. (2014). Association of brain-derived neurotrophic factor gene Val66Met polymorphism with primary dysmenorrhea. *PLoS One*, *9*(11), e112766. doi:10.1371/journal.pone.0112766
- Lee, P. J., Delaney, P., Keogh, J., Sleeman, D., & Shorten, G. D. (2011). Catecholamine-o-methyltransferase polymorphisms are associated with postoperative pain intensity. *Clin J Pain*, *27*(2), 93-101. doi:10.1097/AJP.0b013e3181f15885
- Li, Q. S., Cheng, P., Favis, R., Wickenden, A., Romano, G., & Wang, H. (2015). SCN9A Variants May be Implicated in Neuropathic Pain Associated With Diabetic Peripheral Neuropathy and Pain Severity. *Clin J Pain*, *31*(11), 976-982. doi:10.1097/ajp.0000000000000205
- Li, W., Chen, Y., Yin, B., & Zhang, L. (2014). Pain in Parkinson's disease associated with COMT gene polymorphisms. *Behav Neurol*, *2014*, 304203. doi:10.1155/2014/304203
- Light, K. C., Agarwal, N., Iacob, E., White, A. T., Kinney, A. Y., VanHaitsma, T. A., . . . Light, A. R. (2013). Differing leukocyte gene expression profiles associated with fatigue in patients with prostate cancer versus chronic fatigue syndrome. *Psychoneuroendocrinology*, *38*(12), 2983-2995. doi:10.1016/j.psyneuen.2013.08.008
- Lindstedt, F., Berrebi, J., Greayer, E., Lonsdorf, T. B., Schalling, M., Ingvar, M., & Kosek, E. (2011). Conditioned pain modulation is associated with common polymorphisms in the serotonin transporter gene. *PLoS One*, *6*(3), e18252. doi:10.1371/journal.pone.0018252
- Lindstedt, F., Karshikoff, B., Schalling, M., Olgart Hoglund, C., Ingvar, M., Lekander, M., & Kosek, E. (2012). Serotonin-1A receptor polymorphism (rs6295) associated with thermal pain perception. *PLoS One*, *7*(8), e43221. doi:10.1371/journal.pone.0043221
- Lintermans, A., Van Asten, K., Jongen, L., Van Brussel, T., Laenen, A., Verhaeghe, J., . . . Neven, P. (2016). Genetic variant in the osteoprotegerin gene is associated with aromatase inhibitor-related musculoskeletal toxicity in breast cancer patients. *Eur J Cancer*, *56*, 31-36. doi:10.1016/j.ejca.2015.12.013

- Liu, B. L., Yang, F., Zhan, H. L., Feng, Z. Y., Zhang, Z. G., Li, W. B., & Zhou, X. F. (2014). Increased severity of inflammation correlates with elevated expression of TRPV1 nerve fibers and nerve growth factor on interstitial cystitis/bladder pain syndrome. *Urol Int*, *92*(2), 202-208. doi:10.1159/000355175
- Liu, M., Wang, L., Bongartz, T., Hawse, J. R., Markovic, S. N., Schaid, D. J., . . . Weinshilboum, R. M. (2012). Aromatase inhibitors, estrogens and musculoskeletal pain: estrogen-dependent T-cell leukemia 1A (TCL1A) gene-mediated regulation of cytokine expression. *Breast Cancer Res*, *14*(2), R41. doi:10.1186/bcr3137
- Loncar, Z., Curic, G., Mestrovic, A. H., Mickovic, V., & Bilic, M. (2013). Do IL-1B and IL-1RN modulate chronic low back pain in patients with post-traumatic stress disorder? *Coll Antropol*, *37*(4), 1237-1244.
- Lukkahatai, N., Majors, B., Reddy, S., Walitt, B., & Saligan, L. N. (2013). Gene expression profiles of fatigued fibromyalgia patients with different categories of pain and catastrophizing: a preliminary report. *Nurs Outlook*, *61*(4), 216-224.e212. doi:10.1016/j.outlook.2013.03.007
- Mamie, C., Rebsamen, M. C., Morris, M. A., & Morabia, A. (2013). First evidence of a polygenic susceptibility to pain in a pediatric cohort. *Anesth Analg*, *116*(1), 170-177. doi:10.1213/ANE.0b013e31826f0637
- Martinez-Jauand, M., Sitges, C., Rodriguez, V., Picornell, A., Ramon, M., Buskila, D., & Montoya, P. (2013). Pain sensitivity in fibromyalgia is associated with catechol-O-methyltransferase (COMT) gene. *Eur J Pain*, *17*(1), 16-27. doi:10.1002/j.1532-2149.2012.00153.x
- McCann, B., Miaskowski, C., Koettters, T., Baggott, C., West, C., Levine, J. D., . . . Aouizerat, B. E. (2012). Associations between pro- and anti-inflammatory cytokine genes and breast pain in women prior to breast cancer surgery. *J Pain*, *13*(5), 425-437. doi:10.1016/j.jpain.2011.02.358
- Meloto, C. B., Bortsov, A. V., Bair, E., Helgeson, E., Ostrom, C., Smith, S. B., . . . Diatchenko, L. (2016). Modification of COMT-dependent pain sensitivity by psychological stress and sex. *Pain*, *157*(4), 858-867. doi:10.1097/j.pain.0000000000000449
- Meloto, C. B., Segall, S. K., Smith, S., Parisien, M., Shabalina, S. A., Rizzatti-Barbosa, C. M., . . . Diatchenko, L. (2015). COMT gene locus: new functional variants. *Pain*, *156*(10), 2072-2083. doi:10.1097/j.pain.0000000000000273
- Menon, S., Lea, R. A., Roy, B., Hanna, M., Wee, S., Haupt, L. M., & Griffiths, L. R. (2012). The human mu-opioid receptor gene polymorphism (A118G) is associated with head pain severity in a clinical cohort of female migraine with aura patients. *J Headache Pain*, *13*(7), 513-519. doi:10.1007/s10194-012-0468-z
- Miao, J., Wang, F., Zheng, W., & Zhuang, X. (2015). Association of the Apolipoprotein E polymorphism with migraine: a meta-analysis. *BMC Neurol*, *15*, 138. doi:10.1186/s12883-015-0385-2
- Mickey, B. J., Zhou, Z., Heitzeg, M. M., Heinz, E., Hodgkinson, C. A., Hsu, D. T., . . . Zubieta, J. K. (2011). Emotion processing, major depression, and functional genetic variation of neuropeptide Y. *Arch Gen Psychiatry*, *68*(2), 158-166. doi:10.1001/archgenpsychiatry.2010.197

- Moen, A., Schistad, E. I., Rygh, L. J., Roe, C., & Gjerstad, J. (2014). Role of IL1A rs1800587, IL1B rs1143627 and IL1RN rs2234677 genotype regarding development of chronic lumbar radicular pain; a prospective one-year study. *PLoS One*, *9*(9), e107301. doi:10.1371/journal.pone.0107301
- Moriyama, A., Nishizawa, D., Kasai, S., Hasegawa, J., Fukuda, K., Nagashima, M., . . . Ikeda, K. (2013). Association between genetic polymorphisms of the beta1-adrenergic receptor and sensitivity to pain and fentanyl in patients undergoing painful cosmetic surgery. *J Pharmacol Sci*, *121*(1), 48-57.
- Mu, L., Zheng, W., Wang, L., Chen, X. J., Zhang, X., & Yang, J. H. (2008). Alteration of focal adhesion kinase expression in eutopic endometrium of women with endometriosis. *Fertil Steril*, *89*(3), 529-537. doi:10.1016/j.fertnstert.2007.03.060
- Nicholl, B. I., Holliday, K. L., Macfarlane, G. J., Thomson, W., Davies, K. A., O'Neill, T. W., . . . McBeth, J. (2011). Association of HTR2A polymorphisms with chronic widespread pain and the extent of musculoskeletal pain: results from two population-based cohorts. *Arthritis Rheum*, *63*(3), 810-818. doi:10.1002/art.30185
- Nielsen, L. M., Olesen, A. E., Sato, H., Christrup, L. L., & Drewes, A. M. (2016). Association between Gene Polymorphisms and Pain Sensitivity Assessed in a Multi-Modal Multi-Tissue Human Experimental Model - An Explorative Study. *Basic Clin Pharmacol Toxicol*, *119*(4), 360-366. doi:10.1111/bcpt.12601
- Nishizawa, D., Fukuda, K., Kasai, S., Ogai, Y., Hasegawa, J., Sato, N., . . . Ikeda, K. (2014). Association between KCNJ6 (GIRK2) gene polymorphism rs2835859 and post-operative analgesia, pain sensitivity, and nicotine dependence. *J Pharmacol Sci*, *126*(3), 253-263.
- Nishizawa, D., Nagashima, M., Katoh, R., Satoh, Y., Tagami, M., Kasai, S., . . . Ikeda, K. (2009). Association between KCNJ6 (GIRK2) gene polymorphisms and postoperative analgesic requirements after major abdominal surgery. *PLoS One*, *4*(9), e7060. doi:10.1371/journal.pone.0007060
- Nissenbaum, J., Devor, M., Seltzer, Z., Gebauer, M., Michaelis, M., Tal, M., . . . Darvasi, A. (2010). Susceptibility to chronic pain following nerve injury is genetically affected by CACNG2. *Genome Res*, *20*(9), 1180-1190. doi:10.1101/gr.104976.110
- Ochroch, E. A., Vachani, A., Gottschalk, A., & Kanetsky, P. A. (2012). Natural variation in the mu-opioid gene OPRM1 predicts increased pain on third day after thoracotomy. *Clin J Pain*, *28*(9), 747-754. doi:10.1097/AJP.0b013e3182442b1c
- Oen, K., Malleson, P. N., Cabral, D. A., Rosenberg, A. M., Petty, R. E., Nickerson, P., & Reed, M. (2005). Cytokine genotypes correlate with pain and radiologically defined joint damage in patients with juvenile rheumatoid arthritis. *Rheumatology (Oxford)*, *44*(9), 1115-1121. doi:10.1093/rheumatology/keh689
- Olsen, M. B., Jacobsen, L. M., Schistad, E. I., Pedersen, L. M., Rygh, L. J., Roe, C., & Gjerstad, J. (2012). Pain intensity the first year after lumbar disc herniation is associated with the A118G polymorphism in the opioid receptor mu 1 gene: evidence of a sex and genotype interaction. *J Neurosci*, *32*(29), 9831-9834. doi:10.1523/jneurosci.1742-12.2012
- Olsen, R., Foster, D. J., Upton, R. N., Olesen, A. E., Ross, J. R., Droney, J., . . . Kreilgaard, M. (2016). Modelling the PKPD of oxycodone in experimental pain - Impact of opioid receptor polymorphisms. *Eur J Pharm Sci*, *86*, 41-49. doi:10.1016/j.ejps.2016.02.021

- Omair, A., Holden, M., Lie, B. A., Reikeras, O., & Brox, J. I. (2013). Treatment outcome of chronic low back pain and radiographic lumbar disc degeneration are associated with inflammatory and matrix degrading gene variants: a prospective genetic association study. *BMC Musculoskelet Disord*, *14*, 105. doi:10.1186/1471-2474-14-105
- Omair, A., Lie, B. A., Reikeras, O., Holden, M., & Brox, J. I. (2012). Genetic contribution of catechol-O-methyltransferase variants in treatment outcome of low back pain: a prospective genetic association study. *BMC Musculoskelet Disord*, *13*, 76. doi:10.1186/1471-2474-13-76
- Orrey, D. C., Bortsov, A. V., Hoskins, J. M., Shupp, J. W., Jones, S. W., Cicuto, B. J., . . . McLean, S. A. (2012). Catechol-O-methyltransferase genotype predicts pain severity in hospitalized burn patients. *J Burn Care Res*, *33*(4), 518-523. doi:10.1097/BCR.0b013e31823746ed
- Oshima, T., Nakajima, S., Yokoyama, T., Toyoshima, F., Sakurai, J., Tanaka, J., . . . Miwa, H. (2010). The G-protein beta3 subunit 825 TT genotype is associated with epigastric pain syndrome-like dyspepsia. *BMC Med Genet*, *11*, 13. doi:10.1186/1471-2350-11-13
- Palit, S., Sheaff, R. J., France, C. R., McGlone, S. T., Potter, W. T., Harkness, A. R., . . . Rhudy, J. L. (2011). Serotonin transporter gene (5-HTTLPR) polymorphisms are associated with emotional modulation of pain but not emotional modulation of spinal nociception. *Biol Psychol*, *86*(3), 360-369. doi:10.1016/j.biopsycho.2011.01.008
- Park, J. M., Choi, M. G., Cho, Y. K., Lee, I. S., Kim, S. W., Choi, K. Y., & Chung, I. S. (2011). Cannabinoid receptor 1 gene polymorphism and irritable bowel syndrome in the Korean population: a hypothesis-generating study. *J Clin Gastroenterol*, *45*(1), 45-49. doi:10.1097/MCG.0b013e3181dd1573
- Pata, C., Erdal, E., Yazc, K., Camdeviren, H., Ozkaya, M., & Ulu, O. (2004). Association of the -1438 G/A and 102 T/C polymorphism of the 5-Ht2A receptor gene with irritable bowel syndrome 5-Ht2A gene polymorphism in irritable bowel syndrome. *J Clin Gastroenterol*, *38*(7), 561-566.
- Patruno, C., Napolitano, M., Balato, N., Ayala, F., Megna, M., Patri, A., . . . Balato, A. (2015). Psoriasis and skin pain: instrumental and biological evaluations. *Acta Derm Venereol*, *95*(4), 432-438. doi:10.2340/00015555-1965
- Peters, M. J., Broer, L., Willemen, H. L., Eiriksdottir, G., Hocking, L. J., Holliday, K. L., . . . van Meurs, J. B. (2013). Genome-wide association study meta-analysis of chronic widespread pain: evidence for involvement of the 5p15.2 region. *Ann Rheum Dis*, *72*(3), 427-436. doi:10.1136/annrheumdis-2012-201742
- Potvin, S., Larouche, A., Normand, E., de Souza, J. B., Gaumond, I., Grignon, S., & Marchand, S. (2009). DRD3 Ser9Gly polymorphism is related to thermal pain perception and modulation in chronic widespread pain patients and healthy controls. *J Pain*, *10*(9), 969-975. doi:10.1016/j.jpain.2009.03.013
- Rausch, S. M., Clark, M. M., Patten, C., Liu, H., Felten, S., Li, Y., . . . Yang, P. (2010). Relationship between cytokine gene single nucleotide polymorphisms and symptom burden and quality of life in lung cancer survivors. *Cancer*, *116*(17), 4103-4113. doi:10.1002/cncr.25255

- Rausch, S. M., Gonzalez, B. D., Clark, M. M., Patten, C., Felten, S., Liu, H., . . . Yang, P. (2012). SNPs in PTGS2 and LTA predict pain and quality of life in long term lung cancer survivors. *Lung Cancer*, *77*(1), 217-223. doi:10.1016/j.lungcan.2012.02.017
- Reimann, F., Cox, J. J., Belfer, I., Diatchenko, L., Zaykin, D. V., McHale, D. P., . . . Woods, C. G. (2010). Pain perception is altered by a nucleotide polymorphism in SCN9A. *Proc Natl Acad Sci U S A*, *107*(11), 5148-5153. doi:10.1073/pnas.0913181107
- Reyes-Gibby, C. C., El Osta, B., Spitz, M. R., Parsons, H., Kurzrock, R., Wu, X., . . . Bruera, E. (2008). The influence of tumor necrosis factor-alpha -308 G/A and IL-6 -174 G/C on pain and analgesia response in lung cancer patients receiving supportive care. *Cancer Epidemiol Biomarkers Prev*, *17*(11), 3262-3267. doi:10.1158/1055-9965.epi-08-0125
- Reyes-Gibby, C. C., Shete, S., Yennurajalingam, S., Frazier, M., Bruera, E., Kurzrock, R., . . . Spitz, M. R. (2009). Genetic and nongenetic covariates of pain severity in patients with adenocarcinoma of the pancreas: assessing the influence of cytokine genes. *J Pain Symptom Manage*, *38*(6), 894-902. doi:10.1016/j.jpainsymman.2009.04.019
- Reyes-Gibby, C. C., Spitz, M., Wu, X., Merriman, K., Etzel, C., Bruera, E., . . . Shete, S. (2007). Cytokine genes and pain severity in lung cancer: exploring the influence of TNF-alpha-308 G/A IL6-174G/C and IL8-251T/A. *Cancer Epidemiol Biomarkers Prev*, *16*(12), 2745-2751. doi:10.1158/1055-9965.epi-07-0651
- Reyes-Gibby, C. C., Spitz, M. R., Yennurajalingam, S., Swartz, M., Gu, J., Wu, X., . . . Shete, S. (2009). Role of inflammation gene polymorphisms on pain severity in lung cancer patients. *Cancer Epidemiol Biomarkers Prev*, *18*(10), 2636-2642. doi:10.1158/1055-9965.epi-09-0426
- Reyes-Gibby, C. C., Wang, J., Silvas, M. R., Yu, R., Yeung, S. C., & Shete, S. (2016). MAPK1/ERK2 as novel target genes for pain in head and neck cancer patients. *BMC Genet*, *17*, 40. doi:10.1186/s12863-016-0348-7
- Reyes-Gibby, C. C., Wang, J., Spitz, M., Wu, X., Yennurajalingam, S., & Shete, S. (2013). Genetic variations in interleukin-8 and interleukin-10 are associated with pain, depressed mood, and fatigue in lung cancer patients. *J Pain Symptom Manage*, *46*(2), 161-172. doi:10.1016/j.jpainsymman.2012.07.019
- Rodd, H. D., & Boissonade, F. M. (2000). Substance P expression in human tooth pulp in relation to caries and pain experience. *Eur J Oral Sci*, *108*(6), 467-474.
- Roh, H. L., Lee, J. S., Suh, K. T., Kim, J. I., Lee, H. S., Goh, T. S., & Park, S. H. (2013). Association between estrogen receptor gene polymorphism and back pain intensity in female patients with degenerative lumbar spondylolisthesis. *J Spinal Disord Tech*, *26*(2), E53-57. doi:10.1097/BSD.0b013e318260a09c
- Ruano, G., Thompson, P. D., Windemuth, A., Seip, R. L., Dande, A., Sorokin, A., . . . Wu, A. H. (2007). Physiogenomic association of statin-related myalgia to serotonin receptors. *Muscle Nerve*, *36*(3), 329-335. doi:10.1002/mus.20871
- Rut, M., Machoy-Mokrzynska, A., Reclawowicz, D., Sloniewski, P., Kurzawski, M., Drozdziak, M., . . . Bialecka, M. (2014). Influence of variation in the catechol-O-methyltransferase gene on the clinical outcome after lumbar spine surgery for one-level symptomatic disc disease: a report on 176 cases. *Acta Neurochir (Wien)*, *156*(2), 245-252. doi:10.1007/s00701-013-1895-6

- Sadhasivam, S., Chidambaran, V., Olbrecht, V. A., Esslinger, H. R., Zhang, K., Zhang, X., & Martin, L. J. (2014). Genetics of pain perception, COMT and postoperative pain management in children. *Pharmacogenomics*, *15*(3), 277-284. doi:10.2217/pgs.13.248
- Sato, H., Droney, J., Ross, J., Olesen, A. E., Staahl, C., Andresen, T., . . . Drewes, A. M. (2013). Gender, variation in opioid receptor genes and sensitivity to experimental pain. *Mol Pain*, *9*, 20. doi:10.1186/1744-8069-9-20
- Sato, M., Ohashi, J., Tsuchiya, N., Kashiwase, K., Ishikawa, Y., Arita, H., . . . Yabe, T. (2002). Association of HLA-A*3303-B*4403-DRB1*1302 haplotype, but not of TNFA promoter and NKp30 polymorphism, with postherpetic neuralgia (PHN) in the Japanese population. *Genes Immun*, *3*(8), 477-481. doi:10.1038/sj.gene.6363890
- Schistad, E. I., Jacobsen, L. M., Roe, C., & Gjerstad, J. (2014). The interleukin-1alpha gene C>T polymorphism rs1800587 is associated with increased pain intensity and decreased pressure pain thresholds in patients with lumbar radicular pain. *Clin J Pain*, *30*(10), 869-874. doi:10.1097/ajp.0000000000000048
- Schmahl, C., Ludascher, P., Greffrath, W., Kraus, A., Valerius, G., Schulze, T. G., . . . Bohus, M. (2012). COMT val158met polymorphism and neural pain processing. *PLoS One*, *7*(1), e23658. doi:10.1371/journal.pone.0023658
- Schwahn, C., Grabe, H. J., Meyer zu Schwabedissen, H., Teumer, A., Schmidt, C. O., Brinkman, C., . . . Bernhardt, O. (2012). The effect of catechol-O-methyltransferase polymorphisms on pain is modified by depressive symptoms. *Eur J Pain*, *16*(6), 878-889. doi:10.1002/j.1532-2149.2011.00067.x
- Sery, O., Hrazdilova, O., Didden, W., Klenerova, V., Staif, R., Znojil, V., & Sevcik, P. (2006). The association of monoamine oxidase B functional polymorphism with postoperative pain intensity. *Neuro Endocrinol Lett*, *27*(3), 333-337.
- Shabalina, S. A., Zaykin, D. V., Gris, P., Ogurtsov, A. Y., Gauthier, J., Shibata, K., . . . Diatchenko, L. (2009). Expansion of the human mu-opioid receptor gene architecture: novel functional variants. *Hum Mol Genet*, *18*(6), 1037-1051. doi:10.1093/hmg/ddn439
- Shoskes, D. A., Albakri, Q., Thomas, K., & Cook, D. (2002). Cytokine polymorphisms in men with chronic prostatitis/chronic pelvic pain syndrome: association with diagnosis and treatment response. *J Urol*, *168*(1), 331-335.
- Shrikhande, S. V., Friess, H., di Mola, F. F., Tempia-Caliera, A., Conejo Garcia, J. R., Zhu, Z., . . . Buchler, M. W. (2001). NK-1 receptor gene expression is related to pain in chronic pancreatitis. *Pain*, *91*(3), 209-217.
- Sia, A. T., Lim, Y., Lim, E. C., Goh, R. W., Law, H. Y., Landau, R., . . . Tan, E. C. (2008). A118G single nucleotide polymorphism of human mu-opioid receptor gene influences pain perception and patient-controlled intravenous morphine consumption after intrathecal morphine for postcesarean analgesia. *Anesthesiology*, *109*(3), 520-526. doi:10.1097/ALN.0b013e318182af21
- Sia, A. T., Lim, Y., Lim, E. C., Ocampo, C. E., Lim, W. Y., Cheong, P., & Tan, E. C. (2013). Influence of mu-opioid receptor variant on morphine use and self-rated pain following abdominal hysterectomy. *J Pain*, *14*(10), 1045-1052. doi:10.1016/j.jpain.2013.03.008

- Siqueira, S. R., Alves, B., Malpartida, H. M., Teixeira, M. J., & Siqueira, J. T. (2009). Abnormal expression of voltage-gated sodium channels Nav1.7, Nav1.3 and Nav1.8 in trigeminal neuralgia. *Neuroscience*, *164*(2), 573-577. doi:10.1016/j.neuroscience.2009.08.037
- Skouen, J. S., Smith, A. J., Warrington, N. M., PB, O. S., McKenzie, L., Pennell, C. E., & Straker, L. M. (2012). Genetic variation in the beta-2 adrenergic receptor is associated with chronic musculoskeletal complaints in adolescents. *Eur J Pain*, *16*(9), 1232-1242. doi:10.1002/j.1532-2149.2012.00131.x
- Slade, G. D., Smith, S. B., Zaykin, D. V., Tchivileva, I. E., Gibson, D. G., Yuryev, A., . . . Diatchenko, L. (2013). Facial pain with localized and widespread manifestations: separate pathways of vulnerability. *Pain*, *154*(11), 2335-2343. doi:10.1016/j.pain.2013.07.009
- Smith, S. B., Reenila, I., Mannisto, P. T., Slade, G. D., Maixner, W., Diatchenko, L., & Nackley, A. G. (2014). Epistasis between polymorphisms in COMT, ESR1, and GCH1 influences COMT enzyme activity and pain. *Pain*, *155*(11), 2390-2399. doi:10.1016/j.pain.2014.09.009
- Solovieva, S., Leino-Arjas, P., Saarela, J., Luoma, K., Raininko, R., & Riihimaki, H. (2004). Possible association of interleukin 1 gene locus polymorphisms with low back pain. *Pain*, *109*(1-2), 8-19. doi:10.1016/j.pain.2003.10.020
- Sorge, R. E., Trang, T., Dorfman, R., Smith, S. B., Beggs, S., Ritchie, J., . . . Mogil, J. S. (2012). Genetically determined P2X7 receptor pore formation regulates variability in chronic pain sensitivity. *Nat Med*, *18*(4), 595-599. doi:10.1038/nm.2710
- Spinsanti, G., Zannolli, R., Panti, C., Ceccarelli, I., Marsili, L., Bachiocco, V., . . . Aloisi, A. M. (2008). Quantitative Real-Time PCR detection of TRPV1-4 gene expression in human leukocytes from healthy and hyposensitive subjects. *Mol Pain*, *4*, 51. doi:10.1186/1744-8069-4-51
- Stephens, K., Cooper, B. A., West, C., Paul, S. M., Baggott, C. R., Merriman, J. D., . . . Aouizerat, B. E. (2014). Associations between cytokine gene variations and severe persistent breast pain in women following breast cancer surgery. *J Pain*, *15*(2), 169-180. doi:10.1016/j.jpain.2013.09.015
- Sumitani, M., Nishizawa, D., Nagashima, M., Ikeda, K., Abe, H., Kato, R., . . . Yamada, Y. (2017). Association Between Polymorphisms in the Purinergic P2Y12 Receptor Gene and Severity of Both Cancer Pain and Postoperative Pain. *Pain Med*. doi:10.1093/pm/pnx102
- Tajerian, M., Alvarado, S., Millicamps, M., Dashwood, T., Anderson, K. M., Haglund, L., . . . Stone, L. S. (2011). DNA methylation of SPARC and chronic low back pain. *Mol Pain*, *7*, 65. doi:10.1186/1744-8069-7-65
- Tan, E. C., Lim, E. C., Ocampo, C. E., Allen, J. C., Sng, B. L., & Sia, A. T. (2016). Common variants of catechol-O-methyltransferase influence patient-controlled analgesia usage and postoperative pain in patients undergoing total hysterectomy. *Pharmacogenomics J*, *16*(2), 186-192. doi:10.1038/tpj.2015.33
- Tan, E. C., Lim, E. C., Teo, Y. Y., Lim, Y., Law, H. Y., & Sia, A. T. (2009). Ethnicity and OPRM1 variant independently predict pain perception and patient-controlled analgesia usage for post-operative pain. *Mol Pain*, *5*, 32. doi:10.1186/1744-8069-5-32

- Treister, R., Pud, D., Ebstein, R. P., Laiba, E., Gershon, E., Haddad, M., & Eisenberg, E. (2009). Associations between polymorphisms in dopamine neurotransmitter pathway genes and pain response in healthy humans. *Pain, 147*(1-3), 187-193. doi:10.1016/j.pain.2009.09.001
- Treister, R., Pud, D., Ebstein, R. P., Laiba, E., Raz, Y., Gershon, E., . . . Eisenberg, E. (2011). Association between polymorphisms in serotonin and dopamine-related genes and endogenous pain modulation. *J Pain, 12*(8), 875-883. doi:10.1016/j.jpain.2011.02.348
- Uceyler, N., Riediger, N., Kafke, W., & Sommer, C. (2015). Differential gene expression of cytokines and neurotrophic factors in nerve and skin of patients with peripheral neuropathies. *J Neurol, 262*(1), 203-212. doi:10.1007/s00415-014-7556-8
- Ulirsch, J. C., Weaver, M. A., Bortsov, A. V., Soward, A. C., Swor, R. A., Peak, D. A., . . . McLean, S. A. (2014). No man is an island: living in a disadvantaged neighborhood influences chronic pain development after motor vehicle collision. *Pain, 155*(10), 2116-2123. doi:10.1016/j.pain.2014.07.025
- Valdes, A. M., De Wilde, G., Doherty, S. A., Lories, R. J., Vaughn, F. L., Laslett, L. L., . . . Doherty, M. (2011). The Ile585Val TRPV1 variant is involved in risk of painful knee osteoarthritis. *Ann Rheum Dis, 70*(9), 1556-1561.
- van Meurs, J. B., Uitterlinden, A. G., Stolk, L., Kerkhof, H. J., Hofman, A., Pols, H. A., & Bierma-Zeinstra, S. M. (2009). A functional polymorphism in the catechol-O-methyltransferase gene is associated with osteoarthritis-related pain. *Arthritis Rheum, 60*(2), 628-629. doi:10.1002/art.24175
- Velasco, I., Acien, P., Campos, A., Acien, M. I., & Ruiz-Macia, E. (2010). Interleukin-6 and other soluble factors in peritoneal fluid and endometriomas and their relation to pain and aromatase expression. *J Reprod Immunol, 84*(2), 199-205. doi:10.1016/j.jri.2009.11.004
- Vernon, S. D., Nicholson, A., Rajeevan, M., Dimulescu, I., Cameron, B., Whistler, T., & Lloyd, A. (2006). Correlation of psycho-neuroendocrine-immune (PNI) gene expression with symptoms of acute infectious mononucleosis. *Brain Res, 1068*(1), 1-6. doi:10.1016/j.brainres.2005.11.013
- Vossen, H., Kenis, G., Rutten, B., van Os, J., Hermens, H., & Lousberg, R. (2010). The genetic influence on the cortical processing of experimental pain and the moderating effect of pain status. *PLoS One, 5*(10), e13641. doi:10.1371/journal.pone.0013641
- Wang, X. S., Song, H. B., Chen, S., Zhang, W., Liu, J. Q., Huang, C., . . . Chu, Q. (2015). Association of single nucleotide polymorphisms of ABCB1, OPRM1 and COMT with pain perception in cancer patients. *J Huazhong Univ Sci Technolog Med Sci, 35*(5), 752-758. doi:10.1007/s11596-015-1502-6
- Wei, S. Y., Chao, H. T., Tu, C. H., Lin, M. W., Li, W. C., Low, I., . . . Hsieh, J. C. (2016). The BDNF Val66Met polymorphism is associated with the functional connectivity dynamics of pain modulatory systems in primary dysmenorrhea. *Sci Rep, 6*, 23639. doi:10.1038/srep23639
- Wei, W., Tian, Y., Zhao, C., Sui, Z., Liu, C., Wang, C., & Yang, R. (2015). Correlation of ADRB1 rs1801253 Polymorphism with Analgesic Effect of Fentanyl After Cancer Surgeries. *Med Sci Monit, 21*, 4000-4005.

- Wesmler, S. W., Bender, C. M., Sereika, S. M., Ahrendt, G., Bonaventura, M., Bovbjerg, D. H., & Conley, Y. (2014). Association between serotonin transport polymorphisms and postdischarge nausea and vomiting in women following breast cancer surgery. *Oncol Nurs Forum*, *41*(2), 195-202. doi:10.1188/14.onf.195-202
- White, A. T., Light, A. R., Hughen, R. W., Vanhaitma, T. A., & Light, K. C. (2012). Differences in metabolite-detecting, adrenergic, and immune gene expression after moderate exercise in patients with chronic fatigue syndrome, patients with multiple sclerosis, and healthy controls. *Psychosom Med*, *74*(1), 46-54. doi:10.1097/PSY.0b013e31824152ed
- Williams, F. M., Scollen, S., Cao, D., Memari, Y., Hyde, C. L., Zhang, B., . . . Spector, T. D. (2012). Genes contributing to pain sensitivity in the normal population: an exome sequencing study. *PLoS Genet*, *8*(12), e1003095. doi:10.1371/journal.pgen.1003095
- Xiang, X., Jiang, Y., Ni, Y., Fan, M., Shen, F., Wang, X., . . . Cui, C. (2012). Catechol-O-methyltransferase polymorphisms do not play a significant role in pain perception in male Chinese Han population. *Physiol Genomics*, *44*(5), 318-328. doi:10.1152/physiolgenomics.00162.2011
- Zhang, W., Chang, Y. Z., Kan, Q. C., Zhang, L. R., Lu, H., Chu, Q. J., . . . Zhang, J. (2010). Association of human micro-opioid receptor gene polymorphism A118G with fentanyl analgesia consumption in Chinese gynaecological patients. *Anaesthesia*, *65*(2), 130-135. doi:10.1111/j.1365-2044.2009.06193.x
- Zhou, Q., Yang, L., Larson, S., Basra, S., Merwat, S., Tan, A., . . . Verne, G. N. (2016). Decreased miR-199 augments visceral pain in patients with IBS through translational upregulation of TRPV1. *Gut*, *65*(5), 797-805. doi:10.1136/gutjnl-2013-306464
- Zhou, Z., Zhu, G., Hariri, A. R., Enoch, M. A., Scott, D., Sinha, R., . . . Goldman, D. (2008). Genetic variation in human NPY expression affects stress response and emotion. *Nature*, *452*(7190), 997-1001. doi:10.1038/nature06858
- Zubieta, J. K., Heitzeg, M. M., Smith, Y. R., Bueller, J. A., Xu, K., Xu, Y., . . . Goldman, D. (2003). COMT val158met genotype affects mu-opioid neurotransmitter responses to a pain stressor. *Science*, *299*(5610), 1240-1243. doi:10.1126/science.1078546