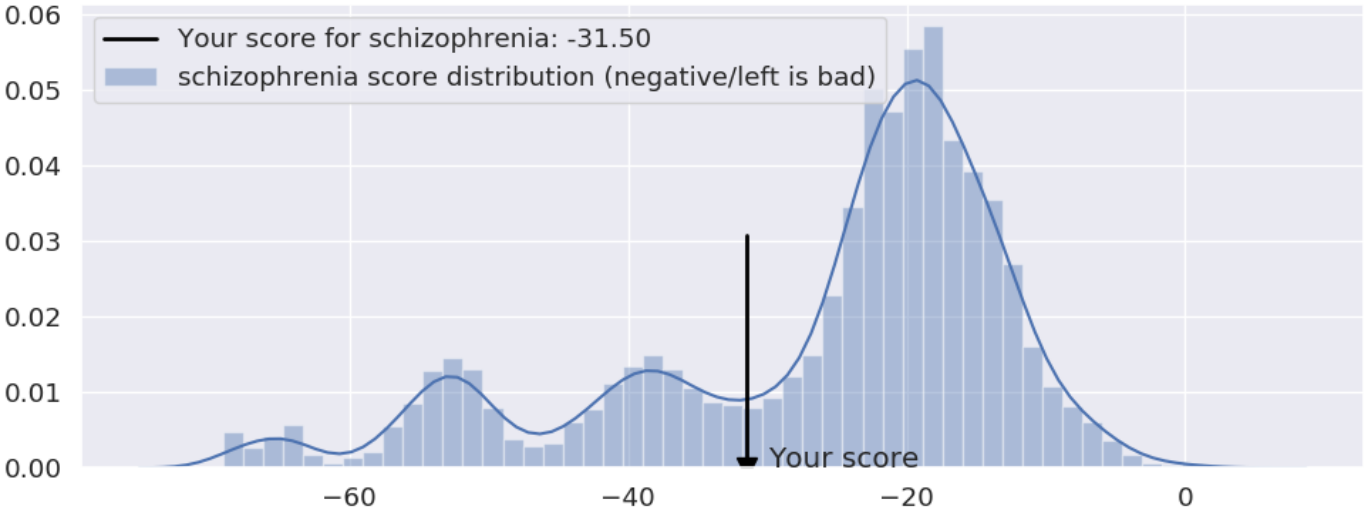
TOPIC: SCHIZOPHRENIA



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★ rs4129148(C;-) warning:2.57 **3x risk of schizophrenia.**

Located in the Pseudoautosomal region

rs4129148, located near the CSF2RA gene, has been reported in a whole genome association study to be associated with schizophrenia.

The risk allele (oriented to the dbSNP entry) is (G); the odds ratio associated with this allele is 3.23 (CI 2.04 - 5.15).

Given the results from the recent massive Psychiatric Genomics Consortium GWAS, it appears very unlikely that any large effect common SNPs exist for schizophrenia. It is not completely clear, though, how the previously
replicated results for rs4129148 might be explained. It is currently predicted that 10,000 SNPs contribute to schizophrenic illness.

The diagnosis for schizophrenia has now possibly shifted from asking: Schizophrenic? Yes or No
to How much Schizophrenic?

Established associations:

schizophrenia **you have 1 copies of the risk allele C**

(risk allele=C, odds ratio/beta 3.23 [2.04-5.15] with pval 4E-7, pubmedid=17522711)

Gene related topics:

schizophrenia(5.00)

Relevant papers and external links:

PMID 17522711

dbSNP: rs4129148 GWAS Catalog: rs4129148 Genecard: CSF2RA chromosome X

SNPedia: rs4129148(C;G)

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★ rs1344706(T;T) warning:2.70 48.37% **1.2x increased risk for schizophrenia**

rs1344706 is a SNP in the ZNF804A gene, and it is probably the first SNP to have been reported as achieving genome-wide significance for psychosis.

Reviews the literature, and concludes that rs1344706 is "robustly, if modestly" associated with increased risk for schizophrenia.

A genome-wide association study of schizophrenia (479 cases, 2,937 controls) followed by additional testing and a meta-analysis concluded that the strongest evidence for association was around ZNF804A (rs1344706; p = 1.61 x 10e-7) and that the finding was strengthened when the affected phenotype included bipolar disorder (p = 9.96 x 10e-9).

Executive function, neural circuitry, and genetic mechanisms in schizophrenia.

Apoptotic engulfment pathway and schizophrenia.

Persistence criteria for susceptibility genes for schizophrenia: a discussion from an evolutionary viewpoint.

Expanding the range of ZNF804A variants conferring risk of psychosis.

Effects of a genome-wide supported psychosis risk variant on neural activation during a theory-of-mind task.

Fine mapping of ZNF804A and genome-wide significant evidence for its involvement in schizophrenia and bipolar disorder.

New Genetic Findings in Schizophrenia: Is there Still Room for the Dopamine Hypothesis of Schizophrenia?

ZNF804A risk allele is associated with relatively intact gray matter volume in patients with schizophrenia.

The impact of a genome-wide supported psychosis variant in the ZNF804A gene on memory function in schizophrenia.

ZNF804A may be associated with executive control of attention.

Evaluation of risk loci for schizophrenia derived from genome-wide association studies in a German population.

Evidence of sex-modulated association of ZNF804A with schizophrenia.

Impact on schizotypal personality trait of a genome-wide supported psychosis variant of the ZNF804A gene.

ANK3, CACNA1C and ZNF804A gene variants in bipolar disorders and psychosis subphenotype.

Altered cortical network dynamics: a potential intermediate phenotype for schizophrenia and association with ZNF804A.

The schizophrenia risk gene ZNF804A influences the antipsychotic response of positive schizophrenia symptoms.

Association of the ZNF804A gene polymorphism rs1344706 with white matter density changes in Chinese schizophrenia.

Genome-wide supported psychosis risk variant in ZNF804A gene and impact on cortico-limbic WM integrity in schizophrenia.

ZNF804a regulates expression of the schizophrenia-associated genes PRSS16, COMT, PDE4B, and DRD2.

The effects of psychosis risk variants on brain connectivity: a review.

Association analysis of ZNF804A (zinc finger protein 804A) rs1344706 with therapeutic response to atypical antipsychotics in first-episode Chinese patients with schizophrenia.

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Established associations:

schizophrenia **you have 2 copies of the risk allele T**

(risk allele=T, odds ratio/beta 1.12 with pval 2E-7, pubmedid=18677311)

Gene related topics:

schizophrenia(5.00) · bipolar disorder(1.00) · personality(1.00) · memory(1.00) · brain(1.00) · PSYCH(0.27) · psychosis(0.27)

Relevant papers and external links:

PMID 20688871

PMID 18677311

OMIM 181500

OMIM 612361

PHARMGKB PA164856914

Evidence: PubMed ID:19407193Rs1344706, found in a separate GWAS to be associated with schizophrenia, was investigated here by Functional Magnetic Resonance Imaging. In 115 healthy German subjects, carriers of the "higher risk" allele(defined in this study as A) showed gene dosage-dependent alterations in functional coupling of dorsolateral prefrontal cortex across hemispheres and with hippocampus and also abnormal coupling of amygdala.

PHARMGKB PA162356547

Evidence: PubMed ID:18677311; Web Resource:External Link Results: Identification of loci associated with schizophrenia by genome-wide association and follow-up (Initial Sample Size: 479 cases, 2,937 controls; Replication Sample Size: 6,666 cases, 9,897 controls; Risk Allele: rs1344706-T). This variant is associated with Schizophrenia.

PMID 19693005

PMID 19721717

PMID 19911060

PMID 20048749

PMID 20231838

PMID 20368704

PMID 20485477

PMID 20934520

PMID 20957649

PMID 21040459

PMID 21302348

PMID 21349497

PMID 21457757

PMID 21767209

PMID 21810628

PMID 21892778

PMID 21911029

PMID 22328493

PMID 22384243

PMID 22416237

PMID 22425527

dbSNP: rs1344706 GWAS Catalog: rs1344706 Genecard: ZNF804A chromosome 2

SNPedia: rs1344706(T;T)

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★ rs2272127(C;C) info:1.74 65.63% **Associated with herpes and schizophrenia**

associations with schizophrenia and herpes

rs2272127 with schizophrenia(P = 0.0007, odds ratio for C allele 1.49, 95% CI: 1.18-1.87; P = 0.03 following correction for multiple comparisons).

rs2272127 was also associated with herpes simplex virus 1 (HSV1) seropositivity in cases (P = 0.04, OR for G allele 1.58, 95% CI: 1.04-2.39).

Gene related topics:

schizophrenia(5.00) · IMMUNE(0.10) · celiac disease(0.10)

Relevant papers and external links:

PMID 18092318

dbSNP: rs2272127 Genecard: IL18RAP chromosome 2 SNPedia: rs2272127(C;C)

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★ rs1858830(C;C) info:1.80 29.43% **2x risk of autism**

The C allele appears to increase risk of autism by an odds ratio of perhaps 1.8x

rs1858830, located in promoter of the MET gene, has been linked to a 2x increase in the risk of autism based on a study of ~700 families.

From OMIM 164860:

"In case-control analysis, the relative risk for autism was 2.27 for the CC genotype and 1.67 for the GC genotype compared to the GG genotype."

The association of rs1858830 in the MET gene with autism failed to replicate in 325 multiplex families and 10 trios of the International Molecular Genetic Study of Autism Consortium (IMGSAC), although another MET SNP did associate with autism (rs38845)

Disruption of cerebral cortex MET signaling in autism spectrum disorder.

Distinct genetic risk based on association of MET in families with co-occurring autism and gastrointestinal conditions.

Association of genetic variation in the MET proto-oncogene with schizophrenia and general cognitive ability.

Further evidence for the role of MET in autism susceptibility.

Gene related topics:

schizophrenia(1.00) · cognitive ability(1.00) · PSYCH(0.12) · autism(0.12)

Relevant papers and external links:

PMID 17053076
PMID 19002214
OMIM 611015
OMIM 164860
PMID 17696172
PMID 19255034
PMID 20080979
PMID 20615438

dbSNP: rs1858830 Genecard: MET chromosome 7 SNPedia: rs1858830(C;C)

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★ rs2007153(G;G) info:1.74 37.48% **increased risk of schizophrenia in limited study**

Associated with schizophrenia in a study of Croatians. Due to the limited number and diversity of the studied population, more study is needed to confirm any link. The G allele was associated with an increased risk of schizophrenia.

Gene related topics:

schizophrenia(5.00) · PSYCH(2.00) · UNKNOWN(2.00) · dopamine beta hydroxylase activity(2.00) · interpersonal sensitivity paranoid ideation psychoticism(2.00) · perceptual disorders(1.00) · NEUROLOGICAL(0.33) · migraine with aura(0.33) · attention deficit hyperactivity disorder(0.21) · CHEMDEPENDENCY(0.16) · smoking behavior(0.16) · adhd attention deficit hyperactivity disorder(0.15) · personality(0.14) · migraine disorders(0.08) · adhd(0.06) · smoking(0.05) · autism(0.03)

Relevant papers and external links:

PMID 19673036

dbSNP: rs2007153 Genecard: DBH chromosome 9 SNPedia: rs2007153(G;G)

★ rs7341475(G;G) info:1.32 72.46% **1.58x increased schizophrenia risk for women**

A total of 2,274 cases of schizophrenia were studied, resulting in an association between rs7341475, exclusively in women. Based on all populations the estimated relative risk for women carrying the common (G;G) genotype is 1.58 (p = 8.8 x 10(-7).

This finding was replicated in a large independent Ashkenazi Jewish collection (721 cases, 259 female; 1455 controls, 834 female), with confirmation that it applies to both schizophrenia and schizoaffective disorder.

Established associations:

schizophrenia **you have 2 copies of the risk allele G**

(risk allele=G, odds ratio/beta 1.58 [1.31-1.89] with pval 9E-7, pubmedid=18282107)

Gene related topics:

schizophrenia(5.00) · UNKNOWN(2.00) · otosclerosis(2.00) · PSYCH(0.22) · autism(0.22)

Relevant papers and external links:

PMID 18282107

PMID 20431428

PHARMGKB PA164740860

Evidence: PubMed ID:18282107; Web Resource:External Link results: Genome-Wide Association Identifies a Common Variant in the Reelin Gene That Increases the Risk of Schizophrenia Only in Women. (Initial Sample Size: 660 cases, 2,271 controls; Replication Sample Size: 2,274 cases, 4,401 controls); (Region: 7q22.1; Reported Gene(s): RELN; Risk Allele: rs7341475-G); (p-value= 8.99999999999999E-07).This variant is associated with Schizophrenia.

dbSNP: rs7341475 GWAS Catalog: rs7341475 Genecard: RELN chromosome 7

SNPedia: rs7341475(G;G)

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★ rs2024513(A;G) info:0.99 36.34% **1.3x higher risk for schizophrenia (among Han Chinese)**

rs2024513 is a SNP in the neurexin-1 NRXN1 gene on chromosome 2p16.3.

Based on a case-control study of 700+ Han Chinese patients with schizophrenia, rs2024513(A) was associated with higher risk, at an odds ratio of 1.3 (CI: 1.07 - 1.56, p=0.006).

Gene related topics:

schizophrenia(5.00) · HEMATOLOGICAL(0.07) · erythrocyte indices(0.07) · RENAL(0.07) · diabetic nephropathies(0.07) · OTHER(0.03) · breath tests(0.03)

Relevant papers and external links:

PMID 21477380

dbSNP: rs2024513 Genecard: NRXN1 chromosome 2 SNPedia: rs2024513(A;G)

★ rs3131296(G;G) warning:2.10 **1.4x increased risk for schizophrenia**

23andMe blog schizophrenia
rs3131296(C) increased the odds of schizophrenia by 1.19x
rs12807809(T) increased the odds of schizophrenia by 1.15x
rs9960767(C) increased the odds of schizophrenia by 1.23 times.

A study of ~2,500 Han Chinese patients with schizophrenia did find rs3131296 to be significantly associated in this population.

Established associations:

schizophrenia **you have 2 copies of the risk allele G**

(risk allele=G, odds ratio/beta 1.19 with pval 2E-10, pubmedid=19571808)

Gene related topics:

PSYCH(0.38) · schizophrenia(0.38) · IMMUNE(0.34) · diabetes mellitus type 1(0.34) · scleroderma systemic(0.15) · lupus erythematosus systemic(0.14) · VISION(0.12) · macular degeneration(0.12) · CARDIOVASCULAR(0.04) · heart rate(0.04)

Relevant papers and external links:

PMID 19571808

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Common variants conferring risk of schizophrenia.

PMID 20673877

dbSNP: rs3131296 GWAS Catalog: rs3131296 Genecard: NOTCH4 chromosome 6

SNPedia: rs3131296(G;G)

★ rs4950928(C;C) info:1.93 61.71% **Normal (higher) risk of Asthma.**

rs4950928 in CHI3L1 is likely to play roles in the predisposition to schizophrenia.

An attempt to repeat the association between rs4950928 and risk for schizophrenia in an ethnically identical population (Japanese) as well as a new population (Han Chinese) failed to show any significant association.

In contrast to previous studies, in this study of 6514 Danish adults the rs4950928(G) allele - rather than the (C) allele - was found to be associated with asthma.

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Established associations:

ykl40 measurement **you have 0 copies of the risk allele G**

(risk allele=G, odds ratio/beta 0.3 ng/ml decrease with pval 1E-13, pubmedid=18403759)

Gene related topics:

asthma(5.00) · schizophrenia(1.00)

Relevant papers and external links:

PMID 18403759
Effect of variation in chi3l1 on serum ykl-40 level, risk of asthma, and lung function.

PMID 17160890

PMID 18767121

PMID 19568425

OMIM 611960

OMIM 181500

OMIM 601525

PHARMGKB PA162356790

Evidence: PubMed ID:18403759; Web Resource:External Link Results: Effect of Variation in CHI31 on Serum YKL-40 Level, Risk of Asthma, and Lung Function (Initial Sample Size: 632 individuals; Replication Sample Size: 206 children; Risk Allele: rs4950928-G). This variant is associated with YKL-40 levels.

OMIM 601525

dbSNP: rs4950928 GWAS Catalog: rs4950928 Genecard: CHI3L1 chromosome 1

SNPedia: rs4950928(C;C)

★ rs6314(C;T) bad:3.02 13.82% **higher risk for RA; better response to paroxetine as treatment for depression**

rheumatoid arthritis risk

rs6314, also known as C1354T or His452Tyr/H452Y, is a SNP in the serotonin 2A receptor HTR2A gene.

Based on a study of 166 Caucasian patients being treated for depression with paroxetine, rs6314 heterozygotes were associated with better response. There was a significantly higher frequency of heterozygotes in the remitter and response groups in comparison to the non-remitter (odds ratio 7.50, p=0.002) and non-response groups (odds ratio 5.25, p=0.01).

rs6314 is part of a 4-SNP haplotype in the serotonin 2A receptor gene HTR2A that has been associated with rheumatoid arthritis in a study of 1800 European patients. The risk allele is rs6314(C). The overall risk for the haplotype CTCC of SNPs rs6311-rs1328674-rs6313-rs6314 is 1.68 (CI: 1.20 - 2.34, p = 0.02).

Note: the orientation of rs1328674 in dbSNP is opposite that cited by this publication; therefore, with respect to dbSNP, the haplotype of risk as cited above is CACC rather than CTCC.

"Haplotype association analysis suggests that the haplotype CCGCA (at SNPs rs3125, rs6314, rs1923886, rs2224721 and rs2770296) is protective against bipolar disorder (P = 0.021, odds ratio 0.63) and the rarer haplotype CCACG confers risk to the disorder (P = 0.0065, odds ratio 3.08)."

Genetic variation in the serotonin 2A receptor and suicidal ideation in a sample of 270 Irish high-density schizophrenia families.

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Gene related topics:

PSYCH(3.00) · anorexia nervosa(3.00) · anorexia nervosa bulimia(3.00) · PHARMACOGENOMIC(2.00) · impulsive behavior(2.00) · olanzapine(2.00) · response to clozapine(2.00) · schizophrenia affective disorder(2.00) · schizophrenia(1.64) · arthritis(1.00) · rheumatoid arthritis(1.00) · bulimia(0.94) · major depression(0.80) · suicidal behavior(0.69) · major depressive disorder(0.68) · depression(0.67) · obsessive compulsive disorder(0.58) · neuroleptic malignant syndrome(0.57) · schizophrenia tardive dyskinesia(0.57) · suicide(0.56) · personality disorders(0.50) · personality traits(0.47) · cognitive function(0.33) · depressive disorder major(0.29) · autism(0.28) · adhd(0.26) · mood disorders(0.23) · panic disorder(0.21) · adhd attention deficit hyperactivity disorder(0.21) · attention deficit hyperactivity disorder(0.21) · tourette syndrome(0.21) · bipolar disorder(0.20) · personality(0.14) · CHEMDEPENDENCY(0.13) · heroin

abuse(0.13) · NEUROLOGICAL(0.11) · migraine(0.11) · tardive dyskinesia(0.11) · smoking behavior(0.09) · CARDIOVASCULAR(0.05) · blood pressure determination(0.05) · alcohol abuse(0.04)

Relevant papers and external links:

PMID 18006541

PHARMGKB PA162181130
Evidence: PubMed ID:11311507; PubMed ID:15052272; PubMed ID:18253134In a study in a unipolar depressive population (n=166) this variant showed an association with remission and response following paroxetine therapy. HTR2A C1354T heterozygotes were significantly associated with improved response to paroxetine therapy. The SNP was also studied as a modifier of antidepressant response in a study in depressed patients (n=173) given a variety of antidepressant treatments with no association found, however another report found the HTR2A T1354 allele to be associated with response to fluoxetine.

PMID 18712714

PHARMGKB PA162181131
Evidence: PubMed ID:14699448; PubMed ID:15891581; PubMed ID:18602445This variant in the gene encoding the serotonin 2A receptor has been associated with human episodic memory performance and with differences in brain volume in memory-related brain regions.

dbSNP: rs6314 Genecard: HTR2A chromosome 13 SNPedia: rs6314(C;T)

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★ rs6313(C;T) warning:2.56 49.31% **higher risk for RA**

rs6313, also known as T102C, is part of a 4-SNP haplotype in the serotonin 2A receptor gene HTR2A that has been associated with rheumatoid arthritis in a study of 1800 European patients. The risk allele is rs6313 (C). The overall risk for the haplotype CTCC of SNPs rs6311-rs1328674-rs6313-rs6314 is 1.68 (CI: 1.20 - 2.34, p = 0.02).

Note: the orientation of rs1328674 in dbSNP is opposite that cited by this publication; therefore, with respect to dbSNP, the haplotype of risk as cited above is CACC rather than CTCC.

see also gs108 and gs226

Polymorphisms in the serotonin receptor gene HTR2A are associated with quantitative traits in panic disorder.

Gene related topics:

PSYCH(3.00) · anorexia nervosa(3.00) · anorexia nervosa bulimia(3.00) · PHARMACOGENOMIC(2.00) · impulsive behavior(2.00) · olanzapine(2.00) · response to clozapine(2.00) · schizophrenia affective disorder(2.00) · schizophrenia(1.64) · arthritis(1.00) · rheumatoid arthritis(1.00) · quantitative traits(1.00) · bulimia(0.94) · major depression(0.80) · suicidal behavior(0.69) · major depressive disorder(0.68) ·

depression(0.67) · obsessive compulsive disorder(0.58) · neuroleptic malignant syndrome(0.57) · schizophrenia tardive dyskinesia(0.57) · suicide(0.56) · personality disorders(0.50) · personality traits(0.47) · cognitive function(0.33) · depressive disorder major(0.29) · autism(0.28) · adhd(0.26) · mood disorders(0.23) · panic disorder(0.21) · adhd attention deficit hyperactivity disorder(0.21) · attention deficit hyperactivity disorder(0.21) · tourette syndrome(0.21) · bipolar disorder(0.20) · personality(0.14) · CHEMDEPENDENCY(0.13) · heroin abuse(0.13) · NEUROLOGICAL(0.11) · migraine(0.11) · tardive dyskinesia(0.11) · smoking behavior(0.09) · CARDIOVASCULAR(0.05) · blood pressure determination(0.05) · alcohol abuse(0.04)

Relevant papers and external links:

PMID 18006541

PHARMGKB PA165109704
Evidence: PubMed ID:19494443Risk or phenotype-associated allele (s): T/T. Phenotype: Patients, with a diagnosis of probable Alzheimer's disease, carrying the TT genotype were the most delusional during the follow-up period of a study evaluating the association of HTR2A 102T/C polymorphism with psychotic symptom severity. Patients with delusion symptoms carrying the CT and TT genotypes were resistant to the treatment with antipsychotic drugs. Study size: 80. Study population/ethnicity: Caucasian

PMID 17440930

PHARMGKB PA164889040
Evidence: PubMed ID:19193342T allele is associated with olanzapine-induced weight gain

dbSNP: rs6313 Genecard: HTR2A chromosome 13 SNPedia: rs6313(C;T)

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★ rs6932590(C;T) info:0.99 33.07% **1.1x increased risk for schizophrenia**

rs6932590 is a SNP that is postulated to have a role in conferring increased susceptibility for schizophrenia. rs6932590 lies in the major histocompatibility complex (MHC) region on chromosome 6, a region that codes for several genes with significant roles in autoimmunity, such as human leukocyte antigens. Specifically, rs6932590 lies in an intergenic region between PRSS16 (a serine protease expressed in the thymus that plays a role in positive T cell selection) and POM121L2 (a membrane glycoprotein) .

The T allele at rs6932590 purportedly confers an increased risk for schizophrenia, with reported odds ratios of 1.16 and 1.31 .

Evidence
One large-scale case-controlled genome-wide association study (GWAS) that examined differential genotypes in individuals with schizophrenia, found five significant schizophrenia-associated SNP markers in the MHC region: rs6913660, rs13219354, rs6932590, rs13211507, and rs3131296, with significant linkage disequilibrium between them. This GWAS was performed by the International Schizophrenia Consortium (ISC), Molecular Genetics of Schizophrenia (MGS), and SGENE and included, in all, 12,945 cases and 34,591 controls. Samples were taken from Caucasian populations across Europe

(eight separate geographical locations) 23andMe blog. rs6932590 was found to be the most significant SNP between cases and controls, with a p-value of 1.4x10e-12. The T allele was found to confer increased risk for schizophrenia with an odds ratio of 1.16.

In a separate GWAS that was designed to examine only the top eight significant SNPs (i.e., candidates) reported by the previous ISC/SGENE/MGS study , 2,496 cases and 5,184 control subjects from the Shanghai, China, population were genotyped. rs6932590 was again found to be significant (corrected p-value of 0.00096), as well as other SNPs in the MHC region (rs3131296, rs3130375) . The 0.00096 p-value is much higher than the one reported by the aforementioned ISC/SGENE/MGS study, however, the investigators deemed it significant. This study also found the T allele at rs6932590 to confer an increased risk for schizophrenia, but with an odds ratio of 1.31. Overall, this study found only four of the eight candidate SNPs from the ISC/SGENE/MGS study to be significant (i.e., validated) in the genotyped Shanghai, China sample.

Importantly, in both of the above studies, rs2958182, a SNP that lies in the TCF4 gene (outside of the MHC region), was also found to be significant. TCF4 codes for a transcription factor that is primarily expressed in pre-B cells and potentially plays a role in cognitive development .

A recent expression quantitative trait locus (eQTL) study investigated whether the SNPs reported by ISC/MGS/SGENE affect gene expression in normal human cortical brain tissue. The study did not find that rs6932590 was associated with any significant differential expression . However, the investigators noted that MHC region SNPs such as rs6932590 may affect gene expression earlier in development, which is difficult to observe temporally, particularly in the elderly, post-mortem brain samples that were used in the eQTL study.

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Biological Explanation

It is still unclear what role immune system genes may have on schizophrenia etiology, or whether the significant genes in the MHC region are even immune genes (there are other, non-immunity genes in the MHC region). One interesting finding is that a single allele variant in a schizophrenia SNP marker in the MHC region, rs3131296 (which has an r^2 of .86 with the HLA-DRB1*03 gene), while conferring risk for schizophrenia, confers increased protection for type-1 diabetes, celiac disease, and systemic lupus erythematosus .

There have been hypotheses that a winter or spring season of birth (i.e., an implicit increased risk of maternal influenza infection during pregnancy; which could lead to inflammation and aberrant neuronal development/growth) or early childhood infections (e.g., measles) may catalyze the development of schizophrenia. However, these hypotheses remain unproven and there was no evidence for them in the ISC/SGENE/MGS patient history data.

Competing/Complementary Theories

The polygenic inheritance model of schizophrenia is predicated on the idea that dozens of common variants combine to increase an individual's risk of schizophrenia. However, there has been limited success in finding significant common SNPs that are associated with schizophrenia. For example, in a study consisting of 1,870 schizophrenia cases and 2,002 controls that were genotyped for 789 SNPs that were hand-picked for their purported significance in schizophrenia susceptibility, no statistically significant associations were found . At

present, the most optimistic estimates of the magnitude of the effect of the polygenic model on disease susceptibility variance is approximately 20% .

The most promising explanation of schizophrenia heritability may come from the significantly increased presence of rare structural variants such as deletions and duplications in individuals with schizophrenia . Certainly, it is possible that certain SNPs, say in brain development or the immune system, may operate in concert with the effects of rare structural variants.

Other theories to explain the missing heritability include effects from certain copy number variations (CNV) and effects from a few of many highly impactful, independent, rare alleles .

As of May 2011, the Psychiatric GWAS Consortium is working on the largest GWAS for schizophrenia ever performed, with 59,000 cases and 7,700 family trios .

References

Common variants conferring risk of schizophrenia.

Common variants in major histocompatibility complex region and TCF4 gene are significantly associated with schizophrenia in Han Chinese

Common polygenic variation contributes to risk of schizophrenia and bipolar disorder

Schizophrenia susceptibility alleles are enriched for alleles that affect gene expression in adult human brain

No significant association of 14 candidate genes with schizophrenia in a large European ancestry sample: implications for psychiatric genetics

Rare structural variants disrupt multiple genes in neurodevelopmental pathways in schizophrenia

Rare structural variants in schizophrenia: one disorder, multiple mutations; one mutation, multiple disorders

Large recurrent microdeletions associated with schizophrenia

Schizophrenia: a common disease caused by multiple rare alleles

A framework for interpreting genome-wide association studies of psychiatric disorders

The human genome browser at UCSC

Cognitive and sensorimotor gating impairments in transgenic mice overexpressing the schizophrenia susceptibility gene Tcf4 in the brain

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Established associations:

schizophrenia **you have 1 copies of the risk allele T**

(risk allele=T, odds ratio/beta 1.16 with pval 1E-12, pubmedid=19571808)

Gene related topics:

schizophrenia(5.00) · celiac disease(1.00) · bipolar disorder(1.00) · brain(1.00) · measles(1.00) · systemic lupus erythematosus(1.00) · OTHER(1.00) · IMMUNE(1.00) · lupus erythematosus(1.00) · psychiatric disorders(1.00) · INFECTION(1.00) · lupus(1.00) · inflammation(1.00)

Relevant papers and external links:

PMID 20673877
PMID 12045153
PMID 19571808
PMID 20673877
PMID 19571808
PMID 19571811
PMID 19571808
PMID 20673877
PMID 20434134
PMID 21339752
PMID 19571808
PMID 18198266
PMID 19571811
PMID 18369103
PMID 19883952
PMID 18668039
PMID 17329737
PMID 19002139
PMID 19571808
PMID 20673877
PMID 19571811
PMID 21339752
PMID 18198266
PMID 18369103
PMID 19883952
PMID 18668039
PMID 17329737
PMID 19002139
PMID 12045153
PMID 20434134
OMIM 181500

dbSNP: rs6932590 GWAS Catalog: rs6932590 Genecard: nan chromosome 6

SNPedia: rs6932590(C;T)

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★ rs1024611(C;T) warning:2.78 46.28% **increased risk of exercise induced ischemia**

rs1024611, also known as the -2578A>G SNP due to its position in the promoter of the monocyte chemoattractant protein-1 MCP-1 CCL2 gene, influences the production of its corresponding protein, a chemokine involved in inflammatory responses.

In a study focusing on 679 apparently healthy siblings of people with premature heart disease, investigators found that carriers of an rs1024611(C) allele - oriented as in dbSNP, not as published - independently predicted the risk of exercise induced ischemia in general. The odds ratio was reported to be 1.86 (CI: 1.14-3.04, p=0.014), regardless of race, age, sex and other factors. However, it is not clear if this risk carries over to individuals who lack siblings with heart disease.

discussed in the 23andMe blog as being relevant to HIV

rs1024611 is not associated with systemic sclerosis in a multicenter study of 345 European patients

tuberculosis

Association study of functional genetic variants of innate immunity related genes in celiac disease.

Polymorphisms in the genes encoding chemokine receptor 5, interleukin-10, and monocyte chemoattractant protein 1 contribute to cytomegalovirus reactivation and disease after allogeneic stem cell transplantation.

Association study of genetic variants of pro-inflammatory chemokine and cytokine genes in systemic lupus erythematosus.

Polymorphisms within inflammatory genes and colorectal cancer.

Association of the -2510A/G chemokine (C-C motif) ligand 2 polymorphism with knee osteoarthritis in a Korean population.

The chemokine network. II. On how polymorphisms and alternative splicing increase the number of molecular species and configure intricate patterns of disease susceptibility.

Genome-wide association with select biomarker traits in the Framingham Heart Study.

A genome-wide association study identifies protein quantitative trait loci (pQTLs).

Polymorphisms affecting gene transcription and mRNA processing in pharmacogenetic candidate genes: detection through allelic expression imbalance in human target tissues.

MCP-1 promoter variant -362C associated with protection from pulmonary tuberculosis in Ghana, West Africa.

Analysis of inflammation- and atherosclerosis-related gene polymorphisms in branch retinal vein occlusion.

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Common variants of inflammatory cytokine genes are associated with risk of nephropathy in type 2 diabetes among Asian Indians.

Single nucleotide polymorphisms in monocyte chemoattractant protein-1 and its receptor act synergistically to increase the risk of carotid atherosclerosis.

Joint effect of MCP-1 genotype GG and MMP-1 genotype 2G/2G increases the likelihood of developing pulmonary tuberculosis in BCG-vaccinated individuals.

Gene-gene interactions in the folate metabolic pathway and the risk of conotruncal heart defects.

The -A2518G polymorphism of monocyte chemoattractant protein-1 is associated with Crohn's disease.

Polymorphisms in IL-1beta, vitamin D receptor Fok1, and Toll-like receptor 2 are associated with extrapulmonary tuberculosis.

CCL2 and CCR2 polymorphisms are associated with markers of exercise-induced skeletal muscle damage.

Combined effect of inflammatory gene polymorphisms and the risk of ischemic stroke in a prospective cohort of subjects with type 2 diabetes: a Go-DARTS study.

CCL3 genotype and current depression increase risk of HIV-associated dementia.

Genetic variants in inflammation-related genes are associated with radiation-induced toxicity following treatment for non-small cell lung cancer.

Monocyte chemoattractant protein-1 in schizophrenia: -2518A/G genetic variant and protein levels in Armenian population.

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Gene related topics:

OTHER(2.00) · carpal tunnel syndrome(2.00) · IMMUNE(1.00) · asthma asthma severity(1.00) · celiac disease(1.00) · atherosclerosis(1.00) · stroke(1.00) · CANCER(1.00) · systemic sclerosis(1.00) · cancer(1.00) · colorectal cancer(1.00) · nephropathy(1.00) · heart disease(1.00) · schizophrenia(1.00) · METABOLIC(1.00) · osteoarthritis(1.00) · lung cancer(1.00) · depression(1.00) · type 2 diabetes(1.00) · vitamin d(1.00) · dementia(1.00) · carotid atherosclerosis(1.00) · lupus(1.00) · inflammation(1.00) · scleroderma systemic(0.35) · RENAL(0.22) · nephropathy iga(0.22) · nephropathy in other diseases(0.19) · INFECTION(0.11) · hiv(0.11) · hepatitis c chronic(0.08) · tuberculosis(0.08) · crohn disease(0.06) · lupus erythematosus(0.06) · tuberculosis pulmonary(0.06) · CARDIOVASCULAR(0.06) · myocardial infarct(0.06) · systemic lupus erythematosus(0.06) · hepatitis b chronic(0.04) · hepatitis c(0.04)

Relevant papers and external links:

PMID 16934270

PMID 19032966

OMIM 158105

OMIM 607948

PMID 16078996

PMID 16672419

PMID 16719905

PMID 17062130
PMID 17763208
PMID 17848170
PMID 17903293
PMID 18464913
PMID 18698231
PMID 18940815
PMID 19347053
PMID 19357773
PMID 19506371
PMID 20111728
PMID 20111745
PMID 20125127
PMID 20196868
PMID 20339010
PMID 20622166
PMID 20725607
PMID 20811626
PMID 22425139

dbSNP: rs1024611 Genecard: nan chromosome 17 SNPedia: rs1024611(C;T)

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★ rs3813929(C;-) info:1.89 74.85% **possible weight gain if taking olanzapine**

rs3813929, also known as -759C/T, is a SNP in the 5-hydroxytryptamine (serotonin) receptor 2C HTR2C gene.

A study of 107 patients with schizophrenia being treated with olanzapine reported a protective effect against weight-gain from the (T) allele of this SNP; zero patients (of 28) with a rs3813929(T) allele had a body mass index increase of >=10% (p=0.002), whereas (C;C) homozygotes did. This effect may also involve nearby SNP rs518147.

T allele showed borderline significant association with higher BMI and incidence of lifetime major depressive disorder among 4978 persons from the European Prospective Investigation into Cancer (EPIC)-Norfolk study, however, only the association with BMI remained borderline significant within the full EPIC-Norfolk cohort (20,981 persons)

The association between HTR2C polymorphisms and obesity in psychiatric patients using antipsychotics: a cross-sectional study.

Association of the HTR2C gene and antipsychotic induced weight gain: a meta-analysis.

The association between HTR2C gene polymorphisms and the metabolic syndrome in patients with schizophrenia.

Multivariate permutation analysis associates multiple polymorphisms with subphenotypes of major depression.

Focus on HTR2C: A possible suggestion for genetic studies of complex disorders.

HTR2C gene polymorphisms and the metabolic syndrome in patients with schizophrenia: a replication study.

Cohort profile: risk patterns and processes for psychopathology emerging during adolescence: the ROOTS project.

Association of polymorphisms of the serotonergic system with smoking initiation in Caucasians.

Pharmacogenetics and antipsychotics: therapeutic efficacy and side effects prediction.

Functional consequences of two HTR2C polymorphisms associated with antipsychotic-induced weight gain.

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Gene related topics:

olanzapine(5.00) · weight(5.00) · METABOLIC(3.60) · weight gain(3.60) · PHARMACOGENOMIC(2.00) · weight gain antipsychotic drug induced(2.00) · weight gain antipsychotic induced(2.00) · OTHER(1.00) · weight loss(1.00) · CANCER(1.00) · body mass(1.00) · cancer(1.00) · bmi(1.00) · metabolic syndrome(1.00) · schizophrenia(1.00) · major depression(1.00) · body mass index(1.00) · obesity(1.00) · depression(1.00) · major depressive disorder(1.00) · smoking(1.00) · PSYCH(0.67) · bipolar affective disorder(0.67) · NEUROLOGICAL(0.33) · migraine with aura(0.33) · mood disorders(0.23) · suicide(0.22) · tardive dyskinesia(0.11) · personality(0.06) · attention deficit hyperactivity disorder(0.05) · personality traits(0.05) · depressive disorder major(0.05) · CHEMDEPENDENCY(0.04) · alcohol abuse(0.04) · autism(0.03)

Relevant papers and external links:

PMID 19434072

PMID 20065966

PHARMGKB PA165109600
Evidence: PubMed ID:19636338Risk or phenotype-associated allele: T. Phenotype: Short-term weight gain under olanzapine therapy was significantly lower for 5-HTR2C -759 T-allele carriers. Study size: 124. Study population/ethnicity: Caucasian; Patients with psychiatric disorders. Significance metric(s): p = 0.011. Type of association: PK.

PHARMGKB PA165108056
Evidence: PubMed ID:15666332Risk or phenotype-associated allele: T. Phenotype: The T allele was more frequently found in subjects not gaining 10% or more of their body weight, compared with those who did gain 10% or more of their body weight. None of the subjects who gained >10% of their initial body weight over 6 weeks carried a T allele (0/11). Study size: 42. Study population/ethnicity: Caucasian acutely ill patients with schizophrenia taking olanzapine. Significance metric(s): p = 0.0035. Type of association: CO.

PHARMGKB PA164924604

Evidence: PubMed ID:19622037This variant is associated with Olanzapine-induced weight gain. The -759T allele confers protective effect towards Olanzapine-induced weight gain in a study consisting of 107 patients with schizophrenia.

PMID 17016522
PMID 17291373
PMID 17632216
PMID 18081710
PMID 18802918
PMID 19142101
PMID 19359258
PMID 20060656
PMID 21162693
PMID 21391883

dbSNP: rs3813929 Genecard: HTR2C chromosome X SNPedia: rs3813929(C;C)

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★ rs464049(T;T) bad:3.38 15.35% **increased risk of schizophrenia in limited study**

Associated with schizophrenia in a study of Croatians. Due to the limited number and diversity of the studied population, more study is needed to confirm any link. The T allele was associated with an increased risk of schizophrenia.

A network of dopaminergic gene variations implicated as risk factors for schizophrenia.

Family based association study of pediatric bipolar disorder and the dopamine transporter gene (SLC6A3).

Genome-wide and candidate gene association study of cigarette smoking behaviors.

Financial and psychological risk attitudes associated with two single nucleotide polymorphisms in the nicotine receptor (CHRNA4) gene.

Two loci control tuberculin skin test reactivity in an area hyperendemic for tuberculosis.

Gene related topics:

PSYCH(9.95) · attention deficit hyperactivity disorder(9.95) · adhd attention deficit hyperactivity disorder(3.41) · schizophrenia methamphetamine abuse(2.00) · CHEMDEPENDENCY(1.25) · smoking behavior(1.25) · perceptual disorders(1.00) · bipolar disorder(1.00) · tuberculosis(1.00) · nicotine(1.00) · personality(0.98) · cocaine related disorders(0.67) · psychosis(0.60) · delirium(0.57) · impulsivity(0.57) · tourette syndrome(0.47) · adhd(0.40) · NEUROLOGICAL(0.40) · parkinson s disease(0.40) · REPRODUCTION(0.36) · prenatal exposure delayed effects(0.36) · schizophrenia(0.27) · substance related disorders(0.27) · heroin dependence(0.25) · bulimia(0.24) · alcohol(0.21) · dyslexia(0.19) · alcohol abuse(0.17) · alcoholism(0.16) · personality traits(0.12) · migraine disorders(0.08) · depression(0.07) · obsessive compulsive disorder(0.06) · autism(0.05) · smoking(0.05) · PHARMACOGENOMIC(0.02)

Relevant papers and external links:

PMID 19673036
PMID 18045777
PMID 18361424
PMID 19247474
PMID 19693267
PMID 19901083

dbSNP: rs464049 Genecard: SLC6A3 chromosome 5 SNPedia: rs464049(T;T)

★ rs4570625(G;G) info:1.18 41.93% **maybe: higher scores on anxiety-related personality traits; greater placebo response**

One study of (only) 25 people shows this genotype was a significant predictor of clinical placebo response, being associated with greater improvement in anxiety symptoms. A criticism of this study has also been published, and it has not been replicated since the original publication years ago.

This SNP has been linked to several psychiatric and/or behavioral phenomena, including:
higher scores on anxiety-related personality traits
obsessive compulsive disorder
panic disorder with a possible gender-dependent effect
rs4570625, also known as G-703T, is a SNP in the tryptophan hydroxylase 2 TPH2 gene. This SNP has been linked to several psychiatric and/or behavioural phenomena, including:

rs4570625 and rs4565946 linked to the pathogenesis of early-onset obsessive compulsive disorder

rs4570625 and rs11178997 in TPH2's regulatory region display preferential transmission

rs4570625(G;G) homozygosity was a significant predictor of clinical placebo response, being associated with greater improvement in anxiety symptoms.

g2b2mh is rs4570625(G;G) is a significant predictor of clinical placebo response? maybe not

panic disorder with a possible gender-dependent effect

Transmission disequilibrium of polymorphic variants in the tryptophan hydroxylase-2 gene in attention-deficit/hyperactivity disorder.

Association between a polymorphism in the promoter region of the TPH2 gene and the personality trait of harm avoidance.

Tryptophan hydroxylase-2 gene variation influences personality traits and disorders related to emotional dysregulation.

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Case-control and family-based association studies of candidate genes in autistic disorder and its endophenotypes: TPH2 and GLO1.

Characterization of a functional promoter polymorphism of the human tryptophan hydroxylase 2 gene in serotonergic raphe neurons.

Genetic variation of serotonin function and cognitive control.

Tryptophan hydroxylase 2 gene and alcohol use among college students.

Resequencing of serotonin-related genes and association of tagging SNPs to citalopram response.

TPH2 gene variants and anxiety during alcohol detoxification outcome.

Epistasis between IL1A, IL1B, TNF, HTR2A, 5-HTTLPR and TPH2 variations does not impact alcohol dependence disorder features.

Alternative splicing and extensive RNA editing of human TPH2 transcripts.

Association study of tryptophan hydroxylase-2 gene in schizophrenia and its clinical features in Chinese Han population.

Pharmacogenetics of antidepressant response.

Serotonin and early cognitive development: variation in the tryptophan hydroxylase 2 gene is associated with visual attention in 7-month-old infants.

Emotion appraisal and the tryptophan hydroxylase 2 (TPH2) gene.

Common variants in the TPH2 promoter confer susceptibility to paranoid schizophrenia.

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Gene related topics:

anxiety(5.00) · personality(5.00) · OTHER(1.00) · chronic fatigue syndrome(1.00) · citalopram(1.00) · obsessive compulsive disorder(1.00) · harm avoidance(1.00) · alcohol(1.00) · alcohol dependence(1.00) · schizophrenia(1.00) · PSYCH(0.56) · suicide(0.56) · METABOLIC(0.45) · waist circumference(0.45) · autism(0.17) · adhd attention deficit hyperactivity disorder(0.15) · depression(0.15) · adhd(0.15) · panic disorder(0.08) · NEUROLOGICAL(0.08) · migraine disorders(0.08) · attention deficit hyperactivity disorder(0.05) · personality traits(0.05) · depressive disorder major(0.05)

Relevant papers and external links:

PMID 19052197
PMID 16146581
PMID 19052197
PMID 19132526
OMIM 143465
OMIM 607478
OMIM 613003
PMID 16116490

PMID 17176491
PMID 17176492
PMID 17346350
PMID 17568567
PMID 17892388
PMID 18782386
PMID 19077664
PMID 19361870
PMID 19742166
PMID 20126463
PMID 20938755
PMID 21172166
PMID 21418063
PMID 22322887
PMID 22392150

dbSNP: rs4570625 Genecard: TPH2 chromosome 12 SNPedia: rs4570625(G;G)

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★ rs16944(G;G) info:1.92 24.07% **Increased risk of mental disorders**

rs16944 is a SNP in the interleukin 1, beta gene, a member of the cytokine family involved in the inflammatory response. The rs16944 G;G genotype is associated with risk for multiple mental illnesses. An increased risk for schizophrenia was found in a genetic association study of 2111 Caucasian individuals with an odds ratio of 1.24 (95% CI 1.09, 1.41) . Studies examining the brains of schizophrenic and bipolar individuals found reduced gray matter and hypoactivity associated with the G;G genotype. Additionally, this genotype is associated with impaired ability to achieve remission in a study of 256 Caucasian individuals with depression (odds ratio = 1.74; 95% confidence interval 1.2-4.3).

The rs16944 A allele increases susceptibility to Osteoarthritis, with 1.80 times for heterozygotes (AG) and 2.90 times for homozygotes (AA)

Gray matter deficits in bipolar disorder rs16944(T;T)

Gene related topics:

mental disorders(5.00) · IMMUNE(4.49) · periodontitis(4.49) · CANCER(4.00) · helicobacter infections stomach neoplasms(4.00) · INFECTION(2.70) · helicobacter infections(2.70) · NEUROLOGICAL(2.40) · seizures febrile(2.40) · UNKNOWN(2.00) · atrophy helicobacter infections(2.00) · dental plaque gingivitis(2.00) · gastritis(2.00) · gastritis helicobacter infections stomach ulcer stomach ulcer(2.00) · stomach neoplasms(1.92) · ige(1.80) · stomatitis aphthous(1.80) · duodenal ulcer helicobacter infections(1.60) · adenocarcinoma helicobacter infections stomach neoplasms(1.50) · helicobacter infections peptic ulcer(1.29) · otitis media recurrence(1.29) · helicobacter pylori infection(1.12) · meningococcal infections(1.12) · alveolar bone loss(1.00) · gastritis atrophic stomach neoplasms(1.00) · gastroesophageal

reflux helicobacter infections(1.00) · helicobacter infections purpura thrombocytopenic idiopathic(1.00) · helicobacter infections stomach ulcer stomach ulcer(1.00) · hepatocellular carcinoma(1.00) · bipolar disorder(1.00) · schizophrenia(1.00) · depression(1.00) · stomach cancer(0.79) · periodontal disease(0.74) · REPRODUCTION(0.69) · premature birth(0.69) · CARDIOVASCULAR(0.67) · heart disease(0.67) · METABOLIC(0.64) · degenerative arthropathy osteoarthritis(0.64) · gastric cancer(0.62) · h pylori infection(0.46) · VISION(0.40) · arthritis rheumatoid rheumatoid arthritis(0.40) · graves ophthalmopathy(0.40) · purpura thrombocytopenic idiopathic werlhof s disease(0.33) · chronic periodontitis(0.31) · meningococcal disease(0.29) · alzheimer s disease(0.26) · osteoarthritis knee(0.24) · mucocutaneous lymph node syndrome(0.22) · carcinoma squamous cell mouth neoplasms squamous cell carcinoma(0.21) · subarachnoid hemorrhage(0.21) · glomerulonephritis iga(0.20) · epilepsy temporal lobe(0.19) · multiple myeloma(0.19) · abortion habitual(0.19) · sepsis(0.18) · adenocarcinoma stomach neoplasms(0.18) · polycystic ovarian syndrome polycystic ovary syndrome(0.16) · osteoarthritis(0.14) · sepsis systemic infection(0.14) · skin cancer non melanoma(0.14) · inflammation(0.13) · arthritis rheumatoid(0.13) · RENAL(0.12) · chronic renal failure kidney failure chronic(0.12) · tuberculosis(0.12) · graves disease graves disease(0.11) · alopecia areata(0.11) · pulmonary disease chronic obstructive(0.10) · PSYCH(0.10) · mood disorders(0.10) · hepatitis b chronic(0.10) · juvenile arthritis(0.09) · rheumatoid spondylitis spondylitis ankylosing(0.09) · ankylosing spondylitis(0.08) · spondylitis ankylosing(0.07) · acute coronary syndrome(0.06) · inflammatory bowel disease(0.06) · c reactive protein(0.06) · arthritis(0.06) · CHEMDEPENDENCY(0.05) · alcohol(0.05) · graft versus host disease(0.05) · endometriosis(0.05) · celiac disease(0.04) · pregnancy loss recurrent(0.04) · NORMALVARIATION(0.04) · normal variation(0.04) · bone mineral density(0.04) · ulcerative colitis(0.04) · sarcoidosis(0.04) · esophageal cancer(0.03) · melanoma(0.03) · cervical cancer(0.02) · OTHER(0.02) · cystic fibrosis(0.02)

Relevant papers and external links:

PMID 16905295

PMID 22763186

PMID 19125864

PMID 20044070

PMID 15077300

PMID 19125864

PHARMGKB PA164926306
Evidence: PubMed ID:16257277This variant was significantly associated with acquired resistance to bisphosphonates treatment in Caucasian patients with Paget's disease of the bone

dbSNP: rs16944 Genecard: IL1B chromosome 2 SNPedia: rs16944(G;G)

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★ rs4444903(A;G) info:1.03 47.79% **3.5x risk of hep-cancer in cirrhosis patients; higher glioma risk**

rs4444903 is a SNP, also known as +61, located in the promoter region of the epidermal growth factor EGF gene that influences the amount of EGF produced. The rs4444903(G) allele appears to produce higher amounts of EGF than the (A) allele.

A study of 2 Caucasian populations of patients with alcoholic cirrhosis indicates that, for these patients, the presence of the risk allele rs4444903(G) increases the chances of developing hepatocellular carcinoma (liver cancer). After adjusting for age, sex, race, etiology, and severity of cirrhosis the number of (G) copies led to an odds ratio for either (G;G) or (A;G) genotypes versus the (A;A) genotype of 3.49 (CI: 1.29-9.44, p=.01).

In another study, analysis of 197 glioma patients showed that the rs4444903(G) allele conferred higher risks for gliomas (odds ratio 1.32, CI: 1.04-1.67), glioblastomas (OR, 1.47, CI: 1.02-2.10), and oligodendrogliomas (OR, 1.55, CI: 1.07-2.23). In general, the risk was about the same for a carrier or one or two (G) alleles, however, no significant association was observed with patients' overall survival.

A study of 126 Indian gallbladder cancer patients concluded that the rs4444903(G;G) genotype was at increased risk, but only in females (odds ratio 3.45, CI: 1.52-7.82, p = 0.003).

effects lots of no known risk
pmids15373782 15729146 16214932 16214933 16214934 16214935 16217151 16217152 16217153

rs4444903, rs2298991, rs7692976 and rs4533485 significantly interacted with gender for acute respiratory distress syndrome risk.

popular in pubmed

Epidermal growth factor gene polymorphism is different between schizophrenia and lung cancer patients in Korean population.

VEGF, FGF1, FGF2 and EGF gene polymorphisms and psoriatic arthritis.

Pathway-based evaluation of 380 candidate genes and lung cancer susceptibility suggests the importance of the cell cycle pathway.

EGFR pathway polymorphisms and bladder cancer susceptibility and prognosis.

Development of a fingerprinting panel using medically relevant polymorphisms.

Genetic factors associated with intestinal metaplasia in a high risk Singapore-Chinese population: a cohort study.

A functional epidermal growth factor (EGF) polymorphism, EGF serum levels and renal cell carcinoma risk in a Chinese population.

A functional polymorphism in the epidermal growth factor gene is associated with risk for hepatocellular carcinoma.

Carriage of the EGF rs4444903 A>G functional polymorphism associates with disease progression in chronic HBV infection.

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Gene related topics:

cirrhosis(5.00) · cancer(5.00) · CANCER(2.00) · malignant melanoma(2.00) · arthritis(1.00) · survival(1.00) · liver cancer(1.00) · cancer susceptibility(1.00) · psoriatic arthritis(1.00) · bladder cancer(1.00) · RENAL(1.00) · respiratory distress syndrome(1.00) · schizophrenia(1.00) · hepatocellular carcinoma(1.00) · lung cancer(1.00) · INFECTION(1.00) · brain cancer(0.50) · brain neoplasms glioma(0.24) · carcinoma squamous cell esophageal neoplasms(0.12) · melanoma(0.11) · glioma(0.11) · stomach cancer(0.06) · melanoma skin neoplasms(0.05)

Relevant papers and external links:

PMID 18167406
PMID 17473192
PMID 18571008
PMID 19010984
OMIM 114550
OMIM 131530
PMID 15663953
PMID 17204151
PMID 18676680
PMID 19372140
PMID 19379518
PMID 19822020
PMID 20203692
PMID 21440548
PMID 22236006

dbSNP: rs4444903 Genecard: EGF chromosome 4 SNPedia: rs4444903(A;G)

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★ rs7997012(G;G) info:0.86 52.89% **~18% less likely to respond to citalopram**

rs7997012, located in an intron of the HTR2A gene, was found to be associated with a somewhat increased rate of successful response to treatment of depression with the drug citalopram.

From this article :

"HTR2A encodes the serotonin 2A receptor, which is downregulated by citalopram. Participants who were homozygous for the A allele had an 18% reduction in absolute risk of having no response to treatment, compared with those homozygous for the other allele."

See also Anxiety Blog posting

Gene related topics:

citalopram(5.00) · PSYCH(3.00) · anorexia nervosa(3.00) · anorexia nervosa bulimia(3.00) · PHARMACOGENOMIC(2.00) · impulsive behavior(2.00) · olanzapine(2.00) · response to clozapine(2.00) · schizophrenia affective disorder(2.00) · schizophrenia(1.64) · anxiety(1.00) · OTHER(1.00) · bulimia(0.94) · major depression(0.80) · suicidal behavior(0.69) · major depressive disorder(0.68) · depression(0.67) · obsessive compulsive disorder(0.58) · neuroleptic malignant syndrome(0.57) · schizophrenia tardive dyskinesia(0.57) · suicide(0.56) · personality disorders(0.50) · personality traits(0.47) · cognitive function(0.33) · depressive disorder major(0.29) · autism(0.28) · adhd(0.26) · mood disorders(0.23) · panic disorder(0.21) · adhd attention deficit hyperactivity disorder(0.21) · attention deficit hyperactivity disorder(0.21) · tourette syndrome(0.21) · bipolar disorder(0.20) · personality(0.14) · CHEMDEPENDENCY(0.13) · heroin abuse(0.13) · NEUROLOGICAL(0.11) · migraine(0.11) · tardive

dyskinesia(0.11) · smoking behavior(0.09) · CARDIOVASCULAR(0.05) · blood pressure determination(0.05) · alcohol abuse(0.04)

Relevant papers and external links:

PMID 16642436

PMID 16642436

OMIM 182135

PHARMGKB PA165109601
Evidence: PubMed ID:19636338Risk or phenotype-associated allele: A. Phenotype: Patients with the 5-HTR2A intron 2 (rs7997012) AA genotype suffered from more pronounced side effects compared to carriers of the GA or GG genotype. Study size: 124. Study population/ethnicity: Caucasian; Patients with psychiatric disorders. Significance metric(s): p = 0.018 and p = 0.002. Type of association: PD.

PHARMGKB PA161614203
Evidence: PubMed ID:16642436In one study, subjects homozygous for allele A had a reduction in absolute risk of having no response to treatment with citalopram for major depressive disorder. The allele was found to be more frequent in white than in black subjects, and this is consistant with racial differences in response to antidepressant treatment.

OMIM 182135

dbSNP: rs7997012 Genecard: HTR2A chromosome 13 SNPedia: rs7997012(G;G)

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★ rs1801131(C;C) bad:3.15 6.22% **Number of risks. Complex.**

MTHFR rs1801131 is involved in converting 5-methylfolate (5MTHF) to tetrahydrofolate (THF). Unlike MTHFR C677T, this mutation does not lead to elevated homocysteine levels.
rs1801131 is a SNP in the MTHFR gene, representing an A>C mutation at mRNA position 1298, resulting in a glu429-to-ala (E429A) substitution (hence this SNP is also known as A1298C or E429A).

A diplotype (according to the authors, but perhaps actually a genoset) of rs1801131 and rs1801133 has been linked to slightly increased risk for several types of brain cancer. The highest risk of meningioma was associated with heterozygosity for both MTHFR SNPs (odds ratio 2.11, CI: 1.42-3.12, p=0.002). The corresponding odds ratio for glioma was 1.23 (CI: 0.91-1.66, p=0.02. In general, risks were increased with genotypes associated with reduced MTHFR activity.

rs1801131 shows no consistent association with schizophrenia overall in 12 studies totaling 3,000+ patients

Gene related topics:

METABOLIC(14.69) · hyperhomocysteinemia(14.69) · DEVELOPMENTAL(14.49) · neural tube defects(14.49) · down syndrome(11.36) · CARDIOVASCULAR(10.00) · coronary artery disease

hyperhomocysteinemia(10.00) · folic acid deficiency(7.00) · homocysteine(6.92) · UNKNOWN(5.00) · chronic renal failure hyperhomocysteinemia kidney failure chronic(5.00) · coronary disease coronary heart disease hyperhomocysteinemia(5.00) · CANCER(4.00) · adenoma colorectal neoplasms neoplasm recurrence local(4.00) · hyperhomocysteinemia retinal vein occlusion(4.00) · spinal dysraphism(3.85) · colorectal cancer(3.74) · arteriosclerosis(3.57) · apoplexy stroke(3.12) · apoplexy brain ischemia hyperhomocysteinemia stroke(3.00) · cardiovascular diseases hyperhomocysteinemia(3.00) · congenital heart defects heart defects congenital(3.00) · diabetes mellitus type ii diabetes mellitus type 2 hyperhomocysteinemia(3.00) · hearing loss sudden(3.00) · hyperhomocysteinemia postoperative complications(3.00) · hyperhomocystinemia(3.00) · vascular diseases(3.00) · cardiovascular diseases(2.93) · apoplexy brain ischemia stroke(2.61) · REPRODUCTION(2.61) · pregnancy loss(2.61) · abortion spontaneous(2.58) · leukemia lymphocytic acute l1 precursor cell lymphoblastic leukemia lymphoma(2.58) · pregnancy complications(2.40) · precursor cell lymphoblastic leukemia lymphoma(2.16) · colonic neoplasms(2.13) · IMMUNE(2.00) · NEUROLOGICAL(2.00) · VISION(2.00) · abortion habitual hyperhomocysteinemia(2.00) · abortion habitual pregnancy complications hematologic thrombophilia(2.00) · abruptio placentae(2.00) · activated protein c resistance hyperhomocysteinemia thrombophilia venous thrombosis(2.00) · acute lymphocytic leukemia hyperhomocysteinemia precursor cell lymphoblastic leukemia lymphoma(2.00) · atherosclerosis thrombosis(2.00) · cardiovascular diseases chronic renal failure hyperhomocysteinemia kidney failure chronic(2.00) · cerebrovascular disease ischemic(2.00) · chronic ulcerative colitis colitis ulcerative folic acid deficiency hyperhomocysteinemia(2.00) · cleft lip cleft palate syndrome(2.00) · epilepsy hyperhomocysteinemia(2.00) · glaucoma angle closure glaucoma open angle(2.00) · heart defects congenital(2.00) · hyperhomocysteinemia hyperlipidemias(2.00) · hyperhomocysteinemia hypertension(2.00) · hyperhomocysteinemia pre eclampsia(2.00) · retinal artery occlusion retinal vein occlusion(2.00) · hyperhomocysteinemia venous thrombosis(1.80) · venous thrombosis(1.78) · abortion habitual thrombophilia(1.71) · stomach neoplasms(1.71) · HEMATOLOGICAL(1.58) · thrombophilia(1.58) · thrombosis(1.44) · PHARMACOGENOMIC(1.39) · methotrexate toxicity(1.39) · thromboembolism venous(1.35) · anemia sickle cell sickle cell anemia(1.29) · cleft lip cleft palate(1.29) · adenocarcinoma stomach neoplasms(1.25) · acute lymphocytic leukemia precursor cell lymphoblastic leukemia lymphoma(1.25) · diabetes mellitus type ii diabetes mellitus type 2 diabetic nephropathies diabetic nephropathy(1.12) · coronary disease coronary heart disease(1.10) · pre eclampsia(1.05) · coronary artery disease(1.04) · antiphospholipid syndrome thrombophilia thrombosis(1.00) · brain ischemia(1.00) · brain neoplasms glioma meningeal neoplasms meningioma(1.00) · carcinoma squamous cell skin neoplasms squamous cell carcinoma(1.00) · cervical intraepithelial neoplasia cervical neoplasm papillomavirus infections uterine cervical neoplasms(1.00) · migraine with aura migraine without aura(1.00) · thrombophilia and vascular disease(1.00) · brain(1.00) · cancer(1.00) · glioma(1.00) · brain cancer(1.00) · breast cancer(0.93) · migraine disorders(0.92) · thrombosis deep vein(0.86) · RENAL(0.84) · diabetic nephropathy(0.84) · pregnancy loss recurrent(0.83) · pre eclampsia thrombophilia(0.82) · esophageal cancer stomach cancer(0.80) · abortion habitual(0.75) · preeclampsia(0.73) · arthritis rheumatoid rheumatoid arthritis(0.71) · PSYCH(0.67) · behcet syndrome venous thrombosis(0.67) · brain ischemia stroke thrombophilia(0.67) · cerebrovascular disorders(0.67) · congenital abnormalities(0.67) · dementia vascular(0.67) · diabetic nephropathies diabetic nephropathy(0.67) · aortic aneurysm abdominal(0.59) · insulin resistance polycystic ovarian syndrome polycystic ovary syndrome(0.57) · heart anomalies congenital(0.53) · leukemia(0.52) · atherosclerosis(0.51) · hypertension(0.51) · cardiovascular risk(0.50) · cerebrovascular disease(0.50) · colonic neoplasms rectal neoplasms(0.50) · thrombosis venous thrombosis(0.50) · chronic renal failure kidney failure chronic(0.49) · esophageal cancer(0.44) · fatty liver(0.44) · adenoma colorectal neoplasms(0.44) · migraine(0.43) · inflammatory bowel disease nos inflammatory bowel diseases(0.43) · OTHER(0.40) · chromosome aberrations dna damage(0.40) · chronic progressive chorea huntington disease(0.40) · infertility male(0.38) · venous thromboembolism(0.36) · alzheimer s disease(0.36) · intima media thickness(0.33) · migraine with aura(0.33) · brain ischemia stroke(0.31) · infertility female(0.31) · stroke ischemic(0.30) · schizophrenia(0.30) · multiple myeloma(0.29) · atherosclerosis coronary(0.29) · schizophrenia bipolar disorder(0.27) · colorectal neoplasms(0.26) · body weight obesity(0.26) · cardiovascular disease(0.25) · stroke(0.24) · bladder neoplasm urinary bladder neoplasms(0.24) · stomach cancer(0.23) · carcinoma squamous cell esophageal neoplasms oesophageal neoplasm squamous cell carcinoma(0.23) · diabetes type 2(0.23) · arthritis rheumatoid(0.23) · myocardial ischemia(0.21) · CHEMDEPENDENCY(0.21) · alcohol(0.21) · bladder cancer(0.20) · kidney transplant complications(0.19) · neoplasms(0.19) · myocardial infarction(0.17) · arthritis juvenile rheumatoid chronic childhood arthritis(0.17) · myocardial infarct(0.16) · cerebral infarction(0.15) · kidney failure chronic(0.14) · lymphoma(0.14) · kidney diseases(0.14) · choroidal neovascularization macular degeneration(0.13) · cleft lip with cleft palate cleft lip without cleft palate(0.12) · restenosis(0.12) · type 2 diabetes(0.12) · carcinoma hepatocellular lcc liver cell carcinoma liver neoplasms(0.11) · INFECTION(0.11) · helicobacter infections(0.11) · depression(0.11) · leukemia lymphocytic chronic b cell(0.11) · carotid artery diseases(0.10) · cerebral palsy(0.09) · AGING(0.08) · longevity(0.08) · cardiovascular(0.08) · carcinoma squamous cell head and neck neoplasms squamous cell carcinoma(0.08) · polycystic ovary syndrome(0.08) · graft vs host disease(0.06) · dna damage(0.06) · autism(0.05) · atrial fibrillation(0.05) · lymphoma non hodgkin(0.05) · NORMALVARIATION(0.04) · normal variation(0.04) · crohn s disease ulcerative colitis(0.04) · dementia(0.04) · osteoporosis(0.04) · coronary disease(0.02) · cervical cancer(0.02)

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Relevant papers and external links:

PMID 18483342

OMIM 607093

PHARMGKB PA165110385
Evidence: PubMed ID:18580170Risk or phenotype-associated allele(s): C/C. Phenotype:Patients with a homozygous MTHFR 1298A>C mutation (n = 25) developed higher plasma homocysteine concentrations (median [interquartile range], 14.9 [10.0-26.4] microm) than wild-type or heterozygous patients (9.3 [7.5-15.5] microm; n = 115). The change in homocysteine after nitrous oxide anesthesia was tripled in homozygous patients compared with wild-type (5.6 microm [+60%] vs. 1.8 microm [+22%]). Study size: 140. Study population/ethnicity: healthy patients undergoing elective surgery. Type of association: GN.

PHARMGKB PA161145164
Evidence: Web Resource:External Link studied, associated with multiple phenotypes.

PHARMGKB PA164918206
Evidence: PubMed ID:15643524In a case control study of Asian gastric cancer (n=633), individuals with 6 variant alleles of three MTHFR common variants (i.e. C677T, A1298C and G1793A) were at increased risk for gastric cardia adenocarcinoma (OR =4.64, 95% CI =1.34-16.01) compared with those having 0-2 variants.

PHARMGKB PA165106617
Evidence: PubMed ID:16572443At 6 months methotrexate and folic acid therapy, of early rheumatoid arthritis patients with the MTHFR 1298AA genotype showed good improvement relative to combined CA and AA genotypes (OR 2.3), while 1298C allele carriers developed more adverse drug events (OR 2.5) (e.g. pneumonitis, gastrointestinal ADEs, skin and mucosal ADEs, and elevated liver enzyme levels). Patients with MTHFR 1298AA / 677CC diplotype showed greater clinical improvement.

PHARMGKB PA165106622
Evidence: PubMed ID:19016697In 330 patients who completed 3 months methotrexate treatment for psoriasis, no significant genotypic associations were found between clinical outcome (e.g. efficacy, toxicity) and 50 SNPs in pathway genes for methotrexate metabolism (ATIC, FPGS, GGH, MTHFR), including 47 common (>5% minor allele frequency) haplotype-tagging SNPs (r(2) > 0.8) plus 3 additional SNPs.

PMID 21302350

dbSNP: rs1801131 Genecard: MTHFR chromosome 1 SNPedia: rs1801131(C;C)

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★ **rs140701(A;G)** info:1.48 50.00% **Increased risk for anxiety disorders**

A study of patients with panic disorder or social anxiety disorder, both moderately heritable anxiety disorders, concluded that the rs140701(A) allele was associated with increased risk for both disorders. This SNP was actually part of a tightly linked haplotype A-A-G (for SNPs rs3794808, rs140701 and rs4583306, respectively) that had 1.7x increased risk for panic disorder (CI: 1.2-2.3).

Gene related topics:

PSYCH(24.57) · depression(24.57) · suicide(6.88) · obsessive compulsive disorder(5.82) · IMMUNE(5.28) · irritable bowel syndrome(5.28) · personality traits(4.75) · anxiety disorder(4.50) · REPRODUCTION(4.00) · depressive disorder major bipolar disorder(4.00) · sexual dysfunction physiological(4.00) · personality disorders(3.78) · depressive disorder major(3.72) · affective disorder(3.12) · anxiety related traits(3.00) · decision making(3.00) · psychoses(3.00) · personality(2.60) · panic disorder(2.19) · autism(2.13) · mood disorders(2.02) · CHEMDEPENDENCY(2.00) · OTHER(2.00) · PHARMACOGENOMIC(2.00) · UNKNOWN(2.00) · alcohol abuse smoking behavior(2.00) · alcoholism attention deficit hyperactivity disorder(2.00) · alcoholism recurrence(2.00) · antidepressant adverse effects(2.00) · anxiety(2.00) · auditory evoked potential(2.00) · bipolar and unipolar disorder(2.00) · eating disorder(2.00) · hallucinations(2.00) · harm avoidance(2.00) · impulse control disorder(2.00) · manic depressive illness(2.00) · personality traits illegal drug use(2.00) · suicidal behavior(1.92) · alcoholism(1.92) · NEUROLOGICAL(1.80) · cocaine dependence(1.80) · major depression(1.80) · migraine migraine with aura(1.80) · neuroticism(1.80) · major depressive disorder(1.73) · migraine(1.73) · substance related disorders(1.67) · bulimia(1.47) · attention deficit hyperactivity disorder(1.16) · adhd attention deficit hyperactivity disorder(1.00) · aggressive behavior(1.00) · alcohol related disorders(1.00) · bipolar disorder depression(1.00) · conduct disorder(1.00) · eating disorders(1.00) · sudden infant death(1.00) · anorexia nervosa(0.93) · CARDIOVASCULAR(0.80) · hypertension pulmonary(0.80) · major psychoses(0.80) · bipolar disorder(0.79) · schizophrenia(0.69) · alcohol abuse(0.68) · bipolar affective disorder(0.67) · fibromyalgia(0.67) · sids sudden infant death syndrome(0.67) · smoking behavior(0.66) · mood disorder(0.60) · psychosis(0.60) · heroin abuse(0.53) · epilepsy temporal lobe(0.43) · sleep disorders(0.36) · cognitive function(0.33) · migraine with aura(0.33) · syncope vasovagal(0.33) · DEVELOPMENTAL(0.27) · mental retardation(0.27) · adhd(0.26) · METABOLIC(0.23) · weight gain(0.23) · smoking(0.21) · tourette syndrome(0.21) · alcohol(0.21) · migraine disorders(0.17) · cognitive ability(0.11) · chronic obstructive pulmonary disease(0.07) · hearing loss(0.07) · AGING(0.04) · longevity(0.04)

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Relevant papers and external links:

PMID 18663369

dbSNP: rs140701 Genecard: SLC6A4 chromosome 17 SNPedia: rs140701(A;G)

★ rs2032652(T;-) info:0.00 47.41%

In silico and in vitro comparative analysis to select, validate and test SNPs for human identification.

MEGF10 association with schizophrenia.

FBXL21 association with schizophrenia in Irish family and case-control samples.

Association of Y chromosome haplogroup I with HIV progression, and HAART outcome.

Gene related topics:

hiv(1.00) · schizophrenia(1.00)

Relevant papers and external links:

PMID 18076761

PMID 18179784
PMID 18404645
PMID 19169712

dbSNP: rs2032652 Genecard: nan chromosome Y SNPedia: rs2032652(T;T)

★ rs10937823(C;C) good:0.00 73.14% **normal**

rs10937823 is a SNP associated with the gene SORCS2, variants of which may play a role in bipolar disorder. The allele most frequently occurring is C, and the variant is T. In the HapMap-CEU population, CC, CT, and TT genotype frequencies were 0.894, 0.097, and 0.009, respectively. However, in the HapMap-CHB population, CT was the most frequently expressed genotype; CC, CT, and TT genotype frequencies were 0.366, 0.439, and 0.195, respectively. In some sample populations, the TT genotype did not exist (TSI, MKK, LWK, ASW). [dbSNP]

The SORCS2 (sortillin-related VPS10 domain containing receptor 2) gene on chromosome 4p16.1 is found to be highly expressed in the mature human brain and kidney. High levels of expression are also seen in the brain during mouse development. [GeneCards] This gene family is responsible for trafficking lysosomal enzymes that are modified within the Golgi to their packaging vacuole. Sortillins have been found to facilitate neurotrophin binding to its receptor, which is necessary for mediating neuronal apoptosis, growth and survival. Given these roles, it has been proposed that alterations to the SORCS2 gene can lead to neuronal dysfunction.

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In 2008, a genome-wide association study indicated the SORCS2 gene in bipolar disorder. The study conducted by Baum et al. analyzed 461 affected individuals and 563 matched controls (from the National Institutes of Mental Health Genetics Initiative, all of European ancestry), and a replication sample of 772 affected individuals and 876 matched controls (affected individuals recruited from German hospital admissions, and controls recruited from a German census). The C allele of rs10937823 was found at a frequency of 0.949 in cases and 0.912 in controls in NIMH cohort (p=0.001); 0.954 in cases and 0.931 in controls in the German cohort (p=0.004). The resulting combined odds ratio was 1.67 between the German and NIMH cohorts. Table 3 Furthermore, with multi-locus analysis, the authors found that the highest risk of bipolar disorder was associated with presence of both rs10937823 and rs1170191, a SNP in diacylglycerol kinase eta (DGKH Rs1170191), suggesting that these SNPs have a combinatorial effect in conferring risk (p=1.2x10-8).

A Finnish bipolar family study in 2009 replicated the association between rs10937823 and bipolar disorder. The researchers genotyped the 26 SNPs most strongly associated SNPs as found by the Wellcome Trust Case Control Consortium, and the aforementioned study by Baum et al. in 723 individuals from 180 families. The study classified individuals as falling into diagnostic classes of bipolar type I disorder (cases = 214; controls = 509) or a broad mood spectrum disorder encompassing all types of bipolar disorder (cases = 298; controls = 495). In an opposite finding to that of Baum et al., the minor allele (T) frequency in the unaffected

individuals was 0.999; in cases, the frequency was 0.112. The lower frequency of the T allele of rs10937823 in cases versus controls was statistically significant (p=0.004187 using broad mood spectrum disorder; p=0.004703 using broad mood spectrum disorder).

In 2011, In a Japanese cohort of 736 individuals, rs10937823 was again found to be significantly associated with bipolar disorder by Takata et al. (363 cases, 370 controls; p=0.0175). However, the results showed that the risk allele (more commonly associated allele in cases) was T, not C. The minor allele frequency in the bipolar disorder sample was 0.275, versus 0.253 in the control sample. An odds ratio for this SNP was not reported.

In 2011, Cristoforou et al. identified an association between rs10937823 and bipolar disorder in a Scottish population (506 cases, 607 controls; p=0.031; OR not reported). Like the Japanese study by Takata et al., the minor allele (T) was found to be associated with bipolar disease. Similar observations of this “flip-flop” phenomenon where opposite alleles appear to confer risk have been reported in other genes, such as COMT gene and schizophrenia, and GSTO1 gene and age of onset in Alzheimer’s Disease. The authors suggest that such different results could be due to allelic heterogeneity, the effects of multiple loci, or varying linkage disequilibrium amongst the subjects, if the findings across the studies and populations are indeed correct.

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Gene related topics:

bipolar disorder(1.00) · survival(1.00) · brain(1.00) · OTHER(1.00) · schizophrenia(1.00)

Relevant papers and external links:

PMID 11165493
PMID 8187177
PMID 14985763
PMID 19002190
PMID 20351716
PMID 17486107
PMID 17486107
PMID 19308021
PMID 21507135
PMID 20351716
PMID 17273975

dbSNP: rs10937823 Genecard: SORCS2 chromosome 4 SNPedia: rs10937823(C;C)

★ rs659734(T;T) good:0.00 84.41% **common in complete genomics**

Genetic variation in the serotonin 2A receptor and suicidal ideation in a sample of 270 Irish high-density schizophrenia families.

Gene related topics:

PSYCH(3.00) · anorexia nervosa(3.00) · anorexia nervosa bulimia(3.00) · PHARMACOGENOMIC(2.00) · impulsive behavior(2.00) · olanzapine(2.00) · response to clozapine(2.00) · schizophrenia affective disorder(2.00) · schizophrenia(1.64) · bulimia(0.94) · major depression(0.80) · suicidal behavior(0.69) · major depressive disorder(0.68) · depression(0.67) · obsessive compulsive disorder(0.58) · neuroleptic malignant syndrome(0.57) · schizophrenia tardive dyskinesia(0.57) · suicide(0.56) · personality disorders(0.50) · personality traits(0.47) · cognitive function(0.33) · depressive disorder major(0.29) · autism(0.28) · adhd(0.26) · mood disorders(0.23) · panic disorder(0.21) · adhd attention deficit hyperactivity disorder(0.21) · attention deficit hyperactivity disorder(0.21) · tourette syndrome(0.21) · bipolar disorder(0.20) · personality(0.14) · CHEMDEPENDENCY(0.13) · heroin abuse(0.13) · NEUROLOGICAL(0.11) · migraine(0.11) · tardive dyskinesia(0.11) · smoking behavior(0.09) · CARDIOVASCULAR(0.05) · blood pressure determination(0.05) · alcohol abuse(0.04)

Relevant papers and external links:

PMID 18712714

dbSNP: rs659734 Genecard: HTR2A chromosome 13 SNPedia: rs659734(T;T)

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★ rs2630351(G;G) good:0.00 82.80% **common in complete genomics**

Gene related topics:

NEUROLOGICAL(3.79) · tardive dyskinesia(3.79) · essential tremor(2.88) · PSYCH(2.37) · schizophrenia(2.37) · CHEMDEPENDENCY(2.00) · UNKNOWN(2.00) · akathisia drug induced(2.00) · cocaine abuse(2.00) · cocaine related disorders(0.67) · schizophrenia tardive dyskinesia(0.57) · tourette syndrome(0.47) · alcohol dependence(0.22) · parkinson s disease(0.14) · personality disorders(0.12) · bipolar disorder(0.10) · obsessive compulsive disorder(0.06) · adhd attention deficit hyperactivity disorder(0.05) · personality traits(0.05) · alcohol abuse(0.04) · smoking behavior(0.04)

Relevant papers and external links:

dbSNP: rs2630351 Genecard: DRD3 chromosome 3 SNPedia: rs2630351(G;G)

★ rs740602(G;G) good:0.00 88.38% **common in complete genomics**

Gene related topics:

UNKNOWN(6.00) · digeorge syndrome pharyngeal pouch syndrome(6.00) · PSYCH(5.72) · schizophrenia(5.72) · CANCER(3.00) · neoplasms pain(3.00) · fibromyalgia(2.67) · NEUROLOGICAL(2.00) · mamographic density(2.00) · pain temporomandibular joint disorders(2.00) · psychosis(1.67) · obsessive compulsive disorder(1.31) · CHEMDEPENDENCY(1.07) · substance related disorders(1.07) · panic disorder(1.03) · adhd attention deficit hyperactivity disorder(1.00) · eating disorders(1.00) · pain(0.94) · breast cancer(0.83) · marijuana abuse(0.67) · mood disorders(0.62) · parkinson s disease(0.62) · DEVELOPMENTAL(0.60) · leiomyoma uterine neoplasms(0.60) · mental retardation(0.60) · schizophrenia bipolar disorder(0.60) · OTHER(0.57) · sleep deprivation(0.57) · bipolar disorder(0.50) · depression(0.50) · fractures bone(0.50) · personality(0.38) · mammographic density(0.36) · personality traits(0.33) · heroin abuse(0.30) · alcoholism(0.29) · adhd(0.26) · cognitive ability(0.25) · heroin dependence(0.25) · bulimia(0.24) · endometrial cancer(0.23) · smoking(0.21) · anorexia nervosa(0.15) · suicide(0.14) · liver cancer(0.13) · tobacco use disorder(0.11) · narcolepsy(0.11) · METABOLIC(0.10) · weight gain(0.10) · smoking behavior(0.09) · endometrial neoplasms(0.07) · attention deficit hyperactivity disorder(0.05) · IMMUNE(0.05) · vitiligo(0.05) · autism(0.03) · REPRODUCTION(0.02) · endometriosis(0.02)

Relevant papers and external links:

dbSNP: rs740602 Genecard: COMT chromosome 22 SNPedia: rs740602(G;G)

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★ rs6280(T;T) info:0.00 26.38% **normal**

rs6280, also known as Ser9Gly, is a SNP in the dopamine receptor D3 DRD3 gene. The rs6280(C) allele encodes a glycine, and the (T) allele encodes a serine (in dbSNP orientation).

In a study of 88 patients being treated for schizophrenia with olanzapine, those who were rs6280(C;C) homozygotes had greater positive symptom remission (endpoint rating of minimal or none on all PANSS clinical response positive items, 39.1%), as compared with (C;T) or (T;T) genotypes (13.8%; p = 0.033).

Ser9Gly has been implicated in executive function in some studies, but the results are conflicting.
Gly/Gly carriers showed significantly (p = 0.002) poorer performance than Ser/Ser carriers on executive functioning tasks in a somewhat small Caucasian sample (84 patients with first-episode psychosis and 85 controls).
Gly/Ser heterozygotes had 23% more preservative errors on the WCST compared to Ser/Ser homozygotes in a small (216) healthy Han Chinese sample (p = 0.009). Differences between homozygotes were not statistically significant.
No association between WCST scores and Ser9Gly was found in 138 schizophrenic patients.

Associated in a family association study and pooled sample of 2,037 with nicotine dependence in Americans of European descent.

Preliminary evidence for an association between a dopamine D3 receptor gene variant and obsessive-compulsive personality disorder in patients with major depression. DRD3 polymorphism for an individual with Gly/Gly (C;C) genotype is 2.4 (P = 0.017) times more likely to be diagnosed with OCPD. Male gender was also found to be a significant predictor of OCPD diagnosis (OR = 2.82, P = 0.001). DRD3 may contribute to the development of OCPD. This association was tested using two independent groups of individuals with a history of depression, from a clinical sample (n = 149) and a family study (n = 213).

Gene related topics:

NEUROLOGICAL(3.79) · tardive dyskinesia(3.79) · essential tremor(2.88) · PSYCH(2.37) · schizophrenia(2.37) · CHEMDEPENDENCY(2.00) · UNKNOWN(2.00) · akathisia drug induced(2.00) · cocaine abuse(2.00) · personality(1.00) · olanzapine(1.00) · nicotine(1.00) · major depression(1.00) · psychosis(1.00) · depression(1.00) · nicotine dependence(1.00) · cocaine related disorders(0.67) · schizophrenia tardive dyskinesia(0.57) · tourette syndrome(0.47) · alcohol dependence(0.22) · parkinson s disease(0.14) · personality disorders(0.12) · bipolar disorder(0.10) · obsessive compulsive disorder(0.06) · adhd attention deficit hyperactivity disorder(0.05) · personality traits(0.05) · alcohol abuse(0.04) · smoking behavior(0.04)

Relevant papers and external links:

PMID 18320559

PMID 18351593

PMID 2186374

PMID 15785860

PMID 18348205

PMID 16583407

PHARMGKB PA165111549
Evidence: PubMed ID:20029384Risk or phenotype-associated allele: Phenotype: This meta-analysis showed no difference in clozipine response between the Ser and Gly allele. Study size: 758 Study population/ethnicity: Patients with Schizophrenia Significance metric(s): OR = 0.82, 95% confidence interval (CI): 0.65-1.04; p = 0.1 Type of association: PD

PHARMGKB PA162316713
Evidence: PubMed ID:18320559A study on 88 olanzapine-treated patients with schizophrenia found that the Gly/gly genotype was significantly associated with greater positive symptom improvement.

PHARMGKB PA164807597
Evidence: PubMed ID:19396436This variant in the DRD3 gene was significantly associated with the therapeutic efficacy of pramipexole in Chinese patients with Parkinson's disease in a study of 30 patients.

PHARMGKB PA165111370
Evidence: PubMed ID:19997080Risk or phenotype-associated allele: C Phenotype: Carriers of the C variant (Gly) of DRD3:Ser9Gly had greater reductions in Autism Treatment Evaluation Checklist (ATEC) scores, indicating improved symptoms and response to risperidone, than TT homozygotes. Study size: 45 Study population/ethnicity: Children with Autism receiving risperidone Significance metric(s): p = 0.012 Type of association: PD

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PHARMGKB PA165110867
Evidence: PubMed ID:16809426Risk or phenotype-associated allele: C. Phenotype: A study comparing 276 patients with essential tremor and 184 normal controls confirmed the association of the Gly-9 variant in the DRD-3 gene with risk and age-at-onset of essential tremor. Study size: 276. Study population/ethnicity: French.

OMIM 126451

dbSNP: rs6280 Genecard: DRD3 chromosome 3 SNPedia: rs6280(T;T)

★ rs1355095(A;A) info:0.00 77.72% **normal**

rs1355095 is associated with schizophrenia

Gene related topics:

schizophrenia(1.00)

Relevant papers and external links:

PMID 18718982

dbSNP: rs1355095 Genecard: MEIKIN chromosome 5 SNPedia: rs1355095(A;A)

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★ rs4648317(C;C) good:0.00 60.83% **normal**

rs4648317, a SNP in the dopamine D2 receptor DRD2 gene, has been linked to higher rates of smoking and higher nicotine dependence scores, based on a study of ~220 adolescents. The risk allele rs4648317 (T).

Gene related topics:

CHEMDEPENDENCY(6.04) · alcoholism(6.04) · alcoholism substance related disorders(4.00) · PSYCH(2.30) · schizophrenia(2.30) · METABOLIC(2.00) · NEUROLOGICAL(2.00) · hyperprolactinaemia hyperprolactinemia(2.00) · nervous system diseases(2.00) · substance withdrawal syndrome(2.00) · substance withdrawal syndrome tobacco use disorder(2.00) · tic combined vocal and multiple motor tourette syndrome(2.00) · smoking behavior(1.74) · UNKNOWN(1.29) · neuroleptic malignant syndrome(1.29) · heroin dependence(1.00) · methamphetamine abuse(1.00) · nicotine(1.00) · nicotine dependence(1.00) · tardive dyskinesia(0.95) · heroin abuse(0.83) · cocaine dependence(0.80) · cocaine related disorders(0.67)

· delirium(0.57) · impulsivity(0.57) · alcohol abuse(0.52) · tobacco use disorder(0.44) · adhd(0.40) · mood disorders(0.40) · parkinson s disease(0.40) · smoking(0.33) · alcohol(0.32) · mood disorder(0.27) · substance related disorders(0.27) · CARDIOVASCULAR(0.25) · atrial natriuretic factor(0.25) · alcohol dependence(0.22) · personality traits(0.21) · tourette syndrome(0.21) · dyslexia(0.19) · migraine disorders(0.17) · adhd attention deficit hyperactivity disorder(0.15) · personality(0.14) · personality disorders(0.12) · depressive disorder major(0.10) · bipolar disorder(0.07) · attention deficit hyperactivity disorder(0.05) · autism(0.03)

Relevant papers and external links:

PMID 18434921

dbSNP: rs4648317 Genecard: DRD2 chromosome 11 SNPedia: rs4648317(C;C)

★ rs12273539(C;C) good:0.00 71.38% **common in complete genomics**

Gene related topics:

PSYCH(2.33) · depression(2.33) · NEUROLOGICAL(2.00) · affective psychoses(2.00) · alzheimer disease amnesia(2.00) · bipolar disorder(1.66) · CHEMDEPENDENCY(1.00) · amphetamine related disorders(1.00) · schizophrenia(0.94) · major depressive disorder(0.68) · alzheimer s disease(0.59) · METABOLIC(0.56) · weight(0.56) · personality(0.55) · obsessive compulsive disorder(0.40) · UNKNOWN(0.36) · dyskinesia drug induced(0.36) · cognitive function(0.33) · parkinsons disease(0.29) · DEVELOPMENTAL(0.27) · IMMUNE(0.27) · dermatitis atopic(0.27) · mental retardation(0.27) · huntington s disease(0.26) · adhd attention deficit hyperactivity disorder(0.21) · anorexia nervosa(0.15) · autism(0.12) · body weight obesity(0.11) · cognitive ability(0.11) · panic disorder(0.08) · migraine disorders(0.08) · attention deficit hyperactivity disorder(0.05) · personality traits(0.05) · smoking(0.05) · epilepsy(0.04) · smoking behavior(0.04) · suicide(0.04)

Relevant papers and external links:

PHARMGKB PA164857049
Evidence: PubMed ID:19414708This intronic variant (T/C) in the BDNF gene was associated with major depressive disorder in a study of 264 controls and 272 Mexican Americans with major depressive disorder. (OR= 1.75; p value=<0.001; risk allele=T)

dbSNP: rs12273539 Genecard: BDNF chromosome 11 SNPedia: rs12273539(C;C)

★ rs2270641(T;T) good:0.00 56.82% **normal**

rs2270641 is a SNP in the vesicular monoamine transporter SLC18A1 gene, encoding a Thr4Pro substitution. In dbSNP orientation, the (G) allele is associated with the Proline.

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A study of 62 patients with schizophrenia concluded that the frequency of rs2270641(G;G) homozygotes was significantly higher. The reported odds ratio was 3.74 (CI: 1.7-8.2, p=0.0006) in this population of European descent.

Note: another SNP, rs56575139, marks the same genomic location as rs2270641.

Gene related topics:

schizophrenia(1.00)

Relevant papers and external links:

PMID 18451639

dbSNP: rs2270641 Genecard: SLC18A1 chromosome 8 SNPedia: rs2270641(T;T)

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★ rs11178997(T;T) info:0.00 72.05% **common for Caucasians on the 23andme platform**

common for Caucasians on the 23andme platform

rs4570625 and rs11178997 in TPH2's regulatory region display preferential transmission

paper Association with and bipolar disorder in a Northern Swedish, Isolated Population. 182 patients and 364 unrelated control individuals. P = .001

rs11178997 significantly reduced TPH2 transcriptional activity by 22% and 7% in cell lines might have implications for the development and function of the serotonergic system in the brain.

paper Carriers of the A-Allele of rs11178997 showed a decreased cortisol and ACTH stimulation. might be crucial factors for major depression

pdf paper associated with bipolar disorder

Minor allele yielded odds ratio of 1.5 (CI:1.2-1.9) for increased risk for bipolar disorder in a study of 883 Russian patients.

Transmission disequilibrium of polymorphic variants in the tryptophan hydroxylase-2 gene in attention-deficit/hyperactivity disorder.

Association of brain-specific tryptophan hydroxylase, TPH2, with unipolar and bipolar disorder in a Northern Swedish, isolated population.

Tryptophan hydroxylase 2 gene and alcohol use among college students.

Investigation of the tryptophan hydroxylase 2 gene in bipolar I disorder in the Romanian population.

Alternative splicing and extensive RNA editing of human TPH2 transcripts.

Pharmacogenetics of antidepressant response.

Common variants in the TPH2 promoter confer susceptibility to paranoid schizophrenia.

Gene related topics:

OTHER(1.00) · chronic fatigue syndrome(1.00) · bipolar disorder(1.00) · brain(1.00) · alcohol(1.00) · schizophrenia(1.00) · major depression(1.00) · PSYCH(0.56) · suicide(0.56) · METABOLIC(0.45) · waist circumference(0.45) · autism(0.17) · adhd attention deficit hyperactivity disorder(0.15) · depression(0.15) · adhd(0.15) · panic disorder(0.08) · NEUROLOGICAL(0.08) · migraine disorders(0.08) · attention deficit hyperactivity disorder(0.05) · personality traits(0.05) · depressive disorder major(0.05)

Relevant papers and external links:

PMID 17568567

PMID 17905754

OMIM 143465

OMIM 607478

OMIM 125480

OMIM 613003

PMID 16116490

PMID 17015812

PMID 18782386

PMID 18797398

PMID 20126463

PMID 21172166

PMID 22392150

dbSNP: rs11178997 Genecard: TPH2 chromosome 12 SNPedia: rs11178997(T;T)

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★ rs8192466(C;C) good:0.00 99.84% **common**

Gene related topics:

PSYCH(2.33) · depression(2.33) · NEUROLOGICAL(2.00) · affective psychoses(2.00) · alzheimer disease amnesia(2.00) · bipolar disorder(1.66) · CHEMDEPENDENCY(1.00) · amphetamine related disorders(1.00) · schizophrenia(0.94) · major depressive disorder(0.68) · alzheimer s disease(0.59) · METABOLIC(0.56) · weight(0.56) · personality(0.55) · obsessive compulsive disorder(0.40) · UNKNOWN(0.36) · dyskinesia drug induced(0.36) · cognitive function(0.33) · parkinsons disease(0.29) · DEVELOPMENTAL(0.27) · IMMUNE(0.27) · dermatitis atopic(0.27) · mental retardation(0.27) · huntington s disease(0.26) · adhd attention deficit hyperactivity disorder(0.21) · anorexia nervosa(0.15) · autism(0.12) · body weight obesity(0.11) · cognitive ability(0.11) · panic disorder(0.08) · migraine disorders(0.08) · attention deficit

hyperactivity disorder(0.05) · personality traits(0.05) · smoking(0.05) · epilepsy(0.04) · smoking behavior(0.04) · suicide(0.04)

Relevant papers and external links:

OMIM 113505

dbSNP: rs8192466 Genecard: BDNF chromosome 11 SNPedia: rs8192466(C;C)

★ rs4606(C;G) info:0.00 45.43% **complex; possible association with anxiety related behaviours**

In mice, the genetic locus best correlated to anxiety-related behaviour contains the 'regulator of G protein signaling 2' gene . In humans, SNPs in the equivalent RGS2 gene have now been studied to see if they are correlated to anxiety related disorders.

In the first part of one study, 119 families including children underwent standard lab-based behavioural assessments of behavioural inhibition, defined as a heritable temperamental profile characterized by a tendency to be shy, avoident, and behaviourally restrained in situations that are novel or unfamiliar. Along with some other RGS2 SNPs, carriers of a rs4606(G) allele were 3 fold more likely to exhibit behavioural inhibition (CI: 1.31-6.84, p = 0.0026).

In the second part of this study, 744 college undergraduates (228 men, 516 women) who had been genotyped completed a personality profile known as the NEO-E (introversion) association test. Consistent with the earlier results, the same RGS2 alleles associated with behavioural inhibition were significantly ($p < 0.05$) associated with introversion (but not neuroticism), including rs4606(G), rs6428136(G), and rs10801152(T).

In the third part of this study, 55 female undergraduates were studied by fMRI (functional MRI) emotional processing tests. Carriers of SNPs rs4606(G) or rs10801152(T) showed increased insular cortex activation, a reflection of anxiety, in these tests.

Based on these results, the authors predict that social anxiety disorder is the most likely anxiety disorder to be associated with SNPs in the RGS2 gene such as rs4606.

SNPs in the RGS2 gene, including rs4606, show association with childhood temperament, adult personality, and brain function.

each rs4606(C) allele was associated with a 2x ($p = .026$) increased risk of generalized anxiety disorder.

173 patients with panic disorder (and 173 matched controls) of German descent analyzed, leading to the conclusion that rs4606(G) carriers were at ~2x increased risk for this disorder. Note that the (G) allele appears to be the minor (rarer) allele in this study.

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Note: given the conflicting reports over whether the (C) or (G) allele is implicated in anxiety-related disorders, Dr. Jordan Smoller was contacted to verify that the orientation was unambiguously reported in the various publications. He has confirmed that the reports truly vary in which allele is considered the risk allele; this may be an example of the "flip-flop" phenomenon .

rs4606 has also been reported to be associated with the development of Parkinson's like symptoms in schizophrenia patients treated with various drugs, as follows:

A replication study was performed in which extrapyramidal symptoms (EPS) were rated in 184 US patients with schizophrenia. This group (115 African Americans, 69 Caucasian) was treated for at least a month with typical antipsychotic drugs (n=45), risperidone (n=46), olanzapine (n=50) or clozapine (n=43). The minor (G) allele showed a protective effect against antipsychotic-induced parkinsonism (AIP), with an odds ratio for AIP among rs4606(G) carriers of 0.23 (CI: 0.10-0.54, p=0.001) for the overall sample.

blog discussion

121 consecutively hospitalized, psychotic patients with Diagnostic and Statistical Manual of Mental Disorder-IV schizophrenia receiving treatment with typical antipsychotic medication (n=72) or typical antipsychotic drugs and risperidone (n=49) for at least 2 weeks were studied. After correction for multiple testing the only RGS2 SNP associated with development or worsening of parkinsonian symptoms was rs4606 (p=0.002).

rs4606 modifies risk of postdisaster and lifetime post-traumatic stress disorder symptoms under conditions of high stressor exposure

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Gene related topics:

anxiety(5.00) · personality(1.00) · neuroticism(1.00) · stress(1.00) · brain(1.00) · olanzapine(1.00) · mental disorder(1.00) · OTHER(1.00) · schizophrenia(1.00) · temperament(1.00) · anxiety disorder(1.00) · CARDIOVASCULAR(0.80) · receptors tumor necrosis factor(0.80) · HEMATOLOGICAL(0.20) · blood coagulation factors(0.20) · PSYCH(0.08) · panic disorder(0.08) · c reactive protein(0.06)

Relevant papers and external links:

PMID 15489855
PMID 18316676
PMID 18316676
PMID 18833580
PMID 16736243
PMID 17273975
PMID 18347610
PMID 17558307
PMID 19162436
PHARMGKB PA164738462

Evidence: PubMed ID:18347610This variant is located in the 3'-regulatory region of RGS2, and is known to influence RGS2 mRNA levels and protein expression. It has been shown to be associated antipsychotic-induced parkinsonism (AIP) with possible protective effect of the minor G allele of rs4606.

dbSNP: rs4606 Genecard: RGS2 chromosome 1 SNPedia: rs4606(C;G)

★ rs11868035(G;G) info:0.00 23.78% **normal; parkinson's disease (you have the risk allele G)**

rs11868035 is one of several SNPs associated with the SREBF1 gene that show a modest association with type-2 diabetes. A study of ~2,000 Caucasian patients (and 10,000+ controls) led to an odds ratio of 1.19 (CI: 1.07-1.33, p=0.002) for the minor (risk) allele, rs11868035(A), in the orientation as in dbSNP.

type-2 diabetes rs2297508(C) and rs11868035(C)

This SNP rs11868035 and rs1057217 are associated with increased risk of schizophrenia in German and Scandinavian samples.

This SNP and rs6812193 are reported to affect risk of Parkinson's disease. plos

Polymorphisms in the gene encoding sterol regulatory element-binding factor-1c are associated with type 2 diabetes.

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Established associations:

parkinson's disease **you have 2 copies of the risk allele G**

(risk allele=G, odds ratio/beta 1.18 [1.11-1.25] with pval 6E-8, pubmedid=21738487)

Gene related topics:

schizophrenia(1.00) · type 2 diabetes(1.00) · METABOLIC(0.15) · hypercholesterolemia(0.15)

Relevant papers and external links:

PMID 18192539
PMID 18692268
PMID 18936756
PMID 21738487
PHARMGKB PA162355925

Evidence: PubMed ID:18936756This SNP in the SREBF1 gene was strongly associated with schizophrenia in German, Danish and Norwegian samples.

PMID 17019602

dbSNP: rs11868035 GWAS Catalog: rs11868035 Genecard: SREBF1 chromosome 17

SNPedia: rs11868035(G;G)

★ rs17101921(G;G) good:0.00 88.68% **common in complete genomics**

A very large (ultimately over 7,000 cases spanning multiple European Caucasians) study concluded that rs17101921 showed evidence for association with schizophrenia, with an odds ratio of 1.17 (CI: 1.06-1.29, p=0.0009).

Gene related topics:

schizophrenia(1.00)

Relevant papers and external links:

PMID 18813210

dbSNP: rs17101921 Genecard: nan chromosome 10 SNPedia: rs17101921(G;G)

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★ rs4846051(A;A) good:0.00 81.53% **common in complete genomics**

Gene related topics:

METABOLIC(14.69) · hyperhomocysteinemia(14.69) · DEVELOPMENTAL(14.49) · neural tube defects(14.49) · down syndrome(11.36) · CARDIOVASCULAR(10.00) · coronary artery disease hyperhomocysteinemia(10.00) · folic acid deficiency(7.00) · homocysteine(6.92) · UNKNOWN(5.00) · chronic renal failure hyperhomocysteinemia kidney failure chronic(5.00) · coronary disease coronary heart disease hyperhomocysteinemia(5.00) · CANCER(4.00) · adenoma colorectal neoplasms neoplasm recurrence local(4.00) · hyperhomocysteinemia retinal vein occlusion(4.00) · spinal dysraphism(3.85) · colorectal cancer(3.74) · arteriosclerosis(3.57) · apoplexy stroke(3.12) · apoplexy brain ischemia hyperhomocysteinemia stroke(3.00) · cardiovascular diseases hyperhomocysteinemia(3.00) · congenital heart defects heart defects congenital(3.00) · diabetes mellitus type ii diabetes mellitus type 2 hyperhomocysteinemia(3.00) · hearing loss sudden(3.00) · hyperhomocysteinemia postoperative complications(3.00) · hyperhomocystinemia(3.00) · vascular diseases(3.00) · cardiovascular diseases(2.93)

· apoplexy brain ischemia stroke(2.61) · REPRODUCTION(2.61) · pregnancy loss(2.61) · abortion spontaneous(2.58) · leukemia lymphocytic acute l1 precursor cell lymphoblastic leukemia lymphoma(2.58) · pregnancy complications(2.40) · precursor cell lymphoblastic leukemia lymphoma(2.16) · colonic neoplasms(2.13) · IMMUNE(2.00) · NEUROLOGICAL(2.00) · VISION(2.00) · abortion habitual hyperhomocysteinemia(2.00) · abortion habitual pregnancy complications hematologic thrombophilia(2.00) · abruptio placentae(2.00) · activated protein c resistance hyperhomocysteinemia thrombophilia venous thrombosis(2.00) · acute lymphocytic leukemia hyperhomocysteinemia precursor cell lymphoblastic leukemia lymphoma(2.00) · atherosclerosis thrombosis(2.00) · cardiovascular diseases chronic renal failure hyperhomocysteinemia kidney failure chronic(2.00) · cerebrovascular disease ischemic(2.00) · chronic ulcerative colitis colitis ulcerative folic acid deficiency hyperhomocysteinemia(2.00) · cleft lip cleft palate syndrome(2.00) · epilepsy hyperhomocysteinemia(2.00) · glaucoma angle closure glaucoma open angle(2.00) · heart defects congenital(2.00) · hyperhomocysteinemia hyperlipidemias(2.00) · hyperhomocysteinemia hypertension(2.00) · hyperhomocysteinemia pre eclampsia(2.00) · retinal artery occlusion retinal vein occlusion(2.00) · hyperhomocysteinemia venous thrombosis(1.80) · venous thrombosis(1.78) · abortion habitual thrombophilia(1.71) · stomach neoplasms(1.71) · HEMATOLOGICAL(1.58) · thrombophilia(1.58) · thrombosis(1.44) · PHARMACOGENOMIC(1.39) · methotrexate toxicity(1.39) · thromboembolism venous(1.35) · anemia sickle cell sickle cell anemia(1.29) · cleft lip cleft palate(1.29) · adenocarcinoma stomach neoplasms(1.25) · acute lymphocytic leukemia precursor cell lymphoblastic leukemia lymphoma(1.25) · diabetes mellitus type ii diabetes mellitus type 2 diabetic nephropathies diabetic nephropathy(1.12) · coronary disease coronary heart disease(1.10) · pre eclampsia(1.05) · coronary artery disease(1.04) · antiphospholipid syndrome thrombophilia thrombosis(1.00) · brain ischemia(1.00) · brain neoplasms glioma meningeal neoplasms meningioma(1.00) · carcinoma squamous cell skin neoplasms squamous cell carcinoma(1.00) · cervical intraepithelial neoplasia cervical neoplasm papillomavirus infections uterine cervical neoplasms(1.00) · migraine with aura migraine without aura(1.00) · thrombophilia and vascular disease(1.00) · breast cancer(0.93) · migraine disorders(0.92) · thrombosis deep vein(0.86) · RENAL(0.84) · diabetic nephropathy(0.84) · pregnancy loss recurrent(0.83) · pre eclampsia thrombophilia(0.82) · esophageal cancer stomach cancer(0.80) · abortion habitual(0.75) · preeclampsia(0.73) · arthritis rheumatoid rheumatoid arthritis(0.71) · PSYCH(0.67) · behcet syndrome venous thrombosis(0.67) · brain ischemia stroke thrombophilia(0.67) · cerebrovascular disorders(0.67) · congenital abnormalities(0.67) · dementia vascular(0.67) · diabetic nephropathies diabetic nephropathy(0.67) · aortic aneurysm abdominal(0.59) · insulin resistance polycystic ovarian syndrome polycystic ovary syndrome(0.57) · heart anomalies congenital(0.53) · leukemia(0.52) · atherosclerosis(0.51) · hypertension(0.51) · cardiovascular risk(0.50) · cerebrovascular disease(0.50) · colonic neoplasms rectal neoplasms(0.50) · thrombosis venous thrombosis(0.50) · chronic renal failure kidney failure chronic(0.49) · esophageal cancer(0.44) · fatty liver(0.44) · adenoma colorectal neoplasms(0.44) · migraine(0.43) · inflammatory bowel disease nos inflammatory bowel diseases(0.43) · OTHER(0.40) · chromosome aberrations dna damage(0.40) · chronic progressive chorea huntington disease(0.40) · infertility male(0.38) · venous thromboembolism(0.36) · alzheimer s disease(0.36) · intima media thickness(0.33) · migraine with aura(0.33) · brain ischemia stroke(0.31) · infertility female(0.31) · stroke ischemic(0.30) · schizophrenia(0.30) · multiple myeloma(0.29) · atherosclerosis coronary(0.29) · schizophrenia bipolar disorder(0.27) · colorectal neoplasms(0.26) · body weight obesity(0.26) · cardiovascular disease(0.25) · stroke(0.24) · bladder neoplasm urinary bladder neoplasms(0.24) · stomach cancer(0.23) · carcinoma squamous cell esophageal neoplasms oesophageal neoplasm squamous cell carcinoma(0.23) · diabetes type 2(0.23) · arthritis rheumatoid(0.23) · myocardial ischemia(0.21) · CHEMDEPENDENCY(0.21) · alcohol(0.21) · bladder cancer(0.20) · kidney transplant complications(0.19) · neoplasms(0.19) · myocardial infarction(0.17) · arthritis juvenile rheumatoid chronic childhood arthritis(0.17) · myocardial infarct(0.16) · cerebral infarction(0.15) · kidney failure chronic(0.14) · lymphoma(0.14) · kidney diseases(0.14) · choroidal neovascularization macular degeneration(0.13) · cleft lip with cleft palate cleft lip without cleft palate(0.12) · restenosis(0.12) · type 2 diabetes(0.12) · carcinoma hepatocellular lcc liver cell carcinoma liver neoplasms(0.11) · INFECTION(0.11) · helicobacter infections(0.11) · depression(0.11) · leukemia lymphocytic chronic b cell(0.11) · carotid artery diseases(0.10) · cerebral palsy(0.09) · AGING(0.08) · longevity(0.08) · cardiovascular(0.08) · carcinoma squamous cell head and neck neoplasms squamous cell carcinoma(0.08) · polycystic ovary syndrome(0.08) · graft vs host disease(0.06) · dna damage(0.06) · autism(0.05) · atrial fibrillation(0.05) · lymphoma non hodgkin(0.05) · NORMALVARIATION(0.04) · normal variation(0.04) · crohn s disease ulcerative colitis(0.04) · dementia(0.04) · osteoporosis(0.04) · coronary disease(0.02) · cervical cancer(0.02)

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Relevant papers and external links:

PHARMGKB PA164918207

Evidence: PubMed ID:16439441The C allele of this variant was associated with increased risk of toxicity in African American Rheumatoid Arthritis patients receiving methotrexate.

dbSNP: rs4846051 Genecard: MTHFR chromosome 1 SNPedia: rs4846051(A;A)

★ rs25533(T;T) good:0.00 85.95% **common in complete genomics**

Gene related topics:

PSYCH(24.57) · depression(24.57) · suicide(6.88) · obsessive compulsive disorder(5.82) · IMMUNE(5.28) · irritable bowel syndrome(5.28) · personality traits(4.75) · anxiety disorder(4.50) · REPRODUCTION(4.00) · depressive disorder major bipolar disorder(4.00) · sexual dysfunction physiological(4.00) · personality disorders(3.78) · depressive disorder major(3.72) · affective disorder(3.12) · anxiety related traits(3.00) · decision making(3.00) · psychoses(3.00) · personality(2.60) · panic disorder(2.19) · autism(2.13) · mood disorders(2.02) · CHEMDEPENDENCY(2.00) · OTHER(2.00) · PHARMACOGENOMIC(2.00) · UNKNOWN(2.00) · alcohol abuse smoking behavior(2.00) · alcoholism attention deficit hyperactivity disorder(2.00) · alcoholism recurrence(2.00) · antidepressant adverse effects(2.00) · anxiety(2.00) · auditory evoked potential(2.00) · bipolar and unipolar disorder(2.00) · eating disorder(2.00) · hallucinations(2.00) · harm avoidance(2.00) · impulse control disorder(2.00) · manic depressive illness(2.00) · personality traits illegal drug use(2.00) · suicidal behavior(1.92) · alcoholism(1.92) · NEUROLOGICAL(1.80) · cocaine dependence(1.80) · major depression(1.80) · migraine migraine with aura(1.80) · neuroticism(1.80) · major depressive disorder(1.73) · migraine(1.73) · substance related disorders(1.67) · bulimia(1.47) · attention deficit hyperactivity disorder(1.16) · adhd attention deficit hyperactivity disorder(1.00) · aggressive behavior(1.00) · alcohol related disorders(1.00) · bipolar disorder depression(1.00) · conduct disorder(1.00) · eating disorders(1.00) · sudden infant death(1.00) · anorexia nervosa(0.93) · CARDIOVASCULAR(0.80) · hypertension pulmonary(0.80) · major psychoses(0.80) · bipolar disorder(0.79) · schizophrenia(0.69) · alcohol abuse(0.68) · bipolar affective disorder(0.67) · fibromyalgia(0.67) · sids sudden infant death syndrome(0.67) · smoking behavior(0.66) · mood disorder(0.60) · psychosis(0.60) · heroin abuse(0.53) · epilepsy temporal lobe(0.43) · sleep disorders(0.36) · cognitive function(0.33) · migraine with aura(0.33) · syncope vasovagal(0.33) · DEVELOPMENTAL(0.27) · mental retardation(0.27) · adhd(0.26) · METABOLIC(0.23) · weight gain(0.23) · smoking(0.21) · tourette syndrome(0.21) · alcohol(0.21) · migraine disorders(0.17) · cognitive ability(0.11) · chronic obstructive pulmonary disease(0.07) · hearing loss(0.07) · AGING(0.04) · longevity(0.04)

Relevant papers and external links:

dbSNP: rs25533 Genecard: SLC6A4 chromosome 17 SNPedia: rs25533(T;T)

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★ rs45590836(G;G) good:0.04 **common in complete genomics**

Gene related topics:

METABOLIC(14.69) · hyperhomocysteinemia(14.69) · DEVELOPMENTAL(14.49) · neural tube defects(14.49) · down syndrome(11.36) · CARDIOVASCULAR(10.00) · coronary artery disease hyperhomocysteinemia(10.00) · folic acid deficiency(7.00) · homocysteine(6.92) · UNKNOWN(5.00) · chronic renal failure hyperhomocysteinemia kidney failure chronic(5.00) · coronary disease coronary heart disease hyperhomocysteinemia(5.00) · CANCER(4.00) · adenoma colorectal neoplasms neoplasm recurrence local(4.00) · hyperhomocysteinemia retinal vein occlusion(4.00) · spinal dysraphism(3.85) · colorectal cancer(3.74) · arteriosclerosis(3.57) · apoplexy stroke(3.12) · apoplexy brain ischemia hyperhomocysteinemia stroke(3.00) · cardiovascular diseases hyperhomocysteinemia(3.00) · congenital heart defects heart defects congenital(3.00) · diabetes mellitus type ii diabetes mellitus type 2

hyperhomocysteinemia(3.00) · hearing loss sudden(3.00) · hyperhomocysteinemia postoperative complications(3.00) · hyperhomocystinemia(3.00) · vascular diseases(3.00) · cardiovascular diseases(2.93) · apoplexy brain ischemia stroke(2.61) · REPRODUCTION(2.61) · pregnancy loss(2.61) · abortion spontaneous(2.58) · leukemia lymphocytic acute l1 precursor cell lymphoblastic leukemia lymphoma(2.58) · pregnancy complications(2.40) · precursor cell lymphoblastic leukemia lymphoma(2.16) · colonic neoplasms(2.13) · IMMUNE(2.00) · NEUROLOGICAL(2.00) · VISION(2.00) · abortion habitual hyperhomocysteinemia(2.00) · abortion habitual pregnancy complications hematologic thrombophilia(2.00) · abruptio placentae(2.00) · activated protein c resistance hyperhomocysteinemia thrombophilia venous thrombosis(2.00) · acute lymphocytic leukemia hyperhomocysteinemia precursor cell lymphoblastic leukemia lymphoma(2.00) · atherosclerosis thrombosis(2.00) · cardiovascular diseases chronic renal failure hyperhomocysteinemia kidney failure chronic(2.00) · cerebrovascular disease ischemic(2.00) · chronic ulcerative colitis colitis ulcerative folic acid deficiency hyperhomocysteinemia(2.00) · cleft lip cleft palate syndrome(2.00) · epilepsy hyperhomocysteinemia(2.00) · glaucoma angle closure glaucoma open angle(2.00) · heart defects congenital(2.00) · hyperhomocysteinemia hyperlipidemias(2.00) · hyperhomocysteinemia hypertension(2.00) · hyperhomocysteinemia pre eclampsia(2.00) · retinal artery occlusion retinal vein occlusion(2.00) · hyperhomocysteinemia venous thrombosis(1.80) · venous thrombosis(1.78) · abortion habitual thrombophilia(1.71) · stomach neoplasms(1.71) · HEMATOLOGICAL(1.58) · thrombophilia(1.58) · thrombosis(1.44) · PHARMACOGENOMIC(1.39) · methotrexate toxicity(1.39) · thromboembolism venous(1.35) · anemia sickle cell sickle cell anemia(1.29) · cleft lip cleft palate(1.29) · adenocarcinoma stomach neoplasms(1.25) · acute lymphocytic leukemia precursor cell lymphoblastic leukemia lymphoma(1.25) · diabetes mellitus type ii diabetes mellitus type 2 diabetic nephropathies diabetic nephropathy(1.12) · coronary disease coronary heart disease(1.10) · pre eclampsia(1.05) · coronary artery disease(1.04) · antiphospholipid syndrome thrombophilia thrombosis(1.00) · brain ischemia(1.00) · brain neoplasms glioma meningeal neoplasms meningioma(1.00) · carcinoma squamous cell skin neoplasms squamous cell carcinoma(1.00) · cervical intraepithelial neoplasia cervical neoplasm papillomavirus infections uterine cervical neoplasms(1.00) · migraine with aura migraine without aura(1.00) · thrombophilia and vascular disease(1.00) · breast cancer(0.93) · migraine disorders(0.92) · thrombosis deep vein(0.86) · RENAL(0.84) · diabetic nephropathy(0.84) · pregnancy loss recurrent(0.83) · pre eclampsia thrombophilia(0.82) · esophageal cancer stomach cancer(0.80) · abortion habitual(0.75) · preeclampsia(0.73) · arthritis rheumatoid rheumatoid arthritis(0.71) · PSYCH(0.67) · behcet syndrome venous thrombosis(0.67) · brain ischemia stroke thrombophilia(0.67) · cerebrovascular disorders(0.67) · congenital abnormalities(0.67) · dementia vascular(0.67) · diabetic nephropathies diabetic nephropathy(0.67) · aortic aneurysm abdominal(0.59) · insulin resistance polycystic ovarian syndrome polycystic ovary syndrome(0.57) · heart anomalies congenital(0.53) · leukemia(0.52) · atherosclerosis(0.51) · hypertension(0.51) · cardiovascular risk(0.50) · cerebrovascular disease(0.50) · colonic neoplasms rectal neoplasms(0.50) · thrombosis venous thrombosis(0.50) · chronic renal failure kidney failure chronic(0.49) · esophageal cancer(0.44) · fatty liver(0.44) · adenoma colorectal neoplasms(0.44) · migraine(0.43) · inflammatory bowel disease nos inflammatory bowel diseases(0.43) · OTHER(0.40) · chromosome aberrations dna damage(0.40) · chronic progressive chorea huntington disease(0.40) · infertility male(0.38) · venous thromboembolism(0.36) · alzheimer s disease(0.36) · intima media thickness(0.33) · migraine with aura(0.33) · brain ischemia stroke(0.31) · infertility female(0.31) · stroke ischemic(0.30) · schizophrenia(0.30) · multiple myeloma(0.29) · atherosclerosis coronary(0.29) · schizophrenia bipolar disorder(0.27) · colorectal neoplasms(0.26) · body weight obesity(0.26) · cardiovascular disease(0.25) · stroke(0.24) · bladder neoplasm urinary bladder neoplasms(0.24) · stomach cancer(0.23) · carcinoma squamous cell esophageal neoplasms oesophageal neoplasm squamous cell carcinoma(0.23) · diabetes type 2(0.23) · arthritis rheumatoid(0.23) · myocardial ischemia(0.21) · CHEMDEPENDENCY(0.21) · alcohol(0.21) · bladder cancer(0.20) · kidney transplant complications(0.19) · neoplasms(0.19) · myocardial infarction(0.17) · arthritis juvenile rheumatoid chronic childhood arthritis(0.17) · myocardial infarct(0.16) · cerebral infarction(0.15) · kidney failure chronic(0.14) · lymphoma(0.14) · kidney diseases(0.14) · choroidal neovascularization macular degeneration(0.13) · cleft lip with cleft palate cleft lip without cleft palate(0.12) · restenosis(0.12) · type 2 diabetes(0.12) · carcinoma hepatocellular lcc liver cell carcinoma liver neoplasms(0.11) · INFECTION(0.11) · helicobacter infections(0.11) · depression(0.11) · leukemia lymphocytic chronic b cell(0.11) · carotid artery diseases(0.10) · cerebral palsy(0.09) · AGING(0.08) · longevity(0.08) · cardiovascular(0.08) · carcinoma squamous cell head and neck neoplasms squamous cell carcinoma(0.08) · polycystic ovary syndrome(0.08) · graft vs host disease(0.06) · dna damage(0.06) · autism(0.05) · atrial fibrillation(0.05) · lymphoma non hodgkin(0.05) · NORMALVARIATION(0.04) · normal variation(0.04) · crohn s disease ulcerative colitis(0.04) · dementia(0.04) · osteoporosis(0.04) · coronary disease(0.02) · cervical cancer(0.02)

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Relevant papers and external links:

OMIM 607093

OMIM 607093

dbSNP: rs45590836 Genecard: MTHFR chromosome 1 SNPedia: rs45590836(G;G)

★ rs6869645(C;C) good:0.03 85.29% **common in complete genomics**

Gene related topics:

PSYCH(9.95) · attention deficit hyperactivity disorder(9.95) · adhd attention deficit hyperactivity disorder(3.41) · schizophrenia methamphetamine abuse(2.00) · CHEMDEPENDENCY(1.25) · smoking behavior(1.25) · perceptual disorders(1.00) · personality(0.98) · cocaine related disorders(0.67) · psychosis(0.60) · delirium(0.57) · impulsivity(0.57) · tourette syndrome(0.47) · adhd(0.40) · NEUROLOGICAL(0.40) · parkinson s disease(0.40) · REPRODUCTION(0.36) · prenatal exposure delayed effects(0.36) · schizophrenia(0.27) · substance related disorders(0.27) · heroin dependence(0.25) · bulimia(0.24) · alcohol(0.21) · dyslexia(0.19) · alcohol abuse(0.17) · alcoholism(0.16) · personality traits(0.12) · migraine disorders(0.08) · depression(0.07) · obsessive compulsive disorder(0.06) · autism(0.05) · smoking(0.05) · PHARMACOGENOMIC(0.02)

Relevant papers and external links:

dbSNP: rs6869645 Genecard: SLC6A3 chromosome 5 SNPedia: rs6869645(C;C)

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★ rs324032(A;A) good:0.02 72.73% **common in complete genomics**

Gene related topics:

NEUROLOGICAL(3.79) · tardive dyskinesia(3.79) · essential tremor(2.88) · PSYCH(2.37) · schizophrenia(2.37) · CHEMDEPENDENCY(2.00) · UNKNOWN(2.00) · akathisia drug induced(2.00) · cocaine abuse(2.00) · cocaine related disorders(0.67) · schizophrenia tardive dyskinesia(0.57) · tourette syndrome(0.47) · alcohol dependence(0.22) · parkinson s disease(0.14) · personality disorders(0.12) · bipolar disorder(0.10) · obsessive compulsive disorder(0.06) · adhd attention deficit hyperactivity disorder(0.05) · personality traits(0.05) · alcohol abuse(0.04) · smoking behavior(0.04)

Relevant papers and external links:

dbSNP: rs324032 Genecard: DRD3 chromosome 3 SNPedia: rs324032(A;A)

★ rs916457(C;C) info:0.12 79.28%

Association and synergistic interaction between promoter variants of the DRD4 gene in Japanese schizophrenics.

Gene related topics:

PSYCH(21.00) · novelty seeking(21.00) · attention deficit hyperactivity disorder(9.95) · adhd(4.13) · OTHER(3.00) · behavior problems(3.00) · temperament(3.00) · personality traits(2.58) · disorganized attachment behavior(2.00) · major psychoses(1.80) · personality disorders(1.53) · impulsivity(1.29) · CHEMDEPENDENCY(1.20) · heroin abuse(1.20) · adhd attention deficit hyperactivity disorder(1.16) · bipolar disorder depression(1.00) · methamphetamine abuse(1.00) · schizophrenia(0.90) · mood disorder(0.60) · METABOLIC(0.53) · body mass(0.53) · NEUROLOGICAL(0.42) · tardive dyskinesia(0.42) · alcohol abuse(0.38) · cognitive function(0.33) · alcoholism(0.29) · psychosis(0.27) · bmi(0.25) · heroin dependence(0.25) · migraine(0.24) · mood disorders(0.23) · weight gain(0.23) · dyslexia(0.19) · smoking behavior(0.16) · obsessive compulsive disorder(0.15) · personality(0.14) · cognitive ability(0.11) · PHARMACOGENOMIC(0.04)

Relevant papers and external links:

PHARMGKB PA164892187
Evidence: PubMed ID:19238168This variant along with 3 other SNPs near DRD4 (4 SNP haplotype: rs3758653; rs916457; rs762502; rs11246226) is associated with tardive dyskinesia in male schizophrenia patients.

PMID 17089069

dbSNP: rs916457 Genecard: DRD4 chromosome 11 SNPedia: rs916457(C;C)

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★ rs1042173(G;T) info:0.38 49.96% **normal**

rs1042173 is a SNP in the solute carrier family 6 (neurotransmitter transporter, serotonin), member 4 SLC6A4 gene.

A study of 275 patients seeking treatment for alcoholism concluded that Caucasians of with the rs1042173 (T;T) genotype consumed an average of 11.17 drinks per drinking day, compared with an average of 8.58 for carriers of a rs1042173(G) allele (p = 0.0034). While this held true for both men and women, this association was not seen in Hispanics.

Gene related topics:

PSYCH(24.57) · depression(24.57) · suicide(6.88) · obsessive compulsive disorder(5.82) · IMMUNE(5.28) · irritable bowel syndrome(5.28) · personality traits(4.75) · anxiety disorder(4.50) · REPRODUCTION(4.00) · depressive disorder major bipolar disorder(4.00) · sexual dysfunction physiological(4.00) · personality disorders(3.78) · depressive disorder major(3.72) · affective disorder(3.12) · anxiety related traits(3.00) ·

decision making(3.00) · psychoses(3.00) · personality(2.60) · panic disorder(2.19) · autism(2.13) · mood disorders(2.02) · CHEMDEPENDENCY(2.00) · OTHER(2.00) · PHARMACOGENOMIC(2.00) · UNKNOWN(2.00) · alcohol abuse smoking behavior(2.00) · alcoholism attention deficit hyperactivity disorder(2.00) · alcoholism recurrence(2.00) · antidepressant adverse effects(2.00) · anxiety(2.00) · auditory evoked potential(2.00) · bipolar and unipolar disorder(2.00) · eating disorder(2.00) · hallucinations(2.00) · harm avoidance(2.00) · impulse control disorder(2.00) · manic depressive illness(2.00) · personality traits illegal drug use(2.00) · suicidal behavior(1.92) · alcoholism(1.92) · NEUROLOGICAL(1.80) · cocaine dependence(1.80) · major depression(1.80) · migraine migraine with aura(1.80) · neuroticism(1.80) · major depressive disorder(1.73) · migraine(1.73) · substance related disorders(1.67) · bulimia(1.47) · attention deficit hyperactivity disorder(1.16) · adhd attention deficit hyperactivity disorder(1.00) · aggressive behavior(1.00) · alcohol related disorders(1.00) · bipolar disorder depression(1.00) · conduct disorder(1.00) · eating disorders(1.00) · sudden infant death(1.00) · anorexia nervosa(0.93) · CARDIOVASCULAR(0.80) · hypertension pulmonary(0.80) · major psychoses(0.80) · bipolar disorder(0.79) · schizophrenia(0.69) · alcohol abuse(0.68) · bipolar affective disorder(0.67) · fibromyalgia(0.67) · sids sudden infant death syndrome(0.67) · smoking behavior(0.66) · mood disorder(0.60) · psychosis(0.60) · heroin abuse(0.53) · epilepsy temporal lobe(0.43) · sleep disorders(0.36) · cognitive function(0.33) · migraine with aura(0.33) · syncope vasovagal(0.33) · DEVELOPMENTAL(0.27) · mental retardation(0.27) · adhd(0.26) · METABOLIC(0.23) · weight gain(0.23) · smoking(0.21) · tourette syndrome(0.21) · alcohol(0.21) · migraine disorders(0.17) · cognitive ability(0.11) · chronic obstructive pulmonary disease(0.07) · hearing loss(0.07) · AGING(0.04) · longevity(0.04)

Relevant papers and external links:

PMID 19032574

dbSNP: rs1042173 Genecard: SLC6A4 chromosome 17 SNPedia: rs1042173(G;T)

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★ **rs6413429(G;G)** **info:0.31** **91.18%**

Gene related topics:

PSYCH(9.95) · attention deficit hyperactivity disorder(9.95) · adhd attention deficit hyperactivity disorder(3.41) · schizophrenia methamphetamine abuse(2.00) · CHEMDEPENDENCY(1.25) · smoking behavior(1.25) · perceptual disorders(1.00) · personality(0.98) · cocaine related disorders(0.67) · psychosis(0.60) · delirium(0.57) · impulsivity(0.57) · tourette syndrome(0.47) · adhd(0.40) · NEUROLOGICAL(0.40) · parkinson s disease(0.40) · REPRODUCTION(0.36) · prenatal exposure delayed effects(0.36) · schizophrenia(0.27) · substance related disorders(0.27) · heroin dependence(0.25) · bulimia(0.24) · alcohol(0.21) · dyslexia(0.19) · alcohol abuse(0.17) · alcoholism(0.16) · personality traits(0.12) · migraine disorders(0.08) · depression(0.07) · obsessive compulsive disorder(0.06) · autism(0.05) · smoking(0.05) · PHARMACOGENOMIC(0.02)

Relevant papers and external links:

dbSNP: rs6413429 Genecard: SLC6A3 chromosome 5 SNPedia: rs6413429(G;G)

★ **rs9960767(A;A)** **good:0.06** **74.24%** **normal**

23andMe blog schizophrenia

rs3131296(C) increased the odds of schizophrenia by 1.19x

rs12807809(T) increased the odds of schizophrenia by 1.15x

rs9960767(C) increased the odds of schizophrenia by 1.23 times.

Established associations:

schizophrenia **you have 0 copies of the risk allele C**

(risk allele=C, odds ratio/beta 1.23 with pval 4E-9, pubmedid=19571808)

Gene related topics:

VISION(2.00) · fuchs endothelial dystrophy(2.00) · schizophrenia(1.00)

Relevant papers and external links:

PMID 19571808
Common variants conferring risk of schizophrenia.

OMIM 181500

dbSNP: rs9960767 GWAS Catalog: rs9960767 Genecard: TCF4 chromosome 18

SNPedia: rs9960767(A;A)

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★ rs12364283(A;A) good:0.15 90.76% **common in complete genomics**

Gene related topics:

CHEMDEPENDENCY(6.04) · alcoholism(6.04) · alcoholism substance related disorders(4.00) · PSYCH(2.30) · schizophrenia(2.30) · METABOLIC(2.00) · NEUROLOGICAL(2.00) · hyperprolactinaemia hyperprolactinemia(2.00) · nervous system diseases(2.00) · substance withdrawal syndrome(2.00) · substance withdrawal syndrome tobacco use disorder(2.00) · tic combined vocal and multiple motor tourette syndrome(2.00) · smoking behavior(1.74) · UNKNOWN(1.29) · neuroleptic malignant syndrome(1.29) · heroin dependence(1.00) · methamphetamine abuse(1.00) · tardive dyskinesia(0.95) · heroin abuse(0.83) · cocaine dependence(0.80) · cocaine related disorders(0.67) · delirium(0.57) · impulsivity(0.57) · alcohol abuse(0.52) · tobacco use disorder(0.44) · adhd(0.40) · mood disorders(0.40) · parkinson s disease(0.40) · smoking(0.33) · alcohol(0.32) · mood disorder(0.27) · substance related disorders(0.27) · CARDIOVASCULAR(0.25) · atrial natriuretic factor(0.25) · alcohol dependence(0.22) · personality

traits(0.21) · tourette syndrome(0.21) · dyslexia(0.19) · migraine disorders(0.17) · adhd attention deficit hyperactivity disorder(0.15) · personality(0.14) · personality disorders(0.12) · depressive disorder major(0.10) · bipolar disorder(0.07) · attention deficit hyperactivity disorder(0.05) · autism(0.03)

Relevant papers and external links:

PHARMGKB PA162355756
Evidence: PubMed ID:18077373; PubMed ID:18829695This promoter variant affects total DRD2 mRNA expression. The C allele is associated with enhanced total DRD2 mRNA expression and is associated with working memory activity in prefrontal cortex and striatum of schizophrenia patients.

dbSNP: rs12364283 Genecard: DRD2 chromosome 11 SNPedia: rs12364283(A;A)

★ rs1018381(C;C) good:0.06 68.70% **normal cognitive ability**

g2b2mh blog In a population of healthy individuals, those that carry common variants (such as rs760761, rs1018381, rs2619522) located in the dysbindin (DTNBP1) gene, a risk factor for schizophrenia, show minor cognitive impairments such as decreased attentional capacity, worse performance on memory tasks, and alterations in schizotypal beliefs and experiences.

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Gene related topics:

PSYCH(1.29) · schizophrenia(1.29) · memory(1.00) · CARDIOVASCULAR(0.29) · blood pressure determination(0.29) · NEUROLOGICAL(0.11) · cognitive ability(0.11) · bipolar disorder(0.07)

Relevant papers and external links:

OMIM 607145

dbSNP: rs1018381 Genecard: DTNBP1 chromosome 6 SNPedia: rs1018381(C;C)

★ rs2630349(G;G) good:0.13 69.07% **common in complete genomics**

Gene related topics:

NEUROLOGICAL(3.79) · tardive dyskinesia(3.79) · essential tremor(2.88) · PSYCH(2.37) ·

schizophrenia(2.37) · CHEMDEPENDENCY(2.00) · UNKNOWN(2.00) · akathisia drug induced(2.00) · cocaine abuse(2.00) · cocaine related disorders(0.67) · schizophrenia tardive dyskinesia(0.57) · tourette syndrome(0.47) · alcohol dependence(0.22) · parkinson s disease(0.14) · personality disorders(0.12) · bipolar disorder(0.10) · obsessive compulsive disorder(0.06) · adhd attention deficit hyperactivity disorder(0.05) · personality traits(0.05) · alcohol abuse(0.04) · smoking behavior(0.04)

Relevant papers and external links:

dbSNP: rs2630349 Genecard: DRD3 chromosome 3 SNPedia: rs2630349(G;G)

★ **rs1800587(C;T)** **info:0.29** **40.19%** **normal**

rs1800587, also known as C-889T, is a SNP in the IL-1 alpha IL1A gene.

A study of 556 adults in the Western Australian coronary heart disease (CHD) population concluded that rs1800587(T;T) homozygotes had larger waist circumference, by 1.8cm on average, compared to major allele (C;C) homozygotes. This association was even more pronounced in patients with higher levels of obesity or inflammatory markers.

rs1800587 increases susceptibility to Intervertebral disc disease 1.31 times for (C;T) heterozygotes and 7.87 times for (T;T) homozygotes

This SNP has also been reported to be associated with Alzheimer's disease in a few studies, but probably ruled out in even more studies, such as this one .

Gene-environment interaction effects on the development of immune responses in the 1st year of life.

Association study of functional genetic variants of innate immunity related genes in celiac disease.

Analysis of polymorphisms in 16 genes in type 1 diabetes that have been associated with other immune-mediated diseases.

Algorithm for automatic genotype calling of single nucleotide polymorphisms using the full course of TaqMan real-time data.

Association study of genetic variants of pro-inflammatory chemokine and cytokine genes in systemic lupus erythematosus.

Inflammatory gene polymorphisms and risk of postoperative myocardial infarction after cardiac surgery.

Interleukin-1 alpha and beta, TNF-alpha and HTTLPR gene variants study on alcohol toxicity and detoxification outcome.

The effect of interleukin-1alpha polymorphisms on bone mineral density and the risk of vertebral fractures.

Prognostic significance of host immune gene polymorphisms in follicular lymphoma survival.

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[A meta-analysis on interleukin-1 gene cluster polymorphism and genetic susceptibility for ankylosing spondylitis].

Optimization of candidate-gene SNP-genotyping by flexible oligonucleotide microarrays; analyzing variations in immune regulator genes of hay-fever samples.

A broad analysis of IL1 polymorphism and rheumatoid arthritis.

Functional genetic polymorphisms and female reproductive disorders: Part I: Polycystic ovary syndrome and ovarian response.

Host immune gene polymorphisms in combination with clinical and demographic factors predict late survival in diffuse large B-cell lymphoma patients in the pre-rituximab era.

Variants in inflammation genes and the risk of biliary tract cancers and stones: a population-based study in China.

Cytokine gene polymorphisms as risk and severity factors for juvenile dermatomyositis.

Association of -31T>C and -511 C>T polymorphisms in the interleukin 1 beta (IL1B) promoter in Korean keratoconus patients.

Organochlorine exposure, immune gene variation, and risk of non-Hodgkin lymphoma.

A meta-analysis of candidate gene polymorphisms and ischemic stroke in 6 study populations: association of lymphotoxin-alpha in nonhypertensive patients.

Interleukin-1alpha -889 C/T polymorphism in Turkish patients with late-onset Alzheimer's disease.

Genetic risk factors in recurrent venous thromboembolism: A multilocus, population-based, prospective approach.

Association of 77 polymorphisms in 52 candidate genes with blood pressure progression and incident hypertension: the Women's Genome Health Study.

A candidate gene association study of 77 polymorphisms in migraine.

Epistasis between IL1A, IL1B, TNF, HTR2A, 5-HTTLPR and TPH2 variations does not impact alcohol dependence disorder features.

An evaluation of candidate genes of inflammation and thrombosis in relation to the risk of venous thromboembolism: The Women's Genome Health Study.

The interleukin-1 cluster gene region is associated with multiple sclerosis in an Italian Caucasian population.

Polymorphisms in IL-1beta, vitamin D receptor Fok1, and Toll-like receptor 2 are associated with extrapulmonary tuberculosis.

Convergent evidence shows a positive association of interleukin-1 gene complex locus with susceptibility to schizophrenia in the Caucasian population.

Allelic variants of IL1R1 gene associate with severe hand osteoarthritis.

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Intermediate phenotypes identify divergent pathways to Alzheimer's disease.

Genetic variants in inflammation-related genes are associated with radiation-induced toxicity following treatment for non-small cell lung cancer.

Association of IL1 gene polymorphisms with chronic periodontitis in Brazilians.

Associations between interleukin-1 (IL-1) gene variations or IL-1 receptor antagonist levels and the development of type 2 diabetes.

Association of interleukin-1 gene polymorphisms with sudden sensorineural hearing loss and Meniere's disease.

Postorthodontic external root resorption is associated with IL1 receptor antagonist gene variations.

Postorthodontic external root resorption in root-filled teeth is influenced by interleukin-1beta polymorphism.

Gene related topics:

IMMUNE(3.52) · periodontitis(3.52) · aggressive periodontitis(3.00) · UNKNOWN(1.00) · alveolar bone loss(1.00) · periodontal diseases(1.00) · celiac disease(1.00) · hearing loss(1.00) · polycystic ovary syndrome(1.00) · tuberculosis(1.00) · survival(1.00) · lymphoma(1.00) · thromboembolism(1.00) · rheumatoid arthritis(1.00) · myocardial infarction(1.00) · stroke(1.00) · blood pressure(1.00) · coronary heart disease(1.00) · chronic periodontitis(1.00) · cancer(1.00) · hypertension(1.00) · multiple sclerosis(1.00) · keratoconus(1.00) · systemic lupus erythematosus(1.00) · OTHER(1.00) · alcohol(1.00) · alcohol dependence(1.00) · venous thromboembolism(1.00) · heart disease(1.00) · schizophrenia(1.00) · type 1 diabetes(1.00) · migraine(1.00) · thrombosis(1.00) · lung cancer(1.00) · obesity(1.00) · ankylosing spondylitis(1.00) · type 2 diabetes(1.00) · waist circumference(1.00) · vitamin d(1.00) · dermatomyositis(1.00) · lupus(1.00) · inflammation(1.00) · NEUROLOGICAL(0.59) · alzheimer s disease(0.59) · multiple system atrophy(0.57) · rhinitis(0.57) · periodontal disease(0.47) · METABOLIC(0.29) · degenerative arthropathy osteoarthritis(0.29) · CARDIOVASCULAR(0.27) · pulmonary fibrosis(0.27) · osteoarthritis knee(0.24) · subarachnoid hemorrhage(0.21) · REPRODUCTION(0.17) · premature birth(0.17) · polycystic ovarian syndrome polycystic ovary syndrome(0.16) · VISION(0.15) · glaucoma open angle(0.15) · cerebral infarction(0.15) · osteoarthritis(0.14) · RENAL(0.12) · chronic renal failure kidney failure chronic(0.12) · alopecia areata(0.11) · juvenile arthritis(0.09) · INFECTION(0.08) · sepsis(0.08) · h pylori infection(0.07) · spondylitis ankylosing(0.07) · CANCER(0.06) · stomach cancer(0.06) · arthritis(0.06) · multiple myeloma(0.05) · hiv infections(0.05) · atopy(0.05) · arthritis rheumatoid rheumatoid arthritis(0.04) · bone mineral density(0.04) · sarcoidosis(0.04) · AGING(0.04) · longevity(0.04) · lupus erythematosus(0.03)

Relevant papers and external links:

PMID 18716798

PMID 17471097

PMID 19158434

PMID 15726497

PMID 16078996

PMID 16519819

PMID 16617143

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PMID 18676870
PMID 19035492
PMID 19043479
PMID 19066394
PMID 19131662
PMID 19155622
PMID 19263529
PMID 19330901
PMID 19559392
PMID 19742166
PMID 20031567
PMID 20192980
PMID 20196868
PMID 20347268
PMID 20353565
PMID 20574532
PMID 20811626
PMID 20934174
PMID 21205020
PMID 21385326
PMID 22035161
PMID 22341060

dbSNP: rs1800587 Genecard: IL1A chromosome 2 SNPedia: rs1800587(C;T)

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★ rs1800443(T;T) good:0.41 97.30% **common in clinvar**

Gene related topics:

PSYCH(21.00) · novelty seeking(21.00) · attention deficit hyperactivity disorder(9.95) · adhd(4.13) · OTHER(3.00) · behavior problems(3.00) · temperament(3.00) · personality traits(2.58) · disorganized

attachment behavior(2.00) · major psychoses(1.80) · personality disorders(1.53) · impulsivity(1.29) · CHEMDEPENDENCY(1.20) · heroin abuse(1.20) · adhd attention deficit hyperactivity disorder(1.16) · bipolar disorder depression(1.00) · methamphetamine abuse(1.00) · schizophrenia(0.90) · mood disorder(0.60) · METABOLIC(0.53) · body mass(0.53) · NEUROLOGICAL(0.42) · tardive dyskinesia(0.42) · alcohol abuse(0.38) · cognitive function(0.33) · alcoholism(0.29) · psychosis(0.27) · bmi(0.25) · heroin dependence(0.25) · migraine(0.24) · mood disorders(0.23) · weight gain(0.23) · dyslexia(0.19) · smoking behavior(0.16) · obsessive compulsive disorder(0.15) · personality(0.14) · cognitive ability(0.11) · PHARMACOGENOMIC(0.04)

Relevant papers and external links:

OMIM 126452

dbSNP: rs1800443 Genecard: DRD4 chromosome 11 SNPedia: rs1800443(T;T)

★ rs27048(C;T) info:0.51 43.64% **normal**

[rs27048]], a SNP in the dopamine transporter SLC6A3 gene, has been associated with more severe symptoms upon alcohol withdrawal, such as seizures, in a study of 250 Caucasian alcohol-dependent patients. Two haplotypes appear to be tagged by this SNP and a neighbor, rs27072.

Variations in the DAT1 gene may affect the inattentive subtype of ADHD.

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Gene related topics:

PSYCH(9.95) · attention deficit hyperactivity disorder(9.95) · adhd attention deficit hyperactivity disorder(3.41) · schizophrenia methamphetamine abuse(2.00) · CHEMDEPENDENCY(1.25) · smoking behavior(1.25) · perceptual disorders(1.00) · seizures(1.00) · personality(0.98) · cocaine related disorders(0.67) · psychosis(0.60) · delirium(0.57) · impulsivity(0.57) · tourette syndrome(0.47) · adhd(0.40) · NEUROLOGICAL(0.40) · parkinson s disease(0.40) · REPRODUCTION(0.36) · prenatal exposure delayed effects(0.36) · schizophrenia(0.27) · substance related disorders(0.27) · heroin dependence(0.25) · bulimia(0.24) · alcohol(0.21) · dyslexia(0.19) · alcohol abuse(0.17) · alcoholism(0.16) · personality traits(0.12) · migraine disorders(0.08) · depression(0.07) · obsessive compulsive disorder(0.06) · autism(0.05) · smoking(0.05) · PHARMACOGENOMIC(0.02)

Relevant papers and external links:

PMID 18070248

PMID 20800641

dbSNP: rs27048 Genecard: SLC6A3 chromosome 5 SNPedia: rs27048(C;T)

★ rs1076560(C;C) info:0.21 59.35% **normal**

rs1076560 is located in intron 6 of the dopamine receptor D2 gene.

In one study of Japanese males, rs1076560(A) alleles were 1.3 fold more associated with Alcoholism than the rs1076560(C) alleles.

The DRD2 risk allele A was more prevalent in the alcoholic patients than in the healthy controls. These data identify rs1076560 as a potentially important variable in the development of alcoholism.

rs1076560 and the DAT 3'-VNTR variant influences memory

Genetic variants altering dopamine D2 receptor expression or function modulate the risk of opiate addiction and the dosage requirements of methadone substitution

Gene related topics:

CHEMDEPENDENCY(6.04) · alcoholism(6.04) · alcoholism substance related disorders(4.00) · PSYCH(2.30) · schizophrenia(2.30) · METABOLIC(2.00) · NEUROLOGICAL(2.00) · hyperprolactinaemia hyperprolactinemia(2.00) · nervous system diseases(2.00) · substance withdrawal syndrome(2.00) · substance withdrawal syndrome tobacco use disorder(2.00) · tic combined vocal and multiple motor tourette syndrome(2.00) · smoking behavior(1.74) · UNKNOWN(1.29) · neuroleptic malignant syndrome(1.29) · heroin dependence(1.00) · methamphetamine abuse(1.00) · memory(1.00) · tardive dyskinesia(0.95) · heroin abuse(0.83) · cocaine dependence(0.80) · cocaine related disorders(0.67) · delirium(0.57) · impulsivity(0.57) · alcohol abuse(0.52) · tobacco use disorder(0.44) · adhd(0.40) · mood disorders(0.40) · parkinson s disease(0.40) · smoking(0.33) · alcohol(0.32) · mood disorder(0.27) · substance related disorders(0.27) · CARDIOVASCULAR(0.25) · atrial natriuretic factor(0.25) · alcohol dependence(0.22) · personality traits(0.21) · tourette syndrome(0.21) · dyslexia(0.19) · migraine disorders(0.17) · adhd attention deficit hyperactivity disorder(0.15) · personality(0.14) · personality disorders(0.12) · depressive disorder major(0.10) · bipolar disorder(0.07) · attention deficit hyperactivity disorder(0.05) · autism(0.03)

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Relevant papers and external links:

PMID 17196743

PMID 19176830

PMID 19373123

PHARMGKB PA162360621
Evidence: PubMed ID:17196743This variant is a potential marker for alcoholism. A allele was more prevalent in the alcoholic patients than in the healthy controls in a study consists of 248 alcoholic patients and 322 healthy controls (all Japanese males).

PHARMGKB PA162355758
Evidence: PubMed ID:18077375; PubMed ID:18829695This variant is in intron 6, and T allele shifts mRNA splicing from the short form (D2S) to the long form (D2L). The T allele carriers are also associated with reduced working memory and attension perfermance.

dbSNP: rs1076560 Genecard: DRD2 chromosome 11 SNPedia: rs1076560(C;C)

★ rs4320932(A;A) info:0.14 53.09% **normal**

rs4320932 is a SNP in the IF2 insulin-like growth factor 2 gene.

A study totaling ~5,000 non-Hispanic white patients with ovarian cancer found a 13% decreased risk of ovarian cancer per copy of the rs4320932(G) allele carried (CI: 0.81-0.93, P-trend=7.4 × 10e-5).

Associated with schizophrenia in a study of Croatians. Due to the limited number (~100 patients) and diversity of the studied population, more study is needed to confirm any link. The G allele was associated with an increased risk of schizophrenia with P < 0.001.

Small size study with 212 cases linked the G allele earlier found protective against ovarian cancer increasing relapse by 3.05 (95% confidence interval CI: 1.47–6.37, P-trend 2*10e-4) and mortality 3.28 (95% CI: 1.64–6.57, P-trend 6*10e-5).

Association of Tagging Single Nucleotide Polymorphisms on 8 Candidate Genes in Dopaminergic Pathway with Schizophrenia in Croatian Population

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Gene related topics:

ovarian cancer(1.00) · CANCER(1.00) · cancer(1.00) · schizophrenia(1.00) · insulin(1.00) · mortality(1.00) · NORMALVARIATION(0.67) · muscle testing(0.67) · METABOLIC(0.57) · insulin obesity(0.57) · body mass(0.24) · UNKNOWN(0.16) · birth weight(0.16) · AGING(0.08) · longevity(0.08) · IMMUNE(0.04) · diabetes mellitus type 1(0.04)

Relevant papers and external links:

PMID 21422097
PMID 19673036
PMID 23677070
PMID 19673036

dbSNP: rs4320932 Genecard: IGF2 chromosome 11 SNPedia: rs4320932(A;A)

★ rs1800496(C;C) good:0.22 99.84% **common in complete genomics**

origins associated with an independent aspect of decision making in a learning paradigm

Gene related topics:

CHEMDEPENDENCY(6.04) · alcoholism(6.04) · alcoholism substance related disorders(4.00) · PSYCH(2.30) · schizophrenia(2.30) · METABOLIC(2.00) · NEUROLOGICAL(2.00) · hyperprolactinaemia hyperprolactinemia(2.00) · nervous system diseases(2.00) · substance withdrawal syndrome(2.00) · substance withdrawal syndrome tobacco use disorder(2.00) · tic combined vocal and multiple motor tourette syndrome(2.00) · smoking behavior(1.74) · UNKNOWN(1.29) · neuroleptic malignant syndrome(1.29) · heroin dependence(1.00) · methamphetamine abuse(1.00) · decision making(1.00) · tardive dyskinesia(0.95) · heroin abuse(0.83) · cocaine dependence(0.80) · cocaine related disorders(0.67) · delirium(0.57) · impulsivity(0.57) · alcohol abuse(0.52) · tobacco use disorder(0.44) · adhd(0.40) · mood disorders(0.40) · parkinson s disease(0.40) · smoking(0.33) · alcohol(0.32) · mood disorder(0.27) · substance related disorders(0.27) · CARDIOVASCULAR(0.25) · atrial natriuretic factor(0.25) · alcohol dependence(0.22) · personality traits(0.21) · tourette syndrome(0.21) · dyslexia(0.19) · migraine disorders(0.17) · adhd attention deficit hyperactivity disorder(0.15) · personality(0.14) · personality disorders(0.12) · depressive disorder major(0.10) · bipolar disorder(0.07) · attention deficit hyperactivity disorder(0.05) · autism(0.03)

Relevant papers and external links:

dbSNP: rs1800496 Genecard: DRD2 chromosome 11 SNPedia: rs1800496(C;C)

★ **rs7598440(C;T)** **info:0.16** **46.04%**

linked to schizophrenia with rs7598440, rs839523, and rs707284

Gene related topics:

NEUROLOGICAL(2.67) · frontal lobe(2.67) · schizophrenia(1.00) · HEMATOLOGICAL(0.76) · factor vii(0.76) · METABOLIC(0.05) · body weights and measures(0.05)

Relevant papers and external links:

OMIM 600543

dbSNP: rs7598440 Genecard: ERBB4 chromosome 2 SNPedia: rs7598440(C;T)

★ **rs28694718(G;-)** **info:0.08** **common**

In the Pseudoautosomal region

rs28694718, located in intron 8 of the CSF2RA gene, is part of a haplotype block that has been reported in a whole genome association study to be associated with schizophrenia. (The other SNP in this block is rs28414810.)

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The risk allele (oriented to the dbSNP entry) is (A); the odds ratio associated with this allele is 2.11.

Gene related topics:

OTHER(1.00) · schizophrenia(1.00)

Relevant papers and external links:

PMID 17522711

dbSNP: rs28694718 Genecard: CSF2RA chromosome X SNPedia: rs28694718(G;G)

★ rs1050450(C;C) good:0.27 61.24% **common in clinvar**

GPX1 Pro198Leu polymorphism, interactions with smoking and alcohol consumption, and risk for lung cancer.

Gene x Gene interaction between MnSOD and GPX-1 and breast cancer risk: a nested case-control study.

Genetic association of glutathione peroxidase-1 with coronary artery calcification in type 2 diabetes: a case control study with multi-slice computed tomography.

Do genetic factors protect for early onset lung cancer? A case control study before the age of 50 years.

A prospective study of genetic polymorphism in MPO, antioxidant status, and breast cancer risk.

Oxidative response gene polymorphisms and risk of adult brain tumors.

The Mn-superoxide dismutase single nucleotide polymorphism rs4880 and the glutathione peroxidase 1 single nucleotide polymorphism rs1050450 are associated with aging and longevity in the oldest old.

Lack of association of GPX1 and MnSOD genes with symptom severity and response to clozapine treatment in schizophrenia subjects.

Extent of differential allelic expression of candidate breast cancer genes is similar in blood and breast.

Gene polymorphisms against DNA damage induced by hydrogen peroxide in leukocytes of healthy humans through comet assay: a quasi-experimental study.

Effects of selenium status and polymorphisms in selenoprotein genes on prostate cancer risk in a prospective study of European men.

Genetic polymorphisms in antioxidative enzymes are associated to forced expiratory volume in 1 s (FEV1) in smokers independently of asthma.

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GPx-1 polymorphism (rs1050450) contributes to tumor susceptibility: evidence from meta-analysis.

Serum selenium and single-nucleotide polymorphisms in genes for selenoproteins: relationship to markers of oxidative stress in men from Auckland, New Zealand.

Antioxidant enzyme polymorphisms and neuropsychological outcomes in medulloblastoma survivors: a report from the Childhood Cancer Survivor Study.

Gene related topics:

aging(1.00) · prostate cancer(1.00) · CANCER(1.00) · stress(1.00) · brain(1.00) · cancer(1.00) · asthma(1.00) · breast cancer(1.00) · alcohol(1.00) · schizophrenia(1.00) · AGING(1.00) · fev1(1.00) · lung cancer(1.00) · type 2 diabetes(1.00) · forced expiratory volume(1.00) · peroxidase(1.00) · longevity(1.00) · smoking(1.00) · response to clozapine(1.00) · oxidative stress(1.00) · RENAL(0.50) · diabetic neuropathy(0.50) · OTHER(0.18) · dna damage(0.18) · METABOLIC(0.04) · metabolic syndrome(0.04)

Relevant papers and external links:

OMIM 138320
PMID 16797832
PMID 16945136
PMID 17825092
PMID 18298806
PMID 18340529
PMID 18682580
PMID 19428448
PMID 19946932
PMID 20003265
PMID 20444272
PMID 20852007
PMID 21595856
PMID 21842217
PMID 22139612
PMID 22661588

dbSNP: rs1050450 Genecard: GPX1 chromosome 3 SNPedia: rs1050450(C;C)

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★ rs1801133(C;C) good:1.98 56.94% **Common genotype: normal homocysteine levels**

rs1801133 is a SNP that is relatively common and has been studied for (relatively) a long time. Also known as C677T, Ala222Val, and A222V, it encodes a variant in the MTHFR gene, which encodes an enzyme

involved in folate metabolism.

Homozygous rs1801133(T;T) individuals have ~30% of the expected MTHFR enzyme activity, and rs1801133(C;T) heterozygotes have ~65% activity, compared to the most common genotype, rs1801133 (C;C).

This reduced activity (i.e. this SNP) has been linked at least once to each of the following disorders (though not necessarily reproducibly):

autism
cancer, including
gastric cancer
lung cancer
head and neck cancer
renal cancer
cleft lip and cleft palate
coronary artery disease
dementia
depression
hyperhomocysteinemia
migraine
neural tube defects
pre-eclampsia (gestational hypertension)
schizophrenia
thrombosis
down syndrome

PubMed lists over 2,300 studies linking Rs1801133 to a long list of disorders in various populations across the world, of which only some are mentioned above. Considering the central role of MTHFR in folate metabolism and in control of homocysteine levels this is not surprising. A nice summary of the pathological significance of elevated homocysteine levels could be found in this article.

With regard to gastric cancer, a meta-analysis combining 16 studies and ~2,700 patients concluded that the increased risk (odds ratio) associated with rs1801133 (T;T) and (C;T) genotypes, was 1.52 (CI 1.31-1.77) and 1.17 (CI 0.99-1.39), respectively, compared to the (C;C) genotype. Roughly the same risks were seen for Caucasians and Asians. Smoking and having low folate levels (presumably from diets low in fruits and veggies) increased the risk for (T;T) individuals from ~1.5x to ~2x, whereas having high folate levels almost reduced the risk for (T;T) genotypes pretty much down to the (C;C) level, ie. the average risk.

Another meta-analysis of three studies on rs1801133 stratified according to dietary folate intake showed an increased risk for individuals with low folate intake (OR=1.37, CI: 0.92-2.06 for head and neck cancer and OR=1.28, CI: 0.97-1.68 for lung) versus high folate intake (OR=0.85, CI: 0.63-1.16 for head and neck cancer, and OR=0.94, CI: 0.79-1.12 for lung).

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rs1801131 and rs1801133 have been linked to increased risk for several types of brain cancer. The highest risk of meningioma was associated with heterozygosity for both MTHFR SNPs (odds ratio 2.11, CI: 1.42-3.12, p=0.002). The corresponding odds ratio for glioma was 1.23 (CI: 0.91-1.66, p=0.02. In general, risks were increased with genotypes associated with reduced MTHFR activity.

Based on a study of 25,000 Caucasian women followed for 11 years (on average), the rs1801133(T;T) genotype individual was less likely to have migraine with aura (odds ratio 0.79, CI: 0.65-0.9 6, p = 0.02) and did not have increased risk for cardiovascular disease. However, if a (T;T) genotype did have migraine with aura, then the risk for cardiovascular disease was increased 3.66 fold (CI: 1.69-7.90, p = 0.001). This was apparently driven by a 4x increased risk for ischemic stroke (multivariable-adjusted relative risk 4.19, CI: 1.38-12.74, p = 0.01).

A study of 677 patients with end-stage renal disease (ESRD) concluded that the adjusted hazard ratio for mortality in all patients was 2.27 (CI: 1.07 - 4.84, p = 0.03) for rs1801133(T;T) homozygotes, in other words, they died at about twice the rate of the other 2 genotypes over the time course of this study.

In a case-control study of 152 cases (men) and 304 age-matched healthy controls conducted in one geographical area of Iran, evidence was seen that the MTHFR polymorphisms might contribute to increased clear cell renal cell carcinoma (CCRCC) risk in men. After controlling for confounding factors, a significant increase in CCRCC risk was found among carriers of the 677CT genotype compared with those with the 677CC genotype (odds ratio 2.21, 95% confidence interval 1.31-3.76), with a significant trend (P=0.014). Statistically significant odds ratios were also found in patients homozygous for MTHFR C677T, who have a 1.58-fold higher risk of developing CCRCC (95% confidence interval=1.21-2.44; P=0.024). Compared with the MTHFR 677CC genotype, the odds ratio (95% confidence interval) for the MTHFR 677TT genotype was 6.18 (95% confidence interval=4.75-8.34) for stage IV cancer and 4.68 (95% confidence interval=2.72-6.54) for grade 3 CCRCC (both P=0.0001). Clin Oncol (R Coll Radiol). 2012 May;24(4):269-81. doi: 10.1016/j.clon.2011.03.005. Epub 2011 Apr 13.

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A 2-year follow-up study of 122 newly diagnosed patients with acute lymphoblastic leukemia (ALL) found that carriers of a rs1801133(T) allele were at increased risk for hepatic toxicity from methotrexate treatment. Hepatic toxicity was increased ~2x and ~5x for heterozygous and homozygous rs1801133(T) genotypes, respectively (p=0.028). If a carrier of a rs1801133(T) allele was also a carrier of a rs70991108 deletion allele, the risk for hepatic toxicity was even higher (odds ratio 6.8, p=0.018).

Note: Another SNP in dbSNP, rs59514310, represents the same location as rs1801133.

blog The MTHFR gene polymorphism is associated with lean body mass but not fat body mass

rs1801133(T;T) post-menopausal women said to be at 2x higher risk for osteoporosis.

MTHFR 677C→T polymorphism is more prevalent among mothers of children with Down syndrome than among control mothers, with an odds ratio of 1.91

Gene-wide association study between the methylenetetrahydrofolate reductase gene (MTHFR) and schizophrenia in the Japanese population, with an updated meta-analysis on currently available data.

rs1801133 shows no consistent association with schizophrenia overall in 12 studies totaling 3,000+ patients

Established associations:

homocysteine measurement **you have 0 copies of the risk allele T**

(risk allele=T, odds ratio/beta 0.1583 [0.14-0.17] unit increase with pval 4E-104, pubmedid=23824729; risk allele=T, WGHS odds ratio/beta 0.05 unit increase in loghomocysteine with pval 8E-35, pubmedid=20031578)

Gene related topics:

METABOLIC(14.69) · hyperhomocysteinemia(14.69) · DEVELOPMENTAL(14.49) · neural tube defects(14.49) · down syndrome(11.36) · CARDIOVASCULAR(10.00) · coronary artery disease hyperhomocysteinemia(10.00) · folic acid deficiency(7.00) · homocysteine(6.92) · UNKNOWN(5.00) · chronic renal failure hyperhomocysteinemia kidney failure chronic(5.00) · coronary disease coronary heart disease hyperhomocysteinemia(5.00) · CANCER(4.00) · adenoma colorectal neoplasms neoplasm recurrence local(4.00) · hyperhomocysteinemia retinal vein occlusion(4.00) · spinal dysraphism(3.85) · colorectal cancer(3.74) · arteriosclerosis(3.57) · apoplexy stroke(3.12) · apoplexy brain ischemia hyperhomocysteinemia stroke(3.00) · cardiovascular diseases hyperhomocysteinemia(3.00) · congenital heart defects heart defects congenital(3.00) · diabetes mellitus type ii diabetes mellitus type 2 hyperhomocysteinemia(3.00) · hearing loss sudden(3.00) · hyperhomocysteinemia postoperative complications(3.00) · hyperhomocystinemia(3.00) · vascular diseases(3.00) · cardiovascular diseases(2.93) · apoplexy brain ischemia stroke(2.61) · REPRODUCTION(2.61) · pregnancy loss(2.61) · abortion spontaneous(2.58) · leukemia lymphocytic acute l1 precursor cell lymphoblastic leukemia lymphoma(2.58) · pregnancy complications(2.40) · precursor cell lymphoblastic leukemia lymphoma(2.16) · colonic neoplasms(2.13) · IMMUNE(2.00) · NEUROLOGICAL(2.00) · VISION(2.00) · abortion habitual hyperhomocysteinemia(2.00) · abortion habitual pregnancy complications hematologic thrombophilia(2.00) · abruptio placentae(2.00) · activated protein c resistance hyperhomocysteinemia thrombophilia venous thrombosis(2.00) · acute lymphocytic leukemia hyperhomocysteinemia precursor cell lymphoblastic leukemia lymphoma(2.00) · atherosclerosis thrombosis(2.00) · cardiovascular diseases chronic renal failure hyperhomocysteinemia kidney failure chronic(2.00) · cerebrovascular disease ischemic(2.00) · chronic ulcerative colitis colitis ulcerative folic acid deficiency hyperhomocysteinemia(2.00) · cleft lip cleft palate syndrome(2.00) · epilepsy hyperhomocysteinemia(2.00) · glaucoma angle closure glaucoma open angle(2.00) · heart defects congenital(2.00) · hyperhomocysteinemia hyperlipidemias(2.00) · hyperhomocysteinemia hypertension(2.00) · hyperhomocysteinemia pre eclampsia(2.00) · retinal artery occlusion retinal vein occlusion(2.00) · hyperhomocysteinemia venous thrombosis(1.80) · venous thrombosis(1.78) · abortion habitual thrombophilia(1.71) · stomach neoplasms(1.71) · HEMATOLOGICAL(1.58) · thrombophilia(1.58) · thrombosis(1.44) · PHARMACOGENOMIC(1.39) · methotrexate toxicity(1.39) · thromboembolism venous(1.35) · anemia sickle cell sickle cell anemia(1.29) · cleft lip cleft palate(1.29) · adenocarcinoma stomach neoplasms(1.25) · acute lymphocytic leukemia precursor cell lymphoblastic leukemia lymphoma(1.25) · diabetes mellitus type ii diabetes mellitus type 2 diabetic nephropathies diabetic nephropathy(1.12) · coronary disease coronary heart disease(1.10) · pre eclampsia(1.05) · coronary artery disease(1.04) · antiphospholipid syndrome thrombophilia thrombosis(1.00) · brain ischemia(1.00) · brain neoplasms glioma meningeal neoplasms meningioma(1.00) · carcinoma squamous cell skin neoplasms squamous cell carcinoma(1.00) · cervical intraepithelial neoplasia cervical neoplasm papillomavirus infections uterine cervical neoplasms(1.00) · migraine with aura migraine without aura(1.00) · thrombophilia and vascular disease(1.00) · gastric cancer(1.00) · metabolism(1.00) · renal cancer(1.00) · brain(1.00) · body mass(1.00) · cancer(1.00) · glioma(1.00) · cleft lip(1.00) · enzyme activity(1.00) · lung cancer(1.00) · mortality(1.00) · brain cancer(1.00) · smoking(1.00) · head and neck cancer(1.00) · breast cancer(0.93) · migraine disorders(0.92) · thrombosis deep vein(0.86) · RENAL(0.84) · diabetic nephropathy(0.84) · pregnancy loss recurrent(0.83) · pre eclampsia thrombophilia(0.82) · esophageal cancer stomach cancer(0.80) · abortion habitual(0.75) · preeclampsia(0.73) · arthritis rheumatoid rheumatoid arthritis(0.71) · PSYCH(0.67) · behcet syndrome venous thrombosis(0.67) · brain ischemia stroke thrombophilia(0.67) · cerebrovascular disorders(0.67) · congenital abnormalities(0.67) · dementia vascular(0.67) · diabetic nephropathies diabetic nephropathy(0.67) · aortic aneurysm abdominal(0.59) · insulin resistance polycystic ovarian syndrome polycystic ovary syndrome(0.57) · heart anomalies congenital(0.53) · leukemia(0.52) · atherosclerosis(0.51) · hypertension(0.51) · cardiovascular risk(0.50) · cerebrovascular disease(0.50) · colonic neoplasms rectal neoplasms(0.50) · thrombosis venous

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thrombosis(0.50) · chronic renal failure kidney failure chronic(0.49) · esophageal cancer(0.44) · fatty liver(0.44) · adenoma colorectal neoplasms(0.44) · migraine(0.43) · inflammatory bowel disease nos inflammatory bowel diseases(0.43) · OTHER(0.40) · chromosome aberrations dna damage(0.40) · chronic progressive chorea huntington disease(0.40) · infertility male(0.38) · venous thromboembolism(0.36) · alzheimer s disease(0.36) · intima media thickness(0.33) · migraine with aura(0.33) · brain ischemia stroke(0.31) · infertility female(0.31) · stroke ischemic(0.30) · schizophrenia(0.30) · multiple myeloma(0.29) · atherosclerosis coronary(0.29) · schizophrenia bipolar disorder(0.27) · colorectal neoplasms(0.26) · body weight obesity(0.26) · cardiovascular disease(0.25) · stroke(0.24) · bladder neoplasm urinary bladder neoplasms(0.24) · stomach cancer(0.23) · carcinoma squamous cell esophageal neoplasms oesophageal neoplasm squamous cell carcinoma(0.23) · diabetes type 2(0.23) · arthritis rheumatoid(0.23) · myocardial ischemia(0.21) · CHEMDEPENDENCY(0.21) · alcohol(0.21) · bladder cancer(0.20) · kidney transplant complications(0.19) · neoplasms(0.19) · myocardial infarction(0.17) · arthritis juvenile rheumatoid chronic childhood arthritis(0.17) · myocardial infarct(0.16) · cerebral infarction(0.15) · kidney failure chronic(0.14) · lymphoma(0.14) · kidney diseases(0.14) · choroidal neovascularization macular degeneration(0.13) · cleft lip with cleft palate cleft lip without cleft palate(0.12) · restenosis(0.12) · type 2 diabetes(0.12) · carcinoma hepatocellular lcc liver cell carcinoma liver neoplasms(0.11) · INFECTION(0.11) · helicobacter infections(0.11) · depression(0.11) · leukemia lymphocytic chronic b cell(0.11) · carotid artery diseases(0.10) · cerebral palsy(0.09) · AGING(0.08) · longevity(0.08) · cardiovascular(0.08) · carcinoma squamous cell head and neck neoplasms squamous cell carcinoma(0.08) · polycystic ovary syndrome(0.08) · graft vs host disease(0.06) · dna damage(0.06) · autism(0.05) · atrial fibrillation(0.05) · lymphoma non hodgkin(0.05) · NORMALVARIATION(0.04) · normal variation(0.04) · crohn s disease ulcerative colitis(0.04) · dementia(0.04) · osteoporosis(0.04) · coronary disease(0.02) · cervical cancer(0.02)

Relevant papers and external links:

PMID 23824729
Common genetic loci influencing plasma homocysteine concentrations and their effect on risk of coronary artery disease.

PMID 20031578
Novel associations of cps1, mut, nox4, and dpep1 with plasma homocysteine in a healthy population: a genome-wide evaluation of 13 974 participants in the women's genome health study.

PMID 18162478

PMID 18789576

PMID 18483342

PMID 18672474

PMID 19272686

PMID 21489764

PMID 19648163

PHARMGKB PA165110386
Evidence: PubMed ID:18580170Risk or phenotype-associated allele(s): T/T. Phenotype:Patients with a homozygous MTHFR 677C>T mutation (n = 25) developed higher plasma homocysteine concentrations (median [interquartile range], 14.9 [10.0-26.4] microm) than wild-type or heterozygous patients (9.3 [7.5-15.5] microm; n = 115). The change in homocysteine after nitrous oxide anesthesia was tripled in homozygous patients compared with wild-type (5.6 microm [+60%] vs. 1.8 microm [+22%]). Study size: 140. Study population/ethnicity: healthy patients undergoing elective surgery. Type of association: GN.

OMIM 607093

PHARMGKB PA161145165
Evidence: Web Resource:External Link studied, associated with multiple phenotypes.

PHARMGKB PA162316602

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Evidence: PubMed ID:17488658This variant is associated with methotrexated-induced mucositis, thrombocytopenia and hepatic toxicity

PHARMGKB PA162316601
Evidence: PubMed ID:18381794This variant is associated with methotrexated-induced alopecia in African Americans with rheumatoid arthritis.

PHARMGKB PA164920416
Evidence: PubMed ID:19581920This variant protein has reduced catalytic activity and thermolability, and is thus associated with elevated homocysteine levels under conditions of impaired folate status.

PHARMGKB PA164918288
Evidence: PubMed ID:19303062The T allele of this SNP was found to be associated with higher blood concentration of homocysteine in Italians (Combined studies of Tuscan Italians (inCHIANTI:N =1175 and Progetto Nutrizione study:N = 687) and Sardinians (SardiNIA: N=1115)) but not in the BLSA cohort (from Baltimore-Washington DC). The study authors inferred that this was related to U.S. food fortification and hence higher folate status.

PHARMGKB PA164918205
Evidence: PubMed ID:15643524In a case control study of Asian gastric cancer (n=633), individuals with 6 variant alleles of three MTHFR common variants (i.e. C677T, A1298C and G1793A) were at increased risk for gastric cardia adenocarcinoma (OR =4.64, 95% CI =1.34-16.01) compared with those having 0-2 variants.

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PHARMGKB PA165106866
Evidence: PubMed ID:12915598In 53 newly diagnosed patients with childhood acute lymphoblastic leukemia who were treated with two courses of high-dose methotrexate (MTX), no association was found between MTX-induced increases in plasma or cerebrospinal fluid homocysteine levels or MTX-induced toxicity (seizures or thrombosis) based upon the MTHFR 677C>T or RFC (SLC19A1) 80G>A genotypes.

PHARMGKB PA165106864
Evidence: PubMed ID:11418485In patients with chronic myelogenous leukemia undergoing bone marrow transplantation and taking methotrexate, carriers of the MTHFR 677TT genotype versus CT and CC genotypes showed significantly greater post-allograft drug-induced toxicity in the form of oral mucositis (p=0.046), and a non-significant trend toward slower platelet recovery.

PHARMGKB PA165108052
Evidence: PubMed ID:17976958Risk or phenotype-associated allele: T. Phenotype: 53% of T allele carriers met metabolic syndrome criteria, compared with 23% in the CC genotype group. Study size: 58. Study population/ethnicity: Individuals with schizophrenia receiving atypical antipsychotics (AAPs) for 12 or more months. Over 85% of the subjects were Caucasian. Significance metric(s): OR = 3.7; p = 0.02. Type of association: CO.

PHARMGKB PA165108053
Evidence: PubMed ID:17976958Risk or phenotype-associated allele: T. Phenotype: Both waist circumference and the MTHFR genotype were significant factors associated with insulin resistance. Study size: 58. Study population/ethnicity: Individuals with schizophrenia receiving atypical antipsychotics (AAPs) for 12 or more months. Over 85% of the subjects were Caucasian. Significance metric(s): p < 0.0001. Type of association: CO.

PHARMGKB PA165106826
Evidence: PubMed ID:11710708MTHFR rs1801133, 667CT or 667TT genotypes were associated with an increased risk of methotrexate treatment discontinuation due to adverse events (relative risk 2.01), mostly as a result of increased risk of elevated levels of liver enzyme alanine aminotransferase (relative risk 2.38) in rheumatoid arthritis patients.

PHARMGKB PA165106865
Evidence: PubMed ID:12453860In a retrospective analysis of 61 Italian patients experiencing methotrexate toxicity during treatment for acute lymphoblastic leukemia or acute promyelocytic leukemia, carriers of the MTHFR 677TT genotype (60%) showed significantly greater drug-induced toxicity (p=0.03) compared to CC and CT genotypes.

PHARMGKB PA165109580
Evidence: PubMed ID:11710708Risk or phenotype-associated allele: CT and TT genotypes. Phenotype: The 677 CT or TT genotypes were associated with greater incidence of discontinuation of methorexate treatment because of adverse events, mainly due to elevation of liver enzymes. Study size: 236. Study population/ethnicity: Patients who started methorexate treatment with (n = 157) or without (n = 79) folic or folinic acid supplementation for rheumatoid arthritis. Significance metric(s): RR = 2.01 Type of association: CO, GN.

PHARMGKB PA165282249
Evidence: PubMed ID:19005482Risk or phenotype-associated allele: T. Phenotype: MTHFR:677T genotype in the transplant recipient was associated with acute graft vs host disease. Study size:107 . Study population/ethnicity: Donors and patients with leukemia after HLA-identical hematopoietic stem cell transplantation, France. Significance metric(s): p = 0.03. Type of association: CO

PHARMGKB PA165106616
Evidence: PubMed ID:16572443Given methotrexate and folic acid therapy, patients with the MTHFR 1298AA / 677CC diplotype showed greater clinical improvement for early rheumatoid arthritis.

PHARMGKB PA165106621
Evidence: PubMed ID:19016697In 330 patients who completed 3 months methotrexate treatment for psoriasis, no significant genotypic associations were found between clinical outcome (e.g. efficacy, toxicity) and 50 SNPs in pathway genes for methotrexate metabolism (ATIC, FPGS, GGH, MTHFR), including 47 common (>5% minor allele frequency) haplotype-tagging SNPs (r(2) > 0.8) plus 3 additional SNPs.

PMID 10930360
PMID 20692813
PMID 21302350
OMIM 607093

dbSNP: rs1801133 GWAS Catalog: rs1801133 Genecard: MTHFR chromosome 1

SNPedia: rs1801133(C;C)

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★ rs821616(A;T) info:0.18 37.52% ?

Women with two rs821616(T) SNPs seem to experience more rapid cognitive decline as they age compared to men.

13 single-nucleotide polymorphisms (SNPs) in 723 members of 179 Finnish Bipolar disorder families.
rs821616 verbal fluency

Gene related topics:

bipolar disorder(1.00) · PSYCH(0.60) · schizophrenia bipolar disorder(0.60) · schizophrenia(0.35) · cognitive function(0.33) · NEUROLOGICAL(0.02) · amyotrophic lateral sclerosis(0.02)

Relevant papers and external links:

PMID 16054297
PMID 17673452

dbSNP: rs821616 Genecard: DISC1 chromosome 1 SNPedia: rs821616(A;T)

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★ rs25531(A;A) info:1.12 74.38% **short form of 5-HTTLPR. lower levels of serotonin, slightly less happy, benefits from more support**

23andMe reports that this genotype is not reliable on their platform. 23andMe users should ignore this result.

This genotype is associated with lower levels of serotonin and appears to have a cognitive effect related to emotions, but the effect is slight and no one in SNPedia has yet found a good description. However the (G;G) genotype generally seems to have more positive associations, while this (A;A) is more negative. Examples of the differences include biased attention for negative word stimuli and gaze bias for emotional information.

More reluctant to endorse utilitarian actions resulting in foreseen harm to an innocent individual

The genotype of this SNP is not meaningful on 23andme v3.
External Link
According to David Hinds of 23andMe on community forums, "nearly everyone (99.97%) is getting called as CC, and there is no clear heterozygote cluster" ... "the genotype calls for rs25531 on our platform are not meaningful." Looking at OpenSNP frequency data, this seems to be universal for direct to consumer genotyping services at this stage.

The minor allele (G) of rs25531 is almost always in phase with the long (L) allele of the 5-HTTLPR, which is the most commonly studied variation in this region. The (L) long allele may be associated with lower levels of serotonin.

The article and video from "The Atlantic" suggests that children with the short allele (A), may need and benefit greatly from more maternal support
External Link

In contrast to earlier reports linking rs25531, a SNP in the serotonin transporter SLC6A4 gene, to obsessive compulsive disorder (OCD), a March 2007 publication finds no significant association studying "the largest sample size of OCD patients (N=347) and controls (N=749) ever investigated".

A separate study of 75 patients suffering mood disorders after traumatic brain injury (TBI) concluded that there was no evidence of association between rs25531 and depression post-TBI.

A small study (62 patients and 62 matched controls) investigated this SNP in relation to blushing. (Blushing is considered to be one of the prime pathophysiological markers of social anxiety disorder.) The less active 5-HTTLPR genotypes were nominally significantly associated with increased blushing propensity in patients with social anxiety disorder, and association remained significant even when statistically controlled for he influence of depression.

A study of 94 depressed patients who attempted suicide compared to 94 without psychiatric disorders found no evidence of an association with rs25531.

A study of 97 "normal" individuals concluded that rs25531(G;G) individuals selectively process positive affective material alongside selective avoidance of negative affective material, in a manner absent among individuals carrying a rs25531(A) allele. To put it another way, if this conclusion drawn from a very small sample of people can be replicated, rs25531(G;G) individuals may have a tendency to be optimists and to be more resilient to stress.

A study published in 2011 of 2,500+ individuals followed from 1995 - 2008 as part of the US National Longitudinal Study of Adolescent Health found that twice as many respondents with two 5-HTTLPR long variants said they were very satisfied with life compared with carriers of two short versions. Conversely, 26% of those carrying two short alleles said they were dissatisfied with life, compared with 20% of people carrying two long variants. This blog post investigates the statistics.

A study of 135 patients with major depressive disorder (mean age 31.1+/-11.6 years, 68% females) treated with escitalopram 10-20 mg/day for 12 weeks concluded that patients carrying the rs25531(A) allele may be at increased risk for side effects (e.g. headaches), but they say no associations with efficacy.

Protocol for genotyping rs25531

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Gene related topics:

PSYCH(24.57) · depression(24.57) · suicide(6.88) · obsessive compulsive disorder(5.82) · IMMUNE(5.28) · irritable bowel syndrome(5.28) · personality traits(4.75) · anxiety disorder(4.50) · REPRODUCTION(4.00) · depressive disorder major bipolar disorder(4.00) · sexual dysfunction physiological(4.00) · personality disorders(3.78) · depressive disorder major(3.72) · affective disorder(3.12) · anxiety related traits(3.00) · decision making(3.00) · psychoses(3.00) · personality(2.60) · panic disorder(2.19) · autism(2.13) · mood disorders(2.02) · CHEMDEPENDENCY(2.00) · OTHER(2.00) · PHARMACOGENOMIC(2.00) · UNKNOWN(2.00) · alcohol abuse smoking behavior(2.00) · alcoholism attention deficit hyperactivity disorder(2.00) · alcoholism recurrence(2.00) · antidepressant adverse effects(2.00) · anxiety(2.00) · auditory

evoked potential(2.00) · bipolar and unipolar disorder(2.00) · eating disorder(2.00) · hallucinations(2.00) · harm avoidance(2.00) · impulse control disorder(2.00) · manic depressive illness(2.00) · personality traits illegal drug use(2.00) · suicidal behavior(1.92) · alcoholism(1.92) · NEUROLOGICAL(1.80) · cocaine dependence(1.80) · major depression(1.80) · migraine migraine with aura(1.80) · neuroticism(1.80) · major depressive disorder(1.73) · migraine(1.73) · substance related disorders(1.67) · bulimia(1.47) · attention deficit hyperactivity disorder(1.16) · adhd attention deficit hyperactivity disorder(1.00) · aggressive behavior(1.00) · alcohol related disorders(1.00) · bipolar disorder depression(1.00) · conduct disorder(1.00) · eating disorders(1.00) · sudden infant death(1.00) · stress(1.00) · brain(1.00) · psychiatric disorders(1.00) · anorexia nervosa(0.93) · CARDIOVASCULAR(0.80) · hypertension pulmonary(0.80) · major psychoses(0.80) · bipolar disorder(0.79) · schizophrenia(0.69) · alcohol abuse(0.68) · bipolar affective disorder(0.67) · fibromyalgia(0.67) · sids sudden infant death syndrome(0.67) · smoking behavior(0.66) · mood disorder(0.60) · psychosis(0.60) · heroin abuse(0.53) · epilepsy temporal lobe(0.43) · sleep disorders(0.36) · cognitive function(0.33) · migraine with aura(0.33) · syncope vasovagal(0.33) · DEVELOPMENTAL(0.27) · mental retardation(0.27) · adhd(0.26) · METABOLIC(0.23) · weight gain(0.23) · smoking(0.21) · tourette syndrome(0.21) · alcohol(0.21) · migraine disorders(0.17) · cognitive ability(0.11) · chronic obstructive pulmonary disease(0.07) · hearing loss(0.07) · AGING(0.04) · longevity(0.04)

Relevant papers and external links:

PMID 8929413

PMID 17375136

PMID 18465388

PMID 18629430

PMID 19103261

PMID 19272758

PHARMGKB PA164920378
Evidence: PubMed ID:15993855This vatiant in the SLC6A4 gene, located upstream of the HTTLPR polymorphism, showed evidence of an association with treatment response, and biochemical experiments showed this polymorphism altered binding of nuclear extracts to a consensus sequence for the activator protein 2 transcription factor, which is believed to be a critical factor in regulating neural gene expression in mammals.

PHARMGKB PA162008701
Evidence: PubMed ID:18618621This promoter SNP is not associated with depression remission frequency upon treatment with citalopram in white Hispanics, white non-Hispanics, or Blacks.

dbSNP: rs25531 Genecard: SLC6A4 chromosome 17 SNPedia: rs25531(A;A)

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★ **rs4251417(G;G)** **info:1.15** **94.53%**

Association between a functional polymorphism in the serotonin transporter gene and diarrhoea predominant irritable bowel syndrome in women.

Sexually dimorphic effects of four genes (COMT, SLC6A2, MAOA, SLC6A4) in genetic associations of ADHD: a preliminary study.

Variants of the serotonin transporter gene and NEO-PI-R Neuroticism: No association in the BLSA and SardiNIA samples.

Gene related topics:

PSYCH(24.57) · depression(24.57) · suicide(6.88) · obsessive compulsive disorder(5.82) · IMMUNE(5.28) · irritable bowel syndrome(5.28) · personality traits(4.75) · anxiety disorder(4.50) · REPRODUCTION(4.00) · depressive disorder major bipolar disorder(4.00) · sexual dysfunction physiological(4.00) · personality disorders(3.78) · depressive disorder major(3.72) · affective disorder(3.12) · anxiety related traits(3.00) · decision making(3.00) · psychoses(3.00) · personality(2.60) · panic disorder(2.19) · autism(2.13) · mood disorders(2.02) · CHEMDEPENDENCY(2.00) · OTHER(2.00) · PHARMACOGENOMIC(2.00) · UNKNOWN(2.00) · alcohol abuse smoking behavior(2.00) · alcoholism attention deficit hyperactivity disorder(2.00) · alcoholism recurrence(2.00) · antidepressant adverse effects(2.00) · anxiety(2.00) · auditory evoked potential(2.00) · bipolar and unipolar disorder(2.00) · eating disorder(2.00) · hallucinations(2.00) · harm avoidance(2.00) · impulse control disorder(2.00) · manic depressive illness(2.00) · personality traits illegal drug use(2.00) · suicidal behavior(1.92) · alcoholism(1.92) · NEUROLOGICAL(1.80) · cocaine dependence(1.80) · major depression(1.80) · migraine migraine with aura(1.80) · neuroticism(1.80) · major depressive disorder(1.73) · migraine(1.73) · substance related disorders(1.67) · bulimia(1.47) · attention deficit hyperactivity disorder(1.16) · adhd attention deficit hyperactivity disorder(1.00) · aggressive behavior(1.00) · alcohol related disorders(1.00) · bipolar disorder depression(1.00) · conduct disorder(1.00) · eating disorders(1.00) · sudden infant death(1.00) · anorexia nervosa(0.93) · CARDIOVASCULAR(0.80) · hypertension pulmonary(0.80) · major psychoses(0.80) · bipolar disorder(0.79) · schizophrenia(0.69) · alcohol abuse(0.68) · bipolar affective disorder(0.67) · fibromyalgia(0.67) · sids sudden infant death syndrome(0.67) · smoking behavior(0.66) · mood disorder(0.60) · psychosis(0.60) · heroin abuse(0.53) · epilepsy temporal lobe(0.43) · sleep disorders(0.36) · cognitive function(0.33) · migraine with aura(0.33) · syncope vasovagal(0.33) · DEVELOPMENTAL(0.27) · mental retardation(0.27) · adhd(0.26) · METABOLIC(0.23) · weight gain(0.23) · smoking(0.21) · tourette syndrome(0.21) · alcohol(0.21) · migraine disorders(0.17) · cognitive ability(0.11) · chronic obstructive pulmonary disease(0.07) · hearing loss(0.07) · AGING(0.04) · longevity(0.04)

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Relevant papers and external links:

PHARMGKB PA164920374
Evidence: PubMed ID:19541292This study identified a two-SNP haplotype proxy for 5HTTLPR (the length polymorphism repeat in the promoter region of the SLC6A4 gene) ; the CA haplotype of SNPs rs4251417 and rs2020934 is coupled with the short allele of 5HTTLPR (r(2) = .72).

PMID 15361494

PMID 18937309

PMID 19199283

dbSNP: rs4251417 Genecard: SLC6A4 chromosome 17 SNPedia: rs4251417(G;G)

★ **rs56164415(G;G)** **good:0.35** **80.85%**

Gene related topics:

PSYCH(2.33) · depression(2.33) · NEUROLOGICAL(2.00) · affective psychoses(2.00) · alzheimer disease amnesia(2.00) · bipolar disorder(1.66) · CHEMDEPENDENCY(1.00) · amphetamine related disorders(1.00) · schizophrenia(0.94) · major depressive disorder(0.68) · alzheimer s disease(0.59) · METABOLIC(0.56) · weight(0.56) · personality(0.55) · obsessive compulsive disorder(0.40) · UNKNOWN(0.36) · dyskinesia drug

induced(0.36) · cognitive function(0.33) · parkinsons disease(0.29) · DEVELOPMENTAL(0.27) · IMMUNE(0.27) · dermatitis atopic(0.27) · mental retardation(0.27) · huntington s disease(0.26) · adhd attention deficit hyperactivity disorder(0.21) · anorexia nervosa(0.15) · autism(0.12) · body weight obesity(0.11) · cognitive ability(0.11) · panic disorder(0.08) · migraine disorders(0.08) · attention deficit hyperactivity disorder(0.05) · personality traits(0.05) · smoking(0.05) · epilepsy(0.04) · smoking behavior(0.04) · suicide(0.04)

Relevant papers and external links:

dbSNP: rs56164415 Genecard: BDNF chromosome 11 SNPedia: rs56164415(G;G)

★ rs1801028(C;C) good:0.35 93.75% **normal risk**

rs1801028 is a SNP in the dopamine D2 receptor DRD2 gene. A meta-analysis comprising 27 samples and over 3,707 schizophrenia patients concluded that Cys/Ser heterozygotes, i.e. rs1801028(C;G) genotypes, were at elevated risk for schizophrenia when compared to either homozygote genotype (rs1801028(C;C) or rs1801028(G;G)). The odds ratio was 1.4 (p<0.005).

An earlier meta-analysis comprising over 9,000 schizophrenia patients concluded pretty much the same thing: the Cys311 (rs1801028(G)) allele frequency led to an odds ratio of 1.43 (CI: 1.16-1.78, p<0.001) for this risk allele.

A study of ~120 Chinese patients with schizophrenia concluded that Cys/Ser heterozygotes may not respond to risperidone treatment as well as Ser/Ser homozygotes.

A paper has been published describing mistakes made in assigning allele status for this SNP:

(free full text) Misassigned alleles can annihilate efforts to control quality in otherwise well-designed genetic association analyses. To date, the issue remains underreported, as is exemplified by studies of a diallelic DRD2 missense variant in schizophrenia. For this variant, allele frequency data have been either misassigned, or incorrectly cited on four consecutive occasions. Contrary to conjecture, low heterozygosity has not guarded against the error with regard to rs1801028, a SNP that features a canonical base pair transversion, G:C.

In the case of rs1801028, rs1801028(C) is the more common allele, encoding the amino acid Serine at position 311, whereas rs1801028(G) encodes Cysteine.

Gene related topics:

CHEMDEPENDENCY(6.04) · alcoholism(6.04) · alcoholism substance related disorders(4.00) · PSYCH(2.30) · schizophrenia(2.30) · METABOLIC(2.00) · NEUROLOGICAL(2.00) · hyperprolactinaemia hyperprolactinemia(2.00) · nervous system diseases(2.00) · substance withdrawal syndrome(2.00) · substance withdrawal syndrome tobacco use disorder(2.00) · tic combined vocal and multiple motor tourette syndrome(2.00) · smoking behavior(1.74) · UNKNOWN(1.29) · neuroleptic malignant syndrome(1.29) · heroin dependence(1.00) · methamphetamine abuse(1.00) · tardive dyskinesia(0.95) · heroin abuse(0.83) ·

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cocaine dependence(0.80) · cocaine related disorders(0.67) · delirium(0.57) · impulsivity(0.57) · alcohol abuse(0.52) · tobacco use disorder(0.44) · adhd(0.40) · mood disorders(0.40) · parkinson s disease(0.40) · smoking(0.33) · alcohol(0.32) · mood disorder(0.27) · substance related disorders(0.27) · CARDIOVASCULAR(0.25) · atrial natriuretic factor(0.25) · alcohol dependence(0.22) · personality traits(0.21) · tourette syndrome(0.21) · dyslexia(0.19) · migraine disorders(0.17) · adhd attention deficit hyperactivity disorder(0.15) · personality(0.14) · personality disorders(0.12) · depressive disorder major(0.10) · bipolar disorder(0.07) · attention deficit hyperactivity disorder(0.05) · autism(0.03)

Relevant papers and external links:

PMID 16402354

PMID 12707934

PMID 15140279

PMID 18154681

PHARMGKB PA161145173
Evidence: Web Resource:External Link variant has decreased affinity for dopamine; no clear concensus on association between Ser311Cys polymorphism and schizophrenia.

dbSNP: rs1801028 Genecard: DRD2 chromosome 11 SNPedia: rs1801028(C;C)

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★ **rs165599(A;G)** **info:0.25** **49.98%**

anxiety-related personality traits, ADHD, schizophrenia

part of a three marker haplotype rs737865-rs4680-rs165599

epistasis between SNPs in COMT (rs2097603, Val158Met (rs4680), rs165599) and polymorphisms in other schizophrenia susceptibility genes

popular in pubmed

is associated with bipolar disorder and influences prefrontal aspects of verbal memory in bipolar patients and healthy controls.

Gene related topics:

UNKNOWN(6.00) · digeorge syndrome pharyngeal pouch syndrome(6.00) · PSYCH(5.72) · schizophrenia(5.72) · CANCER(3.00) · neoplasms pain(3.00) · fibromyalgia(2.67) · NEUROLOGICAL(2.00) · mamographic density(2.00) · pain temporomandibular joint disorders(2.00) · psychosis(1.67) · obsessive compulsive disorder(1.31) · CHEMDEPENDENCY(1.07) · substance related disorders(1.07) · panic disorder(1.03) · adhd attention deficit hyperactivity disorder(1.00) · eating disorders(1.00) · anxiety(1.00) · memory(1.00) · pain(0.94) · breast cancer(0.83) · marijuana abuse(0.67) · mood disorders(0.62) · parkinson s disease(0.62) · DEVELOPMENTAL(0.60) · leiomyoma uterine neoplasms(0.60) · mental retardation(0.60) · schizophrenia bipolar disorder(0.60) · OTHER(0.57) · sleep deprivation(0.57) · bipolar disorder(0.50) · depression(0.50) · fractures bone(0.50) · personality(0.38) · mammographic density(0.36) · personality traits(0.33) · heroin abuse(0.30) · alcoholism(0.29) · adhd(0.26) · cognitive ability(0.25) · heroin dependence(0.25) · bulimia(0.24) · endometrial cancer(0.23) · smoking(0.21) · anorexia nervosa(0.15) · suicide(0.14) · liver cancer(0.13) · tobacco use disorder(0.11) · narcolepsy(0.11) · METABOLIC(0.10) ·

weight gain(0.10) · smoking behavior(0.09) · endometrial neoplasms(0.07) · attention deficit hyperactivity disorder(0.05) · IMMUNE(0.05) · vitiligo(0.05) · autism(0.03) · REPRODUCTION(0.02) · endometriosis(0.02)

Relevant papers and external links:

PMID 17547583

OMIM 104300

OMIM 116790

PHARMGKB PA164888988
Evidence: PubMed ID:19451915In a study of 78 African American and 65 white patients diagnosed with schizophrenia or schizoaffective disorder, this SNP in the COMT gene was found to have significant associations with response to risperidone over 2-12 weeks in both African-American and white patients.

PHARMGKB PA162168065
Evidence: PubMed ID:16876132This variant may predict a favorable outcome for bupropion treatment for smoking cessation

dbSNP: rs165599 Genecard: COMT chromosome 22 SNPedia: rs165599(A;G)

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★ rs28914832(A;A) good:1.40 99.96% **common in complete genomics**

Allelic heterogeneity at the serotonin transporter locus (SLC6A4) confers susceptibility to autism and rigid-compulsive behaviors.

Enhanced activity of human serotonin transporter variants associated with autism.

Characterization of a functional polymorphism in the 3' UTR of SLC6A4 and its association with drinking intensity.

Gene related topics:

PSYCH(24.57) · depression(24.57) · suicide(6.88) · obsessive compulsive disorder(5.82) · IMMUNE(5.28) · irritable bowel syndrome(5.28) · personality traits(4.75) · anxiety disorder(4.50) · REPRODUCTION(4.00) · depressive disorder major bipolar disorder(4.00) · sexual dysfunction physiological(4.00) · personality disorders(3.78) · depressive disorder major(3.72) · affective disorder(3.12) · anxiety related traits(3.00) · decision making(3.00) · psychoses(3.00) · personality(2.60) · panic disorder(2.19) · autism(2.13) · mood disorders(2.02) · CHEMDEPENDENCY(2.00) · OTHER(2.00) · PHARMACOGENOMIC(2.00) · UNKNOWN(2.00) · alcohol abuse smoking behavior(2.00) · alcoholism attention deficit hyperactivity disorder(2.00) · alcoholism recurrence(2.00) · antidepressant adverse effects(2.00) · anxiety(2.00) · auditory evoked potential(2.00) · bipolar and unipolar disorder(2.00) · eating disorder(2.00) · hallucinations(2.00) · harm avoidance(2.00) · impulse control disorder(2.00) · manic depressive illness(2.00) · personality traits illegal drug use(2.00) · suicidal behavior(1.92) · alcoholism(1.92) · NEUROLOGICAL(1.80) · cocaine dependence(1.80) · major depression(1.80) · migraine migraine with aura(1.80) · neuroticism(1.80) · major depressive disorder(1.73) · migraine(1.73) · substance related disorders(1.67) · bulimia(1.47) · attention deficit hyperactivity disorder(1.16) · adhd attention deficit hyperactivity disorder(1.00) · aggressive behavior(1.00) · alcohol related disorders(1.00) · bipolar disorder depression(1.00) · conduct disorder(1.00) · eating disorders(1.00) · sudden infant death(1.00) · anorexia nervosa(0.93) · CARDIOVASCULAR(0.80) · hypertension pulmonary(0.80) · major psychoses(0.80) · bipolar disorder(0.79) · schizophrenia(0.69) ·

alcohol abuse(0.68) · bipolar affective disorder(0.67) · fibromyalgia(0.67) · sids sudden infant death syndrome(0.67) · smoking behavior(0.66) · mood disorder(0.60) · psychosis(0.60) · heroin abuse(0.53) · epilepsy temporal lobe(0.43) · sleep disorders(0.36) · cognitive function(0.33) · migraine with aura(0.33) · syncope vasovagal(0.33) · DEVELOPMENTAL(0.27) · mental retardation(0.27) · adhd(0.26) · METABOLIC(0.23) · weight gain(0.23) · smoking(0.21) · tourette syndrome(0.21) · alcohol(0.21) · migraine disorders(0.17) · cognitive ability(0.11) · chronic obstructive pulmonary disease(0.07) · hearing loss(0.07) · AGING(0.04) · longevity(0.04)

Relevant papers and external links:

OMIM 182138

PMID 15995945

PMID 18957375

PMID 19032574

dbSNP: rs28914832 Genecard: SLC6A4 chromosome 17 SNPedia: rs28914832(A;A)

★ rs37022(T;T) good:1.02 41.52% **common in complete genomics**

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D2 dopamine receptor gene haplotypes and their influence on alcohol and tobacco consumption magnitude in alcohol-dependent individuals.

Neurotransmission and bipolar disorder: a systematic family-based association study.

Association of tagging single nucleotide polymorphisms on 8 candidate genes in dopaminergic pathway with schizophrenia in Croatian population.

Financial and psychological risk attitudes associated with two single nucleotide polymorphisms in the nicotine receptor (CHRNA4) gene.

Gene related topics:

PSYCH(9.95) · attention deficit hyperactivity disorder(9.95) · adhd attention deficit hyperactivity disorder(3.41) · schizophrenia methamphetamine abuse(2.00) · CHEMDEPENDENCY(1.25) · smoking behavior(1.25) · perceptual disorders(1.00) · bipolar disorder(1.00) · nicotine(1.00) · personality(0.98) · cocaine related disorders(0.67) · psychosis(0.60) · delirium(0.57) · impulsivity(0.57) · tourette syndrome(0.47) · adhd(0.40) · NEUROLOGICAL(0.40) · parkinson s disease(0.40) · REPRODUCTION(0.36) · prenatal exposure delayed effects(0.36) · schizophrenia(0.27) · substance related disorders(0.27) · heroin dependence(0.25) · bulimia(0.24) · alcohol(0.21) · dyslexia(0.19) · alcohol abuse(0.17) · alcoholism(0.16) · personality traits(0.12) · migraine disorders(0.08) · depression(0.07) · obsessive compulsive disorder(0.06) · autism(0.05) · smoking(0.05) · PHARMACOGENOMIC(0.02)

Relevant papers and external links:

PMID 17526637

PMID 18444252

PMID 19673036

PMID 19693267

dbSNP: rs37022 Genecard: SLC6A3 chromosome 5 SNPedia: rs37022(T;T)

★ rs821589(G;G) good:0.23 56.64% **common in complete genomics**

Gene related topics:

PSYCH(0.60) · schizophrenia bipolar disorder(0.60) · schizophrenia(0.35) · cognitive function(0.33) · NEUROLOGICAL(0.02) · amyotrophic lateral sclerosis(0.02)

Relevant papers and external links:

dbSNP: rs821589 Genecard: DISC1 chromosome 1 SNPedia: rs821589(G;G)

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★ rs41282918(A;A) good:0.53 **common in complete genomics**

Gene related topics:

PSYCH(2.33) · depression(2.33) · NEUROLOGICAL(2.00) · affective psychoses(2.00) · alzheimer disease amnesia(2.00) · bipolar disorder(1.66) · CHEMDEPENDENCY(1.00) · amphetamine related disorders(1.00) · schizophrenia(0.94) · major depressive disorder(0.68) · alzheimer s disease(0.59) · METABOLIC(0.56) · weight(0.56) · personality(0.55) · obsessive compulsive disorder(0.40) · UNKNOWN(0.36) · dyskinesia drug induced(0.36) · cognitive function(0.33) · parkinsons disease(0.29) · DEVELOPMENTAL(0.27) · IMMUNE(0.27) · dermatitis atopic(0.27) · mental retardation(0.27) · huntington s disease(0.26) · adhd attention deficit hyperactivity disorder(0.21) · anorexia nervosa(0.15) · autism(0.12) · body weight obesity(0.11) · cognitive ability(0.11) · panic disorder(0.08) · migraine disorders(0.08) · attention deficit hyperactivity disorder(0.05) · personality traits(0.05) · smoking(0.05) · epilepsy(0.04) · smoking behavior(0.04) · suicide(0.04)

Relevant papers and external links:

PHARMGKB PA164857053
Evidence: PubMed ID:19414708This variant (A/C) in the 3'UTR of the BDNF gene was associated with major depressive disorder in a study of 264 controls and 272 Mexican Americans with major depressive disorder. (OR= 2.13; p value=0.01; risk allele=A)

dbSNP: rs41282918 Genecard: BDNF chromosome 11 SNPedia: rs41282918(A;A)

★ rs6350(C;C) info:1.39 91.10%

Genetic polymorphisms in monoamine neurotransmitter systems show only weak association with acute post-surgical pain in humans.

SLC6A3 and body mass index in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial.

Familiality and molecular genetics of attention networks in ADHD.

Financial and psychological risk attitudes associated with two single nucleotide polymorphisms in the nicotine receptor (CHRNA4) gene.

Gene related topics:

PSYCH(9.95) · attention deficit hyperactivity disorder(9.95) · adhd attention deficit hyperactivity disorder(3.41) · schizophrenia methamphetamine abuse(2.00) · CHEMDEPENDENCY(1.25) · smoking behavior(1.25) · perceptual disorders(1.00) · ovarian cancer(1.00) · pain(1.00) · CANCER(1.00) · body mass(1.00) · cancer(1.00) · nicotine(1.00) · body mass index(1.00) · personality(0.98) · cocaine related disorders(0.67) · psychosis(0.60) · delirium(0.57) · impulsivity(0.57) · tourette syndrome(0.47) · adhd(0.40) · NEUROLOGICAL(0.40) · parkinson s disease(0.40) · REPRODUCTION(0.36) · prenatal exposure delayed effects(0.36) · schizophrenia(0.27) · substance related disorders(0.27) · heroin dependence(0.25) · bulimia(0.24) · alcohol(0.21) · dyslexia(0.19) · alcohol abuse(0.17) · alcoholism(0.16) · personality traits(0.12) · migraine disorders(0.08) · depression(0.07) · obsessive compulsive disorder(0.06) · autism(0.05) · smoking(0.05) · PHARMACOGENOMIC(0.02)

Relevant papers and external links:

PMID 16848906

PMID 19183461

PMID 19418498

PMID 19693267

dbSNP: rs6350 Genecard: SLC6A3 chromosome 5 SNPedia: rs6350(C;C)

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★ rs2228595(C;C) good:0.11 88.75% **common in complete genomics**

rs2228595 may contribute to risk for schizophrenia by modulating GRM3 splicing

Gene related topics:

schizophrenia(1.00)

Relevant papers and external links:

PMID 18256595

dbSNP: rs2228595 Genecard: GRM3 chromosome 7 SNPedia: rs2228595(C;C)

★ rs9534505(G;G) good:0.48 81.24% **common in complete genomics**

Gene related topics:

PSYCH(3.00) · anorexia nervosa(3.00) · anorexia nervosa bulimia(3.00) · PHARMACOGENOMIC(2.00) · impulsive behavior(2.00) · olanzapine(2.00) · response to clozapine(2.00) · schizophrenia affective disorder(2.00) · schizophrenia(1.64) · bulimia(0.94) · major depression(0.80) · suicidal behavior(0.69) · major depressive disorder(0.68) · depression(0.67) · obsessive compulsive disorder(0.58) · neuroleptic malignant syndrome(0.57) · schizophrenia tardive dyskinesia(0.57) · suicide(0.56) · personality disorders(0.50) · personality traits(0.47) · cognitive function(0.33) · depressive disorder major(0.29) · autism(0.28) · adhd(0.26) · mood disorders(0.23) · panic disorder(0.21) · adhd attention deficit hyperactivity disorder(0.21) · attention deficit hyperactivity disorder(0.21) · tourette syndrome(0.21) · bipolar disorder(0.20) · personality(0.14) · CHEMDEPENDENCY(0.13) · heroin abuse(0.13) · NEUROLOGICAL(0.11) · migraine(0.11) · tardive dyskinesia(0.11) · smoking behavior(0.09) · CARDIOVASCULAR(0.05) · blood pressure determination(0.05) · alcohol abuse(0.04)

Relevant papers and external links:

dbSNP: rs9534505 Genecard: HTR2A chromosome 13 SNPedia: rs9534505(G;G)

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★ rs16856202(T;T) good:0.26 88.15% **common in complete genomics**

Established associations:

amyotrophic lateral sclerosis **you have 0 copies of the risk allele C**

(risk allele=C, susceptibilty odds ratio/beta 2 with pval 8E-6, pubmedid=19451621)

Gene related topics:

PSYCH(0.60) · schizophrenia bipolar disorder(0.60) · schizophrenia(0.35) · cognitive function(0.33) · NEUROLOGICAL(0.02) · amyotrophic lateral sclerosis(0.02)

Relevant papers and external links:

PMID 19451621
Reduced expression of the kinesin-associated protein 3 (kifap3) gene increases survival in sporadic amyotrophic lateral sclerosis.

dbSNP: rs16856202 GWAS Catalog: rs16856202 Genecard: DISC1 chromosome 1

SNPedia: rs16856202(T;T)

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★ rs11214606(C;C) good:0.56 95.77% **common on affy axiom data**

ARVCF single marker and haplotypic association with schizophrenia.

Gene related topics:

CHEMDEPENDENCY(6.04) · alcoholism(6.04) · alcoholism substance related disorders(4.00) · PSYCH(2.30) · schizophrenia(2.30) · METABOLIC(2.00) · NEUROLOGICAL(2.00) · hyperprolactinaemia hyperprolactinemia(2.00) · nervous system diseases(2.00) · substance withdrawal syndrome(2.00) · substance withdrawal syndrome tobacco use disorder(2.00) · tic combined vocal and multiple motor tourette syndrome(2.00) · smoking behavior(1.74) · UNKNOWN(1.29) · neuroleptic malignant syndrome(1.29) · heroin dependence(1.00) · methamphetamine abuse(1.00) · tardive dyskinesia(0.95) · heroin abuse(0.83) · cocaine dependence(0.80) · cocaine related disorders(0.67) · delirium(0.57) · impulsivity(0.57) · alcohol abuse(0.52) · tobacco use disorder(0.44) · adhd(0.40) · mood disorders(0.40) · parkinson s disease(0.40) · smoking(0.33) · alcohol(0.32) · mood disorder(0.27) · substance related disorders(0.27) · CARDIOVASCULAR(0.25) · atrial natriuretic factor(0.25) · alcohol dependence(0.22) · personality traits(0.21) · tourette syndrome(0.21) · dyslexia(0.19) · migraine disorders(0.17) · adhd attention deficit hyperactivity disorder(0.15) · personality(0.14) · personality disorders(0.12) · depressive disorder major(0.10) · bipolar disorder(0.07) · attention deficit hyperactivity disorder(0.05) · autism(0.03)

Relevant papers and external links:

PMID 19508883

dbSNP: rs11214606 Genecard: DRD2 chromosome 11 SNPedia: rs11214606(C;C)

★ rs518147(C;-) info:0.80 47.25% **less weight gain if taking olanzapine**

rs518147, also known as -697G/C, is a SNP in the 5-hydroxytryptamine (serotonin) receptor 2C HTR2C gene.

A study of 107 patients with schizophrenia being treated with olanzapine reported a protective effect against weight-gain from the (C) allele of this SNP; fewer patients (of 28) with a rs518147(C) allele had a body mass index increase of >=10% (p=0.0006), whereas (G;G) homozygotes did. This effect may also involve nearby SNP rs3813929.

The association between HTR2C polymorphisms and obesity in psychiatric patients using antipsychotics: a cross-sectional study.

The association between HTR2C gene polymorphisms and the metabolic syndrome in patients with schizophrenia.

Multivariate permutation analysis associates multiple polymorphisms with subphenotypes of major depression.

HTR2C gene polymorphisms and the metabolic syndrome in patients with schizophrenia: a replication study.

Association of polymorphisms of the serotonergic system with smoking initiation in Caucasians.

HTR2C promoter polymorphisms are associated with risperidone efficacy in Chinese female patients.

Functional consequences of two HTR2C polymorphisms associated with antipsychotic-induced weight gain.

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Gene related topics:

olanzapine(5.00) · weight(5.00) · METABOLIC(3.60) · weight gain(3.60) · PHARMACOGENOMIC(2.00) · weight gain antipsychotic drug induced(2.00) · weight gain antipsychotic induced(2.00) · OTHER(1.00) · weight loss(1.00) · body mass(1.00) · metabolic syndrome(1.00) · schizophrenia(1.00) · major depression(1.00) · body mass index(1.00) · obesity(1.00) · depression(1.00) · smoking(1.00) · PSYCH(0.67) · bipolar affective disorder(0.67) · NEUROLOGICAL(0.33) · migraine with aura(0.33) · mood disorders(0.23) · suicide(0.22) · tardive dyskinesia(0.11) · personality(0.06) · attention deficit hyperactivity disorder(0.05) · personality traits(0.05) · depressive disorder major(0.05) · CHEMDEPENDENCY(0.04) · alcohol abuse(0.04) · autism(0.03)

Relevant papers and external links:

PMID 19434072

PHARMGKB PA164924605
Evidence: PubMed ID:19622037This variant is associated with Olanzapine-induced weight gain. The -697C allele confers protective effect towards Olanzapine-induced weight gain in a study consisting of 107 patients with schizophrenia.

PMID 17016522

PMID 17632216

PMID 18081710
PMID 19142101
PMID 20060656
PMID 20415561
PMID 21391883

dbSNP: rs518147 Genecard: HTR2C chromosome X SNPedia: rs518147(C;C)

★ rs1045642(C;C) info:1.50 36.58% **increased risk of cannabis dependence, lower (normal) cancer risk**

Association between ABCB1 C3435T polymorphism and increased risk of cannabis dependence. (2009). Patients with cannabis dependence (n=40) had a significantly higher 3435C allele frequency (62.5% versus 43.8% respectively, P=0.017) and CC genotype (50% versus 20%, P=0.005, OR=4.00 [1.50-10.60]). The CC genotype was independently associated with cannabis dependence. This is the first time a significant specific genetic marker has been shown in cannabis dependence. ABCB1 polymorphisms may alter Delta9THC distribution, its psychoactive effects and individual vulnerability to dependence.
rs1045642, also known as C3435T, is a SNP located in the ABCB1 gene. It is often studied in conjunction with rs2032582. C3435T has been mentioned by:

A "Silent" Polymorphism in the MDR1 Gene Changes Substrate Specificity (for example, to verapamil)
(R)-lansoprazole (Prevacid) concentrations are significantly increased in CYP2C19 extensive metabolizers with ABCB1 C3435T C allele.
In a Korean population, plasma concentrations of fexofenadine (Allegra) were 17% lower in 2677AA/3435CC subjects and 47% higher in the 2677TT/3435TT subjects compared to 2677GG/3435CC subjects.
In contrast, in this study no association was observed between the C3435T polymorphism and fexofenadine plasma or urine concentrations in a German Caucasian population.
A meta-analysis including 9 case-control studies (totaling ~2,500 patients) found no association between rs1045642 and epilepsy risk

A study of 98 methadone-maintaining patients concluded that the higher (>150 mg/day) and lower (< or =150 mg/day) methadone dose groups differed significantly in their rs1128503 status (experiment-wise p = 0.0325). Furthermore, individuals with the 3-locus genotype pattern (T;T)-(T;T)-(T;T) for SNPs rs1045642, rs2032582 and rs1128503, respectively, had an approximately 5-fold chance of requiring the 'higher' methadone dose, while individuals heterozygous for these three SNPs have an approximately 3-fold chance of stabilizing at the 'lower' methadone dose (point-wise p-value = 0.026).

Identifying candidate causal variants responsible for altered activity of the ABCB1 multidrug resistance gene.

Genetic predictors of the maximum doses patients receive during clinical use of the anti-epileptic drugs carbamazepine and phenytoin.

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ABCB1 genotypes and haplotypes in patients with dementia and age-matched non-demented control patients.

Association of MDR1 genotypes with susceptibility to colorectal cancer in older non-smokers.

Genetic studies of a cluster of acute lymphoblastic leukemia cases in Churchill County, Nevada.

MDR1 gene variants, indoor insecticide exposure, and the risk of childhood acute lymphoblastic leukemia.

No association between MDR1 (ABCB1) 2677G>T and 3435C>T polymorphism and sporadic colorectal cancer among Bulgarian patients.

ABCB1 (MDR1) gene polymorphisms are associated with the clinical response to paroxetine in patients with major depressive disorder.

Pharmacogenetics of minimal residual disease response in children with B-precursor acute lymphoblastic leukemia: a report from the Children's Oncology Group.

Multiplexed genotyping of ABC transporter polymorphisms with the Bioplex suspension array.

A PAI-1 (SERPINE1) polymorphism predicts osteonecrosis in children with acute lymphoblastic leukemia: a report from the Children's Oncology Group.

Association of ABCB1 genetic variants with renal function in Africans and in Caucasians.

Genotyping panel for assessing response to cancer chemotherapy.

Polymorphisms affecting gene transcription and mRNA processing in pharmacogenetic candidate genes: detection through allelic expression imbalance in human target tissues.

Bidirectional translational research: Progress in understanding addictive diseases.

The pharmacokinetics and pharmacogenomics of efavirenz and lopinavir/ritonavir in HIV-infected persons requiring hemodialysis.

No association of ABCB1 polymorphisms with drug-refractory epilepsy in a north Indian population.

Germline genetic variations in drug action pathways predict clinical outcomes in advanced lung cancer treated with platinum-based chemotherapy.

Prevalence in the United States of selected candidate gene variants: Third National Health and Nutrition Examination Survey, 1991-1994.

Opiate and cocaine addiction: from bench to clinic and back to the bench.

Investigation of candidate polymorphisms and disease activity in rheumatoid arthritis patients on methotrexate.

Steroid biosynthesis and renal excretion in human essential hypertension: association with blood pressure and endogenous ouabain.

Genetic determinants of target and novelty-related event-related potentials in the auditory oddball response.

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ABCB1 (MDR1) rs1045642 is associated with increased overall survival in plasma cell myeloma.

No significant effect of ABCB1 haplotypes on the pharmacokinetics of fluvastatin, pravastatin, lovastatin, and rosuvastatin.

Influence of ABCB1 polymorphisms and haplotypes on tacrolimus nephrotoxicity and dosage requirements in children with liver transplant.

Polymorphisms in the xenobiotic transporter Multidrug Resistance 1 (MDR1) and interaction with meat intake in relation to risk of colorectal cancer in a Danish prospective case-cohort study.

Effect of CYP3A and ABCB1 single nucleotide polymorphisms on the pharmacokinetics and pharmacodynamics of calcineurin inhibitors: Part I.

Effect of CYP3A and ABCB1 single nucleotide polymorphisms on the pharmacokinetics and pharmacodynamics of calcineurin inhibitors: Part II.

Explaining variability in ciclosporin exposure in adult kidney transplant recipients.

Pazopanib-induced hyperbilirubinemia is associated with Gilbert's syndrome UGT1A1 polymorphism.

ABCB1/MDR1 gene polymorphisms as a prognostic factor in colorectal cancer.

ABCB1 gene polymorphisms are associated with the severity of major depressive disorder and its response to escitalopram treatment.

Cytochrome P450 genetic polymorphisms influence the serum concentration of calcineurin inhibitors in allogeneic hematopoietic SCT recipients.

Pharmacogenetics of antidepressant response.

Correlation between genetic polymorphisms of the hOCT1 and MDR1 genes and the response to imatinib in patients newly diagnosed with chronic-phase chronic myeloid leukemia.

Impact of ABCB1 C3435T polymorphism on lymph node regression in multimodality treatment of locally advanced esophageal cancer.

Ultra-resistant schizophrenia is not associated with the multidrug-resistant transporter 1 (MDR1) gene rs1045642 variant.

The effects of CYP3A4, CYP3A5, ABCB1, ABCC2, ABCG2 and SLCO1B3 single nucleotide polymorphisms on the pharmacokinetics and pharmacodynamics of docetaxel in nasopharyngeal carcinoma patients.

Expression of CYP3A5 and P-glycoprotein in renal allografts with histological signs of calcineurin inhibitor nephrotoxicity.

Polymorphisms of the MDR1 and MIF genes in children with nephrotic syndrome.

The clinical impact of ABCB1 polymorphisms on the treatment of psychiatric diseases.

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Association of ABCB1, 5-HT3B receptor and CYP2D6 genetic polymorphisms with ondansetron and metoclopramide antiemetic response in Indonesian cancer patients treated with highly emetogenic chemotherapy.

Polymorphisms in genes that regulate cyclosporine metabolism affect cyclosporine blood levels and clinical outcomes in patients who receive allogeneic hematopoietic stem cell transplantation.

Common variants in ABCB1, ABCC2 and ABCG2 genes and clinical outcomes among women with advanced stage ovarian cancer treated with platinum and taxane-based chemotherapy: a Gynecologic Oncology Group study.

ABCB1 haplotype is associated with major molecular response in chronic myeloid leukemia patients treated with standard-dose of imatinib.

Variants in ABCB1, TGFB1, and XRCC1 genes and susceptibility to viral hepatitis A infection in Mexican Americans.

Influence of genomic ancestry on the distribution of SLCO1B1, SLCO1B3 and ABCB1 gene polymorphisms among Brazilians.

Association between the functional polymorphism (C3435T) of the gene encoding P-glycoprotein (ABCB1) and major depressive disorder in the Japanese population.

MDR1 C3435T polymorphism and cancer risk: a meta-analysis based on 39 case-control studies.

A comprehensive investigation on common polymorphisms in the MDR1/ABCB1 transporter gene and susceptibility to colorectal cancer.

Neither P-gp SNP variants, P-gp expression nor functional P-gp activity predicts MDR in a preliminary study of plasma cell myeloma.

PharmGKB summary: phenytoin pathway.

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Gene related topics:

PHARMACOGENOMIC(8.52) · tacrolimus pharmacokinetics(8.52) · NEUROLOGICAL(7.60) · epilepsy(7.60) · digoxin serum concentration(6.00) · cancer(5.00) · 9 hydroxyrisperidone risperidone(2.00) · CARDIOVASCULAR(2.00) · OTHER(2.00) · digoxin pharmacokinetics(2.00) · docetaxel pharmacokinetics(2.00) · drug related genes(2.00) · heart transplant(2.00) · lymphoproliferative disorders(2.00) · tacrolimus pharmcokinetics(2.00) · tacrolimus(1.64) · RENAL(1.00) · UNKNOWN(1.00) · acute coronary syndrome cardiovascular diseases(1.00) · femur head necrosis(1.00) · myocardial infarction stroke(1.00) · renal insufficiency(1.00) · saquinavir pharmacokinetics(1.00) · ovarian cancer(1.00) · arthritis(1.00) · metabolism(1.00) · carbamazepine(1.00) · survival(1.00) · rheumatoid arthritis(1.00) · blood pressure(1.00) · hematopoietic stem cell transplantation(1.00) · esophageal cancer(1.00) · hypertension(1.00) · colorectal cancer(1.00) · hyperbilirubinemia(1.00) · nephrotic syndrome(1.00) · schizophrenia(1.00) · nasopharyngeal carcinoma(1.00) · myeloid leukemia(1.00) · lung cancer(1.00) · dementia(1.00) · major depressive disorder(1.00) · essential hypertension(1.00) · phenytoin(1.00) · INFECTION(0.69) · hiv(0.69) · voriconazole(0.67) · IMMUNE(0.61) · crohn s disease ulcerative colitis(0.61) · pravastatin kinetics(0.57) · kidney transplant complications(0.53) · nevirapine(0.50) · paclitaxel pharmacokinetics(0.50) · cyclosporine(0.40) · liver transplant(0.40) · hiv 1(0.33) · CANCER(0.31) · leukemia lymphoid(0.31) · hiv infections(0.29) · leukemia myelogenous chronic bcr abl positive(0.26) · leukemia(0.26) · precursor cell lymphoblastic leukemia lymphoma(0.24) · cirrhosis biliary primary(0.19) · epilepsy temporal lobe(0.19) · irinotecan pharmacokinetics(0.19) · hiv infections x human immunodeficiency virus disease(0.19) · inflammatory bowel disease(0.17) · coronary artery disease myocardial infarction(0.11) · multiple

myeloma(0.11) · METABOLIC(0.09) · body weight(0.09) · ulcerative colitis(0.09) · kidney transplant(0.08) · hypercholesterolemia(0.04) · leukemia myeloid acute(0.04) · arthritis rheumatoid(0.03) · crohn disease(0.03) · stomach neoplasms(0.02)

Relevant papers and external links:

PHARMGKB PA161145208
Evidence: Web Resource:External Link SNP is well-studied but there is no clear consensus on its significance for drug disposition, response or toxicity.

PHARMGKB PA161868039
Evidence: PubMed ID:17185560rs1045642 is associated with altered inhibition by verapamil and cyclosporin A of substrate uptake in vitro.

PHARMGKB PA162290073
Evidence: PubMed ID:12082591Individuals that are homozygotes for 3435T alleles of ABCB1 have increased risk of developing nortriptyline-induced postural hypotension.This variant is also associated with expression level and in vivo function of ABCB1.

PHARMGKB PA162355845
Evidence: PubMed ID:12082591The T allele of this SNP is associated with nortriptyline-induced postural hypotension in patients treated for major depression. This SNP is not associated with response to treatment with nortriptyline or fluoxetine.

PHARMGKB PA162363714
Evidence: PubMed ID:19093297Indian rheumatoid arthritis patients heterozygous for this SNP (CT genotype) had about double the risk of non-response to methotrexate.

PHARMGKB PA162928798
Evidence: PubMed ID:16912956Decreased risk of hepatotoxicity was associated with ABCB1:3435C>T in a study of HIV patients receiving either efavirenz- or nevirapine-containing drug regimens.

PHARMGKB PA162928797
Evidence: PubMed ID:16912957In a study of HIV patients in South Africa, participants who experienced hepatotoxicity were less likely to have at least one T allele of the variant ABCB1:3435C>T.

PHARMGKB PA162372986
Evidence: PubMed ID:17112805; PubMed ID:19106083The C3435T variant (rs1045642) at exon 26 in the ABCB1 was showed to influence clopidogrel absorption in patients with a cardiovascular disease. Plasma concentrations of clopidogrel and its active metabolite were reduced in patients carrying the TT genotype.

PHARMGKB PA162652705
Evidence: PubMed ID:17190370(R)-lansoprazole concentrations significantly increased in CYP2C19 extensive metabolizers with the ABCB1 C3435T C allele, but not TT genotype, after renal transplantation and treatment with tacrolimus and lansoprazole.

PHARMGKB PA164920327
Evidence: PubMed ID:16950614Patients with both rs1045642 and rs2032582 variants have been associated with neutropenia from paclitaxel.

PHARMGKB PA164920323
Evidence: PubMed ID:18836089Patients with this variant with metastatic breast cancer treated with palitaxel showed a significantly lower disease control rate and lower overall survival rate than the CC variant allele.

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PHARMGKB PA165107206
Evidence: PubMed ID:19752884In Slovak (White) breast cancer patients (n=221) receiving anthracycline-based chemotherapy, the CC genotype of ABCB1:3435C>T was associated with longer time to progression.

PHARMGKB PA164946503
Evidence: PubMed ID:12352921; Web Resource:External Link or phenotype-associated allele: T allele. Phenotype: Decreased drug-induced neurotoxicity (e.g. convulsion, tremor, leukoencephalopathy) in recipients of liver transplantation associated with the T allele in combination with other factors (e.g. ABCB1:2677G>T/A, tacrolimus trough concentration, aspartate aminotransferase, ratio of graft weight-to-recipient's standard liver volume). Study size: 17 (6 with and 11 without neurotoxicity). Study population/ethnicity: Liver transplant patients from Kyushu University Hospital in Japan. Significance metric(s): chi-squared = 7.91; $p < 0.005$. Type of association: GN; PK; PD; TOX; ADR.

PHARMGKB PA165108055
Evidence: PubMed ID:17038883Risk or phenotype-associated allele: T. Phenotype: In subjects carrying one or two T alleles of this variant, the plasma olanzapine level alone was positively associated with percent change in Brief Psychiatric Rating Scale (BPRS) score. As olanzapine plasma levels increased, the BPRS score increased. Study size: 41. Study population/ethnicity: Patients with schizophrenia; > 90% Caucasian. Significance metric(s): $p = 0.02$. Type of association: CO.

PHARMGKB PA164953199
Evidence: PubMed ID:16331627Clinical outcome and P-gp activity was studied in Asian patients with de novo acute myeloid leukemia taking cytarabine and idarubicin, relative to ABCB1 genotypes, C3435T (rs1045642) and G2677T/A (rs2032582, Ala893Ser/Thr). Three-year event-free survival (EFS) was higher in 2677 GG homozygotes (893Ala/Ala) (60.6%) versus non-GG genotypes (893Ser allele-harboring subjects) (21.9%; $p = 0.02$), and in 3435 CC homozygotes versus non-CC genotypes ($p = 0.01$), and for 2677GG (893Ala/Ala)/3435CC diplotypes (58.2%) versus other diplotypes (22.6%; $p = 0.04$); although no significant genotypic or haplotypic association was observed for overall survival (OS). The rate of complete remission was significantly higher in 3435 CC ($p = 0.05$) and 2677 GG (893Ala/Ala) ($p = 0.04$) homozygotes, and for the 3435CC/2677GG diplotype ($p = 0.03$) compared to non-GC haplotype homozygotes. Using an in vitro daunorubicin accumulation assay with leukemic mononuclear cells from AML patients, 3435 CC homozygotes showed significantly lower P-gp activity (7.5%) than for CT (10.7%) and TT (19.9%) genotypes ($p = 0.029$); and G2677T/A (Ala893Ser/Thr) genotype had no effect ($p = 0.181$).

PHARMGKB PA164944054
Evidence: PubMed ID:115030143435TT homozygotes showed statistically different fenofexadine area under the concentration curve (AUC) values for 0-4 hours ($p = 0.036$) than CC homozygotes.

PHARMGKB PA164953179
Evidence: PubMed ID:17206635There was no significant association between the genotype C3435T distribution and the risk of Cyclosporin A failure in steroid resistance ulcerative colitis ($p = 0.23$).

PHARMGKB PA165291614
Evidence: PubMed ID:14711599Risk or phenotype-associated allele: none. Phenotype: Efavirenz and lopinavir plasma levels. Study size: 67. Study population/ethnicity: HIV patients. Significance metric(s): not available from abstract. Type of association: GN; PK.

PHARMGKB PA165291617

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Evidence: PubMed ID:15452306Risk or phenotype-associated allele: TT gentoype and T allele. Phenotype: Risk of antiepileptic drug resistance (refractory epilepsy) is not associated with the 3435 SNP, although the T allele (p = 0.013) and TT gentoype (OR = 2.67; p = 0.026) were associated with temporal lobe epilepsy (TLE) with hippocampal sclerosis (HS) compared to TLE without HS in a subgroup. Study size: 609 (401 drug-resistant and 208 drug-responsive); 226 TLE subgroup (116 with HS, 110 without HS). Study population/ethnicity: Ethnically-matched drug-resistant and drug-responsive epilepsy patients. Significance metric(s): p = 0.013 (allelic); OR = 2.67, p = 0.026 (genotypic). Type of association: GN; CO.

PHARMGKB PA165291616
Evidence: PubMed ID:15280437Risk or phenotype-associated allele: TT genotype. Phenotype: Decreased ABCB1 (P-gp) expression in placenta and liver. Study size: 115 (96 placental and 19 liver tissue samples). Study population/ethnicity: Japanese. Significance metric(s): p < 0.05. Type of association: GN; FA.

PHARMGKB PA165291615
Evidence: PubMed ID:14747421Risk or phenotype-associated allele: CC genotype. Phenotype: CC genotype associated with decreased tacrolimus levels after 1 and 3 months (p < 0.05), but no genotypic association at 6, 9, and 12 months (p > 0.05) post-transplantation immunosuppressive therapy. Study size: 83. Study population/ethnicity: Adult lung transplant recipients, from the USA. Significance metric(s): p < 0.05 (1, 3 months Tx); p > 0.05 (6, 9, 12 months Tx). Type of association: GN; PK.

PHARMGKB PA165291811
Evidence: PubMed ID:18377430Risk or phenotype-associated allele: T. Phenotype: A haplotype of ABCB1 c.1236C>T, c.2677G>A/T, and c.3435C>T (rs1128503, rs2032582 and rs1045642) was associated with increased drug exposure and reduced clearance. Study size: . Study population/ethnicity: Asian patients with Breast Neoplasms treated with doxorubicin. Significance metric(s): p = 0.03 (exposure); p= 0.01 (clearance). Type of association: PK.

PHARMGKB PA165374698
Evidence: PubMed ID:20801498Risk or phenotype-associated genotype: CC. Phenotype: In patients with or without ST-elevation acute coronary syndrome a higher rate of of ischaemic events were observed for patients with the ABCB1 3435 CC genotype (high-expression group) than for those with polymorphisms of intermediate (CT) or low expression (TT) who were on clopidogrel. Study size: 5148 patients receiving 75 mg clopidogrel once daily Study population/ethnicity: predominantly white (98%) Type of association: GN

PHARMGKB PA165110268
Evidence: PubMed ID:12781336Functional study of rs1045642 (3435C>T) and rs1128503 (2677G>T/A): in LLC-PK1 cells expressing wild-type (2677G/3435C) or polymorphic (2677G/3435T, 2677A/3435C, 2677A/3435T, 2677T/3435C, 2677T/3435T) constructs of ABCB1 in vitro, no significant differences were observed in transcellular efflux of structurally diverse P-gp substrates, verapamil, digoxin, vinblastine or cyclosporin A.

PHARMGKB PA165110368
Evidence: PubMed ID:12781336Functional study of rs1045642 (3435C>T) and rs2032582 (2677G>T/A): in LLC-PK1 cells expressing wild-type (2677G/3435C) or polymorphic (2677G/3435T, 2677A/3435C, 2677A/3435T, 2677T/3435C, 2677T/3435T) constructs of ABCB1 in vitro, no significant differences were observed in transcellular efflux of structurally diverse P-gp substrates, verapamil, digoxin, vinblastine or cyclosporin A.

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PHARMGKB PA165110372
Evidence: PubMed ID:15521904Haplotypes derived from the SNPs 2677G > T (rs2032582) and 3435C > T (rs1045642) do not influence the pharmacokinetics of tacrolimus in renal transplant patients

PHARMGKB PA165110370
Evidence: PubMed ID:14600574No significant association between allelic ABCB1 variants, C3435T (rs1045642) and G2677T/A (Ala893Ser) (rs2032582), and phase 1 or phase 2 viral decay, changes in lymphocyte subsets over time, or plasma trough ritonavir concentrations among 31 HIV-infected individuals initiating antiretroviral therapy.

PHARMGKB PA165110749
Evidence: PubMed ID:18851956Risk or phenotype-associated allele: 3435 CT and TT genotypes. Phenotype: ABCB1 polymorphisms were associated with risk for coronary artery disease (CAD) ($p<0.05$). Carriers of 3435 CT and TT genotypes (63%) and 2677 non-GG (non 893Ala/Ala) genotypes (64%) had higher frequency of family history of coronary artery disease (CAD) than the 3435CC (44%, $p = 0.042$) and 2677GG (46%, $p = 0.043$) carriers. The frequency of CAD in those carrying the 3435/2677 T/T haplotype (67%) was higher than that found in 3435/2677 non-T/T individuals (47%, $p = 0.021$). ABCB1 substrates (antiarrhythmics, beta-blockers, diuretics, ACE inhibitors, and others) or inhibitors (antiarrhythmics, calcium antagonists, calcium channel blockers, antidepressants and others) did not affect the baseline ABCB1 expression, but ABCB1 inhibitors reversed the effects of atorvastatin on both ABCB1 and ABCC1 transporters. Study size: 136. Study population/ethnicity: Hypercholesterolemic individuals, treated with atorvastatin (10mg/day/4 weeks), evaluated for CAD risk factors at the Institute Dante Pazzanese of Cardiology and the Hospital of the Sao Paulo University in Sao Paulo City, Brazil. Significance metric(s): $p < 0.05$. Type of association: GN; PD; FA

PHARMGKB PA165111311
Evidence: PubMed ID:15122075Risk or phenotype-associated allele: none. Phenotype: There was no significant association between systemic exposure of tipifarnib (AUC levels) and rs1045642 genotype. Study size: 28 (16 male). Study population/ethnicity: Caucasian cancer patients, aged 34-75. Significance metric(s): Not significant, $p = 0.92$. Type of association: GN; PK

PHARMGKB PA165291600
Evidence: PubMed ID:11809184Risk or phenotype-associated allele: TT allele. Phenotype: Increased efavirenz and nelfinavir response after 6 months treatment. Study size: 123. Study population/ethnicity: White HIV patients. Significance metric(s): $p = 0.0001$. Type of association: GN; PD.

PHARMGKB PA165110748
Evidence: PubMed ID:12781336Risk or phenotype-associated allele: None. Phenotype: Efflux of P-glycoprotein substrates (verapamil; digoxin; vinblastine; cyclosporin A) in vitro were not significantly affected by combined mutations for rs1128503 (2677G>T/A) and rs1045642 (3435C>T) in LLC-PK1 cell lines. Study size: Triplicate cell assays. Study population/ethnicity: N/A. Significance metric(s): Not significant, $p > 0.05$. Type of association: FA

PHARMGKB PA165111621
Evidence: PubMed ID:20017669Risk or phenotype-associated allele: C. Phenotype: This variant is associated with nevirapine-induced hepatotoxicity in patients from Mozambique, with the T allele showing a protective effect. Study size: 156 (78 with nevirapine-induced hepatotoxicity and 78 without adverse events).

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Study population/ethnicity: HIV infected patients from Mozambique. Significance metric(s): p = 0.038; odds ratio: 0.42. Type of association: GN; CO

PHARMGKB PA165291599
Evidence: PubMed ID:11434506Risk or phenotype-associated allele: TT genotype. Phenotype: Decreased ABCB1 (P-gp) expression in leukocytes isolated from subjects, and increased in vitro rhodamine exposure in peripheral blood cells isolated from subjects. Study size: 31. Study population/ethnicity: Caucasians from Germany. Significance metric(s): p < 0.01. Type of association: GN; FA.

PHARMGKB PA165291598
Evidence: PubMed ID:10716719Risk or phenotype-associated allele: TT genotype. Phenotype: Decreased expression of intestinal ABCB1 (P-gp) (p = 0.056, n = 21), and increased plasma levels of digoxin relative to the CC genotype (p = 0.006, n = 14). Study size: 21 duodenum samples, and 14 PK subjects. Study population/ethnicity: Caucasians from Germany. Significance metric(s): p = 0.006 - 0.056. Type of association: GN; PK; FA.

PHARMGKB PA165291619
Evidence: PubMed ID:15778422Risk or phenotype-associated allele: none. Phenotype: No genetic association with dicloxacillin pharmacokinetics given 1g dicloxacillin prior to or after 600 mg rifampin (ABCB1 (P-gp) inducer). Study size: 18 (13 male). Study population/ethnicity: Healthy volunteers (12 Caucasian, 5 Asian, 1 African American, 1 subject undetermined) from San Francisco, California, USA. Significance metric(s): not significant. Type of association: GN; PK.

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PHARMGKB PA165291623
Evidence: PubMed ID:12492608; Web Resource:External Link or phenotype-associated allele: none. Phenotype: No association with digoxin disposition (AUC, C(max), T(max)) after a single oral dose. Study size: 50. Study population/ethnicity: Healthy, unrelated, white male non-smokers, aged 18-40, from Berlin, Germany. Significance metric(s): p >= 0.3. Type of association: GN; PK.

PHARMGKB PA165291622
Evidence: PubMed ID:12175731; Web Resource:External Link or phenotype-associated allele: CC genotype. Phenotype: Increased time to wean from steroid treatment in pediatric heart transplantation. Study size: 69. Study population/ethnicity: Pediatric heart transplant patients from the Children's Hospital of Pittsburgh, Pennsylvania, USA. Significance metric(s): p = 0.04. Type of association: GN; PD.

PHARMGKB PA165291625
Evidence: PubMed ID:12686700; Web Resource:External Link or phenotype-associated allele: CC genotype. Phenotype: Increased antiepileptic drug resistance. Study size: 315 (200 drug-resistant, 115 drug-responsive). Study population/ethnicity: Epilepsy patients from England, classified as drug-resistant or drug-responsive. Significance metric(s): OR = 2.66; p = 0.006. Type of association: GN; PD.

PHARMGKB PA165291624
Evidence: PubMed ID:12684679; Web Resource:External Link or phenotype-associated allele: TT genotype. Phenotype: Increased drug response to anthracyclines and taxanes in breast cancer. Study size: 68. Study population/ethnicity: Locally advanced stage breast cancer patients undergoing preoperative chemotherapy. Significance metric(s): p = 0.029. Type of association: GN; PD.

PHARMGKB PA165291627

Evidence: PubMed ID:12969965; Web Resource:External Link or phenotype-associated allele: CC genotype. Phenotype: Increased etoposide clearance. Study size: 109 (104 whites, 42 blacks). Study population/ethnicity: Black and white children, newly diagnosed with acute lymphoblastic leukemia, from the USA. Significance metric(s): p = 0.027. Type of association: GN; PK.

PHARMGKB PA165291626
Evidence: PubMed ID:12739761; Web Resource:External Link or phenotype-associated allele: TT genotype. Phenotype: Decreased digoxin absorption after direct delivery to the surface of the duodenum by endoscope. Study size: 11 (5 CC genotype, 6 TT genotype). Study population/ethnicity: Unrelated, healthy subjects from Kobe, Japan. Significance metric(s): p = 0.007. Type of association: GN; PK.

PHARMGKB PA165291629
Evidence: PubMed ID:14586389; Web Resource:External Link or phenotype-associated allele: none. Phenotype: No association with plasma levels after a single dose of loperamide, nor drug-induced respiratory depression (pharmacodynamic evidence of brain penetration as an unintended drug target). Study size: 16 (8 TT genotype, 8 CC genotype). Study population/ethnicity: Healthy Caucasians from San Francisco, California, USA. Significance metric(s): p > 0.05. Type of association: GN; PK; ADR.

PHARMGKB PA165291628
Evidence: PubMed ID:14583680; Web Resource:External Link or phenotype-associated allele: TT genotype. Phenotype: Decreased tacrolimus levels in a subset of 29 post-operative kidney transplant patients (p < 0.01), and lower incidence of steroid-induced osteonecrosis in 136 patients (OR = 0.1; p = 0.034). Study size: 136 (30 osteonecrosis cases, 106 without osteonecrosis for 2 years post-transplant). Study population/ethnicity: Post-operative kidney transplant patients from Japan. Significance metric(s): OR = 0.10, p = 0.034 (osteonecrosis incidence); p < 0.01 (tacrolimus levels). Type of association: GN; PK; ADR.

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PHARMGKB PA165291621
Evidence: PubMed ID:12142082; Web Resource:External Link or phenotype-associated allele: TT genotype. Phenotype: Decreased or no ABCB1 (P-gp) expression in mammary and ovarian carcinoma cell lines. Study size: < 40. Study population/ethnicity: not stated. Significance metric(s): p = 0.0448. Type of association: GN; FA.

PHARMGKB PA165291620
Evidence: PubMed ID:11994059; Web Resource:External Link or phenotype-associated allele: TT genotype. Phenotype: Increased cellular rhodamine levels in leukocytes isolated from subjects (p < 0.05), but no association with fexofenadine plasma levels in the subjects. Study size: 20. Study population/ethnicity: Caucasian volunteers from Germany. Significance metric(s): p < 0.05 Type of association: GN; PK; FA.

PHARMGKB PA165291630
Evidence: PubMed ID:16267764; Web Resource:External Link or phenotype-associated allele: T allele, TT genotype. Phenotype: Association with decreased virologic failure (p = 0.05, TT vs. CC/CT), decreased drug resistance (OR = 0.56, p = 0.05), and increased toxicity-related treatment failure (p = 0.05) with efavirenz (EFV); however, no association with nelfinavir (NLF) or efavirenz response (e.g. increase in CD4 T cell count) (p > 0.1) nor nelfinavir or efavirenz exposure. Study size: 504 (340 efavirenz, 348 nelfinavir, 184 both drugs). Study population/ethnicity: Subset of larger study of 504 (49% whites, 31% blacks, 19% Hispanics from the USA and Italy) randomized antiretroviral-naive HIV-1 patients who were administered efavirenz plus

two nucleoside analogues. Significance metric(s): p = 0.05 (ERV: less virologic failure, drug resistance, tox-related Tx failure); p > 0.1 (EFV/NLF response); not significant (EFV/NLF exposure). Type of association: GN; PK; PD; TOX; ADR.

PHARMGKB PA165374665
Evidence: PubMed ID:20801494Risk or phenotype-associated genotype: TT. Phenotype: ABCB1 3435C>T genotype was significantly associated with the risk of cardiovascular death, myocardial infarction, or stroke (p=0.0064). ABCB1 3435 TT homozygotes had a 72% increased risk of cardiovascular death, myocardial infarction, or stroke compared with CT/CC individuals HR 1.72, 95% CI 1.22-2.44, p=0.002). CT heterozygotes were at similar risk to CC individuals (HR 0.94, 0.58-1.51). Study size/population: 1471 patients with acute coronary syndromes taking clopidogrel. Type of association: CO; GN; ADR

PHARMGKB PA165292171
Evidence: PubMed ID:15778422Risk or phenotype-associated allele: none. Phenotype: No association with dicloxacillan pharmacokinetics given 1g dicloxacillan prior to or after 600 mg rifampin (ABCB1 (P-gp) inducer). Study size: 18 (13 male). Study population/ethnicity: Healthy volunteers (12 Caucasian, 5 Asian, 1 African American, 1 subject undetermined) from San Francisco, California, USA. Significance metric(s): not significant. Type of association: GN; PK.

OMIM 171050

PHARMGKB PA165110728
Evidence: PubMed ID:12914549ABCB1 rs2032582 and rs1045642 genotype and peripheral blood lymphocyte efflux of P-gp substrate, rhodamine 123 (Rh123), in vitro, in healthy males: there was no significant difference in Rh123 efflux in CD56+ NK cells after 5, 10, 15, and 30 min efflux, or in CD4+ T-helper cells after 15, 30, 60, and 90 min between individuals with different genotypes. Rh123 efflux was not enhanced by a 10-day administration of P-gp inducer, rifampin, in vivo in 15 individuals before and after rifampin treatment. No genotypic effect was observed for inhibition of Rh123 efflux by P-pg inhibitor, verapamil, in vitro with CD56+ and CD4+.

PMID 17185560
PMID 17190370
PMID 15536457
PMID 11994059
PMID 20491876
PMID 18424454
OMIM 171050
OMIM 610064
PMID 15197162
PMID 15805193
PMID 16999857
PMID 17146660
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PMID 18182569
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PMID 21468756
PMID 21544031
PMID 21553324
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PMID 22134106
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PMID 22306099
PMID 22311042

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PMID 22396794
PMID 22434582
PMID 22569204

dbSNP: rs1045642 Genecard: ABCB1 chromosome 7 SNPedia: rs1045642(C;C)

★ rs27072(C;T) good:2.07 32.60% **Lower risk of alcohol withdrawal seizures, and perhaps lower odds of ADHD.**

Alcoholics with this are less likely to have seizures during alcohol withdrawal.
rs27072, a SNP in the dopamine transporter SLC6A3 gene, has been associated with more severe symptoms upon alcohol withdrawal, such as seizures, in a study of 250 Caucasian alcohol-dependent patients. Two haplotypes appear to be tagged by this SNP and a neighbor, rs27048. The rs27072 polymorphism has been shown to be significantly associated with ADHD in clinical samples of Canadian children aged 6 to 16 [Feng et al., 2005] and the significant association was also reported by Ouellet-Morin et al. in a Canadian twin study, 2008 (Am. J. of Medical Genetics Part B, 147B:1442-1449 (2008).

The interaction between the dopamine transporter gene and age at onset in relation to tobacco and alcohol use among 19-year-olds.

Association of promoter variants of human dopamine transporter gene with schizophrenia in Han Chinese.

Dopamine Transporter Gene Variant Affecting Expression in Human Brain is Associated with Bipolar Disorder.

Sequence variation in the 3'-untranslated region of the dopamine transporter gene and attention-deficit hyperactivity disorder (ADHD).

Association of the dopamine transporter gene and ADHD symptoms in a Canadian population-based sample of same-age twins.

Candidate gene studies of ADHD: a meta-analytic review.

Association between polymorphism of the dopamine transporter gene and early smoking onset: an interaction risk on nicotine dependence.

Gene and gene by sex associations with initial sensitivity to nicotine in nonsmokers.

Financial and psychological risk attitudes associated with two single nucleotide polymorphisms in the nicotine receptor (CHRNA4) gene.

Haplotypes of dopamine and serotonin transporter genes are associated with antisocial personality disorder in alcoholics.

Pharacogenetic effects of dopamine transporter gene polymorphisms on response to chlorpromazine and clozapine and on extrapyramidal syndrome in schizophrenia.

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The role of dopamine transporter (SLC6A3) and dopamine D2 receptor/ankyrin repeat and kinase domain containing 1 (DRD2/ANKK1) gene polymorphisms in personality traits.

Alcohol Dependence

Gene related topics:

PSYCH(9.95) · attention deficit hyperactivity disorder(9.95) · seizures(5.00) · adhd attention deficit hyperactivity disorder(3.41) · schizophrenia methamphetamine abuse(2.00) · CHEMDEPENDENCY(1.25) · smoking behavior(1.25) · perceptual disorders(1.00) · bipolar disorder(1.00) · brain(1.00) · antisocial personality disorder(1.00) · nicotine(1.00) · alcohol dependence(1.00) · nicotine dependence(1.00) · personality(0.98) · cocaine related disorders(0.67) · psychosis(0.60) · delirium(0.57) · impulsivity(0.57) · tourette syndrome(0.47) · adhd(0.40) · NEUROLOGICAL(0.40) · parkinson s disease(0.40) · REPRODUCTION(0.36) · prenatal exposure delayed effects(0.36) · schizophrenia(0.27) · substance related disorders(0.27) · heroin dependence(0.25) · bulimia(0.24) · alcohol(0.21) · dyslexia(0.19) · alcohol abuse(0.17) · alcoholism(0.16) · personality traits(0.12) · migraine disorders(0.08) · depression(0.07) · obsessive compulsive disorder(0.06) · autism(0.05) · smoking(0.05) · PHARMACOGENOMIC(0.02)

Relevant papers and external links:

PMID 18070248
OMIM 143465
OMIM 126455
PMID 19740369
PMID 19879111
PMID 21525861
PMID 16082693
PMID 18165969
PMID 19506906
PMID 14685824
PMID 18690117
PMID 19693267
PMID 20505557
PMID 20580759
PMID 21354244

dbSNP: rs27072 Genecard: SLC6A3 chromosome 5 SNPedia: rs27072(C;T)

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★ **rs1328674(G;G)** good:0.70 89.85% **average**

rs1328675 is part of a 4-SNP haplotype in the serotonin 2A receptor gene HTR2A that has been associated with rheumatoid arthritis in a study of 1800 European patients. The risk allele is rs1328674(A)

in dbSNP orientation. The overall risk for the haplotype CTCC of SNPs rs6311-rs1328674-rs6313-rs6314 is 1.68 (CI: 1.20 - 2.34, p = 0.02). This is actually quite close to the odds ratio calculated for rs1328674 by itself; OR of 1.62 (p = 0.007).

Note: the orientation of rs1328674 in dbSNP is opposite that cited by this publication; therefore, with respect to dbSNP, the haplotype of risk as cited above should be CACC, rather than CTCC as published.

Gene related topics:

PSYCH(3.00) · anorexia nervosa(3.00) · anorexia nervosa bulimia(3.00) · PHARMACOGENOMIC(2.00) · impulsive behavior(2.00) · olanzapine(2.00) · response to clozapine(2.00) · schizophrenia affective disorder(2.00) · schizophrenia(1.64) · arthritis(1.00) · rheumatoid arthritis(1.00) · bulimia(0.94) · major depression(0.80) · suicidal behavior(0.69) · major depressive disorder(0.68) · depression(0.67) · obsessive compulsive disorder(0.58) · neuroleptic malignant syndrome(0.57) · schizophrenia tardive dyskinesia(0.57) · suicide(0.56) · personality disorders(0.50) · personality traits(0.47) · cognitive function(0.33) · depressive disorder major(0.29) · autism(0.28) · adhd(0.26) · mood disorders(0.23) · panic disorder(0.21) · adhd attention deficit hyperactivity disorder(0.21) · attention deficit hyperactivity disorder(0.21) · tourette syndrome(0.21) · bipolar disorder(0.20) · personality(0.14) · CHEMDEPENDENCY(0.13) · heroin abuse(0.13) · NEUROLOGICAL(0.11) · migraine(0.11) · tardive dyskinesia(0.11) · smoking behavior(0.09) · CARDIOVASCULAR(0.05) · blood pressure determination(0.05) · alcohol abuse(0.04)

Relevant papers and external links:

PMID 18006541

dbSNP: rs1328674 Genecard: HTR2A chromosome 13 SNPedia: rs1328674(G;G)

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★ **rs769224(G;G)** **good:0.54** **90.19%**

The complex global pattern of genetic variation and linkage disequilibrium at catechol-O-methyltransferase.

Influence and interaction of genetic polymorphisms in catecholamine neurotransmitter systems and early life stress on antidepressant drug response.

Gene related topics:

UNKNOWN(6.00) · digeorge syndrome pharyngeal pouch syndrome(6.00) · PSYCH(5.72) · schizophrenia(5.72) · CANCER(3.00) · neoplasms pain(3.00) · fibromyalgia(2.67) · NEUROLOGICAL(2.00) · mamographic density(2.00) · pain temporomandibular joint disorders(2.00) · psychosis(1.67) · obsessive compulsive disorder(1.31) · CHEMDEPENDENCY(1.07) · substance related disorders(1.07) · panic disorder(1.03) · adhd attention deficit hyperactivity disorder(1.00) · eating disorders(1.00) · stress(1.00) · pain(0.94) · breast cancer(0.83) · marijuana abuse(0.67) · mood disorders(0.62) · parkinson s disease(0.62) · DEVELOPMENTAL(0.60) · leiomyoma uterine neoplasms(0.60) · mental retardation(0.60) · schizophrenia bipolar disorder(0.60) · OTHER(0.57) · sleep deprivation(0.57) · bipolar disorder(0.50) · depression(0.50) · fractures bone(0.50) · personality(0.38) · mammographic density(0.36) · personality traits(0.33) · heroin abuse(0.30) · alcoholism(0.29) · adhd(0.26) · cognitive ability(0.25) · heroin dependence(0.25) · bulimia(0.24) · endometrial cancer(0.23) · smoking(0.21) · anorexia nervosa(0.15) · suicide(0.14) · liver

cancer(0.13) · tobacco use disorder(0.11) · narcolepsy(0.11) · METABOLIC(0.10) · weight gain(0.10) · smoking behavior(0.09) · endometrial neoplasms(0.07) · attention deficit hyperactivity disorder(0.05) · IMMUNE(0.05) · vitiligo(0.05) · autism(0.03) · REPRODUCTION(0.02) · endometriosis(0.02)

Relevant papers and external links:

PMID 18574484

PMID 21680027

dbSNP: rs769224 Genecard: COMT chromosome 22 SNPedia: rs769224(G;G)

★ rs460000(C;C) info:2.06 33.60% **Better response to amphetamine**

Individuals with the C/C genotype at rs460000 (N = 83) reported approximately twofold higher ratings of stimulation and euphoria relative to the A/A+A/C (N = 69) genotype group, at both the 10 and 20 mg doses.

[PMID 20091113]

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Gene related topics:

PSYCH(9.95) · attention deficit hyperactivity disorder(9.95) · adhd attention deficit hyperactivity disorder(3.41) · schizophrenia methamphetamine abuse(2.00) · CHEMDEPENDENCY(1.25) · smoking behavior(1.25) · perceptual disorders(1.00) · personality(0.98) · cocaine related disorders(0.67) · psychosis(0.60) · delirium(0.57) · impulsivity(0.57) · tourette syndrome(0.47) · adhd(0.40) · NEUROLOGICAL(0.40) · parkinson s disease(0.40) · REPRODUCTION(0.36) · prenatal exposure delayed effects(0.36) · schizophrenia(0.27) · substance related disorders(0.27) · heroin dependence(0.25) · bulimia(0.24) · alcohol(0.21) · dyslexia(0.19) · alcohol abuse(0.17) · alcoholism(0.16) · personality traits(0.12) · migraine disorders(0.08) · depression(0.07) · obsessive compulsive disorder(0.06) · autism(0.05) · smoking(0.05) · PHARMACOGENOMIC(0.02)

Relevant papers and external links:

dbSNP: rs460000 Genecard: SLC6A3 chromosome 5 SNPedia: rs460000(C;C)

★ rs25532(C;T) info:3.02 **may be part of a haplotype associated with OCD**

rs25532 is a SNP in a regulatory region upstream of the serotonin transporter SLC6A4 gene. The more common allele, rs25532(C), is the higher-expressing allele.

A study of patients with obsessive compulsive disorder (OCD) concluded that the major allele of rs25532 was a major contributor to the association of a corresponding haplotype with this disorder.

Gene related topics:

PSYCH(24.57) · depression(24.57) · suicide(6.88) · obsessive compulsive disorder(5.82) · IMMUNE(5.28) · irritable bowel syndrome(5.28) · personality traits(4.75) · anxiety disorder(4.50) · REPRODUCTION(4.00) · depressive disorder major bipolar disorder(4.00) · sexual dysfunction physiological(4.00) · personality disorders(3.78) · depressive disorder major(3.72) · affective disorder(3.12) · anxiety related traits(3.00) · decision making(3.00) · psychoses(3.00) · personality(2.60) · panic disorder(2.19) · autism(2.13) · mood disorders(2.02) · CHEMDEPENDENCY(2.00) · OTHER(2.00) · PHARMACOGENOMIC(2.00) · UNKNOWN(2.00) · alcohol abuse smoking behavior(2.00) · alcoholism attention deficit hyperactivity disorder(2.00) · alcoholism recurrence(2.00) · antidepressant adverse effects(2.00) · anxiety(2.00) · auditory evoked potential(2.00) · bipolar and unipolar disorder(2.00) · eating disorder(2.00) · hallucinations(2.00) · harm avoidance(2.00) · impulse control disorder(2.00) · manic depressive illness(2.00) · personality traits illegal drug use(2.00) · suicidal behavior(1.92) · alcoholism(1.92) · NEUROLOGICAL(1.80) · cocaine dependence(1.80) · major depression(1.80) · migraine migraine with aura(1.80) · neuroticism(1.80) · major depressive disorder(1.73) · migraine(1.73) · substance related disorders(1.67) · bulimia(1.47) · attention deficit hyperactivity disorder(1.16) · adhd attention deficit hyperactivity disorder(1.00) · aggressive behavior(1.00) · alcohol related disorders(1.00) · bipolar disorder depression(1.00) · conduct disorder(1.00) · eating disorders(1.00) · sudden infant death(1.00) · anorexia nervosa(0.93) · CARDIOVASCULAR(0.80) · hypertension pulmonary(0.80) · major psychoses(0.80) · bipolar disorder(0.79) · schizophrenia(0.69) · alcohol abuse(0.68) · bipolar affective disorder(0.67) · fibromyalgia(0.67) · sids sudden infant death syndrome(0.67) · smoking behavior(0.66) · mood disorder(0.60) · psychosis(0.60) · heroin abuse(0.53) · epilepsy temporal lobe(0.43) · sleep disorders(0.36) · cognitive function(0.33) · migraine with aura(0.33) · syncope vasovagal(0.33) · DEVELOPMENTAL(0.27) · mental retardation(0.27) · adhd(0.26) · METABOLIC(0.23) · weight gain(0.23) · smoking(0.21) · tourette syndrome(0.21) · alcohol(0.21) · migraine disorders(0.17) · cognitive ability(0.11) · chronic obstructive pulmonary disease(0.07) · hearing loss(0.07) · AGING(0.04) · longevity(0.04)

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Relevant papers and external links:

PMID 18055562

PHARMGKB PA164920373

Evidence: PubMed ID:18055562This study found that the minor allele of the functional C > T single nucleotide polymorphism, rs25532, located less than 150 nucleotides centromeric of the serotonin transporter-linked polymorphic region indel (known as 5-HTTLPR) significantly decreased luciferase reporter gene expression levels by 15-80%, depending on 5-HTTLPR allele background and cell type.

dbSNP: rs25532 Genecard: SLC6A4 chromosome 17 SNPedia: rs25532(C;T)

★ rs11246226(A;C) good:1.81 49.90% **decreased risk of schizophrenia in limited study**

Associated with schizophrenia in a study of Croatians. Due to the limited number and diversity of the studied population, more study is needed to confirm any link. The C allele was associated with an decreased risk of schizophrenia.

Gene related topics:

PSYCH(21.00) · novelty seeking(21.00) · attention deficit hyperactivity disorder(9.95) · adhd(4.13) · OTHER(3.00) · behavior problems(3.00) · temperament(3.00) · personality traits(2.58) · disorganized attachment behavior(2.00) · major psychoses(1.80) · personality disorders(1.53) · impulsivity(1.29) · CHEMDEPENDENCY(1.20) · heroin abuse(1.20) · adhd attention deficit hyperactivity disorder(1.16) · bipolar disorder depression(1.00) · methamphetamine abuse(1.00) · schizophrenia(0.90) · mood disorder(0.60) · METABOLIC(0.53) · body mass(0.53) · NEUROLOGICAL(0.42) · tardive dyskinesia(0.42) · alcohol abuse(0.38) · cognitive function(0.33) · alcoholism(0.29) · psychosis(0.27) · bmi(0.25) · heroin dependence(0.25) · migraine(0.24) · mood disorders(0.23) · weight gain(0.23) · dyslexia(0.19) · smoking behavior(0.16) · obsessive compulsive disorder(0.15) · personality(0.14) · cognitive ability(0.11) · PHARMACOGENOMIC(0.04)

Relevant papers and external links:

PMID 19673036

PHARMGKB PA164892188

Evidence: PubMed ID:19238168This variant along with 3 other SNPs near DRD4 (4 SNP haplotype: rs3758653; rs916457; rs762502; rs11246226) is associated with tardive dyskinesia in male schizophrenia patients.

dbSNP: rs11246226 Genecard: DRD4 chromosome 11 SNPedia: rs11246226(A;C)

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★ rs1800458(G;G) good:0.72 95.38% **common in clinvar**

Transthyretin: no association between serum levels or gene variants and schizophrenia.

Association of TTR polymorphisms with hippocampal atrophy in Alzheimer disease families.

Gene related topics:

NEUROLOGICAL(3.00) · amyloid neuropathies familial(3.00) · familial amyloidotic polyneuropathy(3.00) · familial amyloid polyneuropathy(2.00) · schizophrenia(1.00) · alzheimer disease(1.00) · atrophy(1.00)

Relevant papers and external links:

OMIM 176300

PMID 16716350

PMID 19328595

dbSNP: rs1800458 Genecard: TTR chromosome 18 SNPedia: rs1800458(G;G)

★ rs4633(C;C) info:0.65 39.49% **normal**

rs4633 is a variant at codon 62 of the COMT gene, however, it does not change the amino acid sequence of the COMT protein.

In a study of 150 (Caucasian) cases of endometrial cancer, a significant increase in rs4633(T;T) genotype was observed in patients compared to controls (OR = 2.39, CI: 1.31-4.37, p = 0.004). Furthemore, the frequency of the C-G haplotype of rs4633-rs4680 was significantly higher in controls (p < 0.0001) than in patients. This correlated with lower expression levels of the COMT protein in carriers of these alleles.

pubmed 1180576 Schizophrenia Susceptibility

Genetic basis for individual variations in pain perception and the development of a chronic pain condition

Gene related topics:

UNKNOWN(6.00) · digeorge syndrome pharyngeal pouch syndrome(6.00) · PSYCH(5.72) · schizophrenia(5.72) · CANCER(3.00) · neoplasms pain(3.00) · fibromyalgia(2.67) · NEUROLOGICAL(2.00) · mamographic density(2.00) · pain temporomandibular joint disorders(2.00) · psychosis(1.67) · obsessive compulsive disorder(1.31) · CHEMDEPENDENCY(1.07) · substance related disorders(1.07) · panic disorder(1.03) · adhd attention deficit hyperactivity disorder(1.00) · eating disorders(1.00) · cancer(1.00) · pain(0.94) · breast cancer(0.83) · marijuana abuse(0.67) · mood disorders(0.62) · parkinson s disease(0.62) · DEVELOPMENTAL(0.60) · leiomyoma uterine neoplasms(0.60) · mental retardation(0.60) · schizophrenia bipolar disorder(0.60) · OTHER(0.57) · sleep deprivation(0.57) · bipolar disorder(0.50) · depression(0.50) · fractures bone(0.50) · personality(0.38) · mammographic density(0.36) · personality traits(0.33) · heroin abuse(0.30) · alcoholism(0.29) · adhd(0.26) · cognitive ability(0.25) · heroin dependence(0.25) · bulimia(0.24) · endometrial cancer(0.23) · smoking(0.21) · anorexia nervosa(0.15) · suicide(0.14) · liver cancer(0.13) · tobacco use disorder(0.11) · narcolepsy(0.11) · METABOLIC(0.10) · weight gain(0.10) · smoking behavior(0.09) · endometrial neoplasms(0.07) · attention deficit hyperactivity disorder(0.05) · IMMUNE(0.05) · vitiligo(0.05) · autism(0.03) · REPRODUCTION(0.02) · endometriosis(0.02)

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Relevant papers and external links:

PMID 18324659

PMID 15537663

OMIM 116790

PHARMGKB PA164944060

Evidence: PubMed ID:15537663On the basis of subjects' pain responsiveness, haplotypes involving rs6269 (A/G), rs4633 (C/T), rs4818 (C/G), and rs4680 (G/A) were designated as low (low pain sensitivity (LPS) haplotype; GCGG), average (average pain sensitivity (APS) haplotype; ATCA), or high (high pain sensitivity (HPS) haplotype; ACCG) pain sensitive.

dbSNP: rs4633 Genecard: COMT chromosome 22 SNPedia: rs4633(C;C)

★ rs5443(C;C) good:1.35 **normal, but higher risk for several conditions**

ostensibly the 'normal' form, however variation is common, and each genotype seems to show some good and bad consequences.
rs5443, a SNP in the G-protein beta3 subunit (GNB3) gene that is more commonly known as the C825T variant, has been linked to a number of metabolic conditions including obesity, coronary artery disease, insulin resistance and therefore diabetes, left ventricular hypertrophy, and hypertension. It has also been linked to how well a patient responds to Viagra (sildenafil). Several studies have been unable to replicate one or more of the associations in at least some populations between this SNP and these conditions. The more notable studies include:

rs5443(T) allele carriers are 2-3 fold more likely to be obese in Caucasian, Chinese, and African American populations.

rs5443(T) carriers are clearly at higher risk for hypertension, but this review indicates that whether they are also at increased risk for stroke and left ventricular hypertrophy remains controversial.

rs5443(T;T) women gain significantly more weight during pregnancy than rs5443(C;T) or rs5443(C;C) women, and had a significantly higher pre-pregnancy body mass index.

rs5443(T;T) genotypes respond to Viagra better. 91% of them have a "positive erectile response" upon taking Viagra, whereas only around 50% of rs5443(C;T) and rs5443(C;C) individuals respond equivalently to the drug. The odds ratio for the positive response was 10.0 (CI: 1.2 - 81.1, p = 0.01).

rs5443(T;T) patients receiving clozapine over a long term for the treatment of schizophrenia gain significantly more weight (16%) compared to patients carrying at least one rs5443(C) allele in a study of Chinese patients.

rs5443(T) carriers taking triptans for the treatment of migraines or cluster headaches were ~3 fold more likely to respond positively compared with rs5443(C;C) homozygotes (OR 2.96, CI:1.34 - 6.56, p=0.0074) in a study of ~200 Caucasian patients.

rs5443(C;T) genotypes are more prevalent in gastroesophageal reflux disease (GERD) patients relative to healthy controls (odds ratio 1.43, CI: 1.04–1.98).

rs5443(C;C) individuals do not lose weight under sibutramine therapy whereas (C;T) and (T;T) individuals do, based on a study of 131 obese Taiwanese patients. 23andMe blog

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Gene related topics:

METABOLIC(2.00) · UNKNOWN(2.00) · dyspepsia(2.00) · obesity hypertension(2.00) · CARDIOVASCULAR(1.42) · hypertension(1.42) · left ventricular hypertrophy(1.00) · insulin resistance(1.00) · stroke(1.00) · body mass(1.00) · weight(1.00) · schizophrenia(1.00) · coronary artery disease(1.00) · gastroesophageal reflux disease(1.00) · body mass index(1.00) · obesity(1.00) · insulin(1.00) · IMMUNE(0.78) · irritable bowel syndrome(0.78) · obesity weight loss(0.57) · weight gain(0.23) · NEUROLOGICAL(0.17) · migraine disorders(0.17) · PSYCH(0.11) · major depressive disorder(0.11) · depressive disorder major(0.10) · hypercholesterolemia(0.08) · RENAL(0.06) · kidney failure chronic(0.06) · blood pressure arterial(0.06) · REPRODUCTION(0.05) · pre eclampsia(0.05) · metabolic syndrome(0.04) · diabetes mellitus type 2(0.02)

Relevant papers and external links:

PMID 10477144
PMID 12530935
PMID 12668921
PMID 12576843
PMID 16141801
PMID 17361120
PMID 19174793
PMID 19687782

PHARMGKB PA165109228
Evidence: PubMed ID:19247266Risk or phenotype-associated allele: T. Phenotype: Among GNB3 T allele carriers, the risk of diabetes due to thiazide use was less increased than among homozygous GNB3 CC subjects . Study size: 497 incident cases of type 2 diabetes and 2,633 controls. metric(s): (SI 0.62 (95% CI: 0.41-0.93). Type of association: GN.

PHARMGKB PA161145077
Evidence: PubMed ID:1600156; PubMed ID:16707857; PubMed ID:17278960; PubMed ID:17663734; PubMed ID:17701674; PubMed ID:17785925Extensively studied, found to be associated with many things, including blood pressure and hypertension.

PHARMGKB PA161822201
Evidence: PubMed ID:12576843This variant is associated with sildenafil response for erectile dysfunction patients.

PHARMGKB PA161845790
Evidence: PubMed ID:18551043This variant is associated with statin response. Patients carring T allele have less risk of MI and are more likely to benefit from statin therapy in a hypercholesterolemic population of antihypertensive drug users.

PHARMGKB PA161845791
Evidence: PubMed ID:17136758This variant (C allele carriers) is associated with an increased risk for the development of oncocytic thyroid tumours.

PHARMGKB PA162263548
Evidence: PubMed ID:17361120A study on A total of 180 migraine and cluster headache patients found that pain relief by triptans is significantly modulated by this common genetic GNB3 variant.

PHARMGKB PA162364006
Evidence: PubMed ID:17361120A study on a total of 180 migraine and cluster headache patients found that pain relief by triptans is significantly modulated by this common genetic GNB3 variant.

PHARMGKB PA164889042
Evidence: PubMed ID:19193342T allele is associated with olanzapine-induced weight gain

dbSNP: rs5443 Genecard: GNB3 chromosome 12 SNPedia: rs5443(C;C)

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★ rs2287939(C;C) info:0.27 51.10%

Chromosome 5p Region SNPs Are Associated with Risk of NSCLC among Women.

Non-synonymous variants in the AMACR gene are associated with schizophrenia.

Gene related topics:

schizophrenia(1.00)

Relevant papers and external links:

PMID 20445798
PMID 20875727

dbSNP: rs2287939 Genecard: AMACR chromosome 5 SNPedia: rs2287939(C;C)

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★ rs1799978(A;A) good:1.30 77.61%

Association between ADORA2A and DRD2 polymorphisms and caffeine-induced anxiety.

Physiogenomic analysis of localized FMRI brain activity in schizophrenia.

Evaluation of genetic variability in the dopamine receptor D2 in relation to behavioral inhibition and impulsivity/sensation seeking: an exploratory study with d-amphetamine in healthy participants.

Pharmacogenetics and antipsychotics: therapeutic efficacy and side effects prediction.

Gene related topics:

CHEMDEPENDENCY(6.04) · alcoholism(6.04) · alcoholism substance related disorders(4.00) · PSYCH(2.30) · schizophrenia(2.30) · METABOLIC(2.00) · NEUROLOGICAL(2.00) · hyperprolactinaemia hyperprolactinemia(2.00) · nervous system diseases(2.00) · substance withdrawal syndrome(2.00) · substance withdrawal syndrome tobacco use disorder(2.00) · tic combined vocal and multiple motor tourette syndrome(2.00) · smoking behavior(1.74) · UNKNOWN(1.29) · neuroleptic malignant syndrome(1.29) · heroin dependence(1.00) · methamphetamine abuse(1.00) · anxiety(1.00) · brain(1.00) · tardive dyskinesia(0.95) · heroin abuse(0.83) · cocaine dependence(0.80) · cocaine related disorders(0.67) · delirium(0.57) · impulsivity(0.57) · alcohol abuse(0.52) · tobacco use disorder(0.44) · adhd(0.40) · mood disorders(0.40) · parkinson s disease(0.40) · smoking(0.33) · alcohol(0.32) · mood disorder(0.27) · substance related disorders(0.27) · CARDIOVASCULAR(0.25) · atrial natriuretic factor(0.25) · alcohol dependence(0.22) · personality traits(0.21) · tourette syndrome(0.21) · dyslexia(0.19) · migraine disorders(0.17) · adhd attention deficit hyperactivity disorder(0.15) · personality(0.14) · personality disorders(0.12) · depressive disorder major(0.10) · bipolar disorder(0.07) · attention deficit hyperactivity disorder(0.05) · autism(0.03)

Relevant papers and external links:

PHARMGKB PA165108051
Evidence: PubMed ID:19339912Risk or phenotype-associated allele: A. Phenotype: Having the AA genotype of this variant was associated with a protective effect from increased prolactin concentration. Study size: 90. Study population/ethnicity: 7-17-year-old patients chronically treated with risperidone; non-Hispanic Caucasians. Significance metric(s): p = 0.002. Type of association: CO.

PHARMGKB PA162356251
Evidence: PubMed ID:18855532This SNP is significant predictor of treatment response to risperidone in first-episode schizophrenia.

PMID 18305461

PMID 18330705

PMID 19968402

PMID 21162693

dbSNP: rs1799978 Genecard: DRD2 chromosome 11 SNPedia: rs1799978(A;A)

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★ rs6267(G;G) good:0.92 97.34% **common**

Gene related topics:

UNKNOWN(6.00) · digeorge syndrome pharyngeal pouch syndrome(6.00) · PSYCH(5.72) · schizophrenia(5.72) · CANCER(3.00) · neoplasms pain(3.00) · fibromyalgia(2.67) · NEUROLOGICAL(2.00) · mamographic density(2.00) · pain temporomandibular joint disorders(2.00) · psychosis(1.67) · obsessive compulsive disorder(1.31) · CHEMDEPENDENCY(1.07) · substance related disorders(1.07) · panic disorder(1.03) · adhd attention deficit hyperactivity disorder(1.00) · eating disorders(1.00) · pain(0.94) · breast cancer(0.83) · marijuana abuse(0.67) · mood disorders(0.62) · parkinson s disease(0.62) · DEVELOPMENTAL(0.60) · leiomyoma uterine neoplasms(0.60) · mental retardation(0.60) · schizophrenia bipolar disorder(0.60) · OTHER(0.57) · sleep deprivation(0.57) · bipolar disorder(0.50) · depression(0.50) · fractures bone(0.50) · personality(0.38) · mammographic density(0.36) · personality traits(0.33) · heroin abuse(0.30) · alcoholism(0.29) · adhd(0.26) · cognitive ability(0.25) · heroin dependence(0.25) · bulimia(0.24) · endometrial cancer(0.23) · smoking(0.21) · anorexia nervosa(0.15) · suicide(0.14) · liver cancer(0.13) · tobacco use disorder(0.11) · narcolepsy(0.11) · METABOLIC(0.10) · weight gain(0.10) · smoking behavior(0.09) · endometrial neoplasms(0.07) · attention deficit hyperactivity disorder(0.05) · IMMUNE(0.05) · vitiligo(0.05) · autism(0.03) · REPRODUCTION(0.02) · endometriosis(0.02)

Relevant papers and external links:

OMIM 116790

PHARMGKB PA164944058
Evidence: PubMed ID:18163386This study showed a highly significant association between a COMT haplotype of two functional SNPs (Ala72Ser and Val158Met) and aggressive behavior in schizophrenia.

dbSNP: rs6267 Genecard: COMT chromosome 22 SNPedia: rs6267(G;G)

★ rs6675281(C;T) info:0.67 17.33% **None**

linked to schizophrenia

Gene related topics:

PSYCH(0.60) · schizophrenia bipolar disorder(0.60) · schizophrenia(0.35) · cognitive function(0.33) · NEUROLOGICAL(0.02) · amyotrophic lateral sclerosis(0.02)

Relevant papers and external links:

OMIM 605210

dbSNP: rs6675281 Genecard: DISC1 chromosome 1 SNPedia: rs6675281(C;T)

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★ rs6265(G;G) good:1.55 63.80% **common/normal**

Val/val (normal) variant of the Val66Met snp in the BDNF gene that codes for brain-derived neurotrophic factor. Met/met is associated with susceptibility to neuropsychiatric disorders.
rs6265, also known as Val66Met, is a SNP in brain-derived neurotrophic factor BDNF gene. The more common G allele encodes the Val, while the A allele encodes Met.

Met/A allele associated with introversion

The A allele may also be protective against depression when subjected to repeated defeat g2b2mh blog

On a driving-based motor learning task subjects with this genotype showed greater error during short-term learning and poorer retention over 4 days, relative to subjects without the polymorphism. The presence of this BDNF polymorphism is associated with differences in brain motor system function, altered short-term plasticity, and greater error in short-term motor learning.

Wired discusses the research as does 23andMe blog.

Alzheimer's disease risk for non ApoE4 carriers is affected by the heterozygous form of rs6265, as well as the diplotypes of rs6265, rs11030104, and rs2049045.

Depressed patients who had (GA or AA) appeared to show a significantly increased risk of suicidal behaviour

In 2 studies of British women, rs6265(A;A) women had a lower body mass index than rs6265(G) allele carriers, with the difference being -0.57-0.911 kg/m(2), depending on the study.

Established associations:

smoking behavior **you have 2 copies of the risk allele G**

(risk allele=G, smoking initiation odds ratio/beta 1.06 [1.04-1.08] with pval 2E-8, pubmedid=20418890)

body mass index **you have 2 copies of the risk allele G**

(risk allele=G, odds ratio/beta 4.58 [3.07-6.09] % SD with pval 5E-10, pubmedid=19079260)

body weight **you have 2 copies of the risk allele G**

(risk allele=G, odds ratio/beta 4 [2.47-5.53] % SD with pval 2E-7, pubmedid=19079260)

Gene related topics:

PSYCH(2.33) · depression(2.33) · NEUROLOGICAL(2.00) · affective psychoses(2.00) · alzheimer disease amnesia(2.00) · bipolar disorder(1.66) · CHEMDEPENDENCY(1.00) · amphetamine related disorders(1.00) · brain(1.00) · body mass(1.00) · body mass index(1.00) · schizophrenia(0.94) · major depressive disorder(0.68) · alzheimer s disease(0.59) · METABOLIC(0.56) · weight(0.56) · personality(0.55) · obsessive compulsive disorder(0.40) · UNKNOWN(0.36) · dyskinesia drug induced(0.36) · cognitive function(0.33) · parkinsons disease(0.29) · DEVELOPMENTAL(0.27) · IMMUNE(0.27) · dermatitis atopic(0.27) · mental retardation(0.27) · huntington s disease(0.26) · adhd attention deficit hyperactivity disorder(0.21) · anorexia nervosa(0.15) · autism(0.12) · body weight obesity(0.11) · cognitive ability(0.11) · panic disorder(0.08) · migraine disorders(0.08) · attention deficit hyperactivity disorder(0.05) · personality traits(0.05) · smoking(0.05) · epilepsy(0.04) · smoking behavior(0.04) · suicide(0.04)

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Relevant papers and external links:

PMID 19079260
Genome-wide association yields new sequence variants at seven loci that associate with measures of obesity.

PMID 20418890
Genome-wide meta-analyses identify multiple loci associated with smoking behavior.

PMID 20042999

PMID 17956738

PMID 19745020

PMID 17293537

PMID 18600033

PMID 19209189

OMIM 113505

PHARMGKB PA164857051
Evidence: PubMed ID:19414708This nonsynonymous variant (G/A) in an exon in BDNF gene was associated with major depressive disorder in a study of 264 controls and 272 Mexican Americans with major depressive disorder. (OR= 1.66; p value=0.009; risk allele=G)

PHARMGKB PA162364070

Evidence: PubMed ID:18319075In DNA from frontal-cortex brain tissue of a group of Schizophrenia, Bipolar Disorder and Control individuals, this SNP was found to be associated with methylation at CpG sites surrounding the gene. CC genotype was associated with a higher level of methylation.

PHARMGKB PA164740154
Evidence: PubMed ID:19079260; Web Resource:External Link results: Genome-wide association yields new sequence variants at seven loci that associate with measures of obesity. (Initial Sample Size: 80,969 individuals; Replication Sample Size: 11,036 individuals); (Region: 11p14.1; Reported Gene(s): BDNF; Risk Allele: rs6265-G); (p-value= 0.0000000005).This variant is associated with Body mass index.

PHARMGKB PA164740174
Evidence: PubMed ID:19079260; Web Resource:External Link results: Genome-wide association yields new sequence variants at seven loci that associate with measures of obesity. (Initial Sample Size: 80,969 individuals; Replication Sample Size: 11,036 individuals); (Region: 11p14.1; Reported Gene(s): BDNF; Risk Allele: rs6265-G); (p-value= 0.0000002).This variant is associated with Weight.

OMIM 113505

dbSNP: rs6265 GWAS Catalog: rs6265 Genecard: BDNF chromosome 11

SNPedia: rs6265(G;G)

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★ rs167771(A;A) info:1.19 34.65% **Possibly more "Insistence on Sameness" on ADI-R test. Possibly increased FTND nicotine dependence.**

Possibly more "Insistence on Sameness" on ADI-R test.
Possibly increased FTND nicotine dependence.
rs167771 was significantly associated with autism spectrum disorder in a study of 144 patients.

G allele associated with increased extra-pyramidal symptom risk as a result of risperidone treatment in a study of 321 psychiatric inpatients (81 presenting with EPS and 189 without)

Gene related topics:

nicotine(5.00) · nicotine dependence(5.00) · NEUROLOGICAL(3.79) · tardive dyskinesia(3.79) · essential tremor(2.88) · PSYCH(2.37) · schizophrenia(2.37) · CHEMDEPENDENCY(2.00) · UNKNOWN(2.00) · akathisia drug induced(2.00) · cocaine abuse(2.00) · autism(1.00) · cocaine related disorders(0.67) · schizophrenia tardive dyskinesia(0.57) · tourette syndrome(0.47) · alcohol dependence(0.22) · parkinson s disease(0.14) · personality disorders(0.12) · bipolar disorder(0.10) · obsessive compulsive disorder(0.06) · adhd attention deficit hyperactivity disorder(0.05) · personality traits(0.05) · alcohol abuse(0.04) · smoking behavior(0.04)

Relevant papers and external links:

PMID 19058789
PMID 19506579

PHARMGKB PA165109604
Evidence: PubMed ID:19506579Risk or phenotype-associated allele: G. Phenotype: The G variant of rs167771 was associated with increased risk for extrapyramidal symptoms in psychiatric patients receiving risperidone. Study size: 132. Study population/ethnicity: Patients with Schizophrenia or Bipolar disorder receiving antipsychotics; Caucasians; Spain; Catalonia. Significance metric(s): OR = 3.3; p = 0.00013. Type of association: PD.

dbSNP: rs167771 Genecard: DRD3 chromosome 3 SNPedia: rs167771(A;A)

★ rs1049353(G;G) info:1.93 75.80% **more resistant to treatment for depression**

Based on a study of 256 Caucasian patients being treated for depression, carriers of a rs1049353(G) allele were less likely to respond favorably, particularly if they were females with comorbid anxiety.

rs806368(C) together with rs1049353(A) or rs1049353(G) make up a haplotype associated with PTSD, with the C-A haplotype somewhat associated (p=0.04) with higher risk of PTSD and the C-G haplotype associated (p=0.01) with a lower risk of PTSD.

Cannabis receptor haplotype associated with fewer cannabis dependence symptoms in adolescents.

No evidence for an involvement of variants in the cannabinoid receptor gene (CNR1) in obesity in German children and adolescents.

The G1422A variant of the cannabinoid receptor gene (CNR1) is associated with abdominal adiposity in obese men.

No association of CNR1 gene variations with susceptibility to schizophrenia.

Polymorphisms of the cannabinoid 1 receptor gene and cognitive impairment in multiple sclerosis.

Association between single nucleotide polymorphisms in the cannabinoid receptor gene (CNR1) and impulsivity in southwest California Indians.

Cannabinoid receptor 1 gene association with nicotine dependence.

Cannabinoid type-1 receptor gene polymorphisms are associated with central obesity in a Southern Brazilian population.

Lack of association of genetic variants in genes of the endocannabinoid system with anorexia nervosa.

Evidence for association between polymorphisms in the cannabinoid receptor 1 (CNR1) gene and cannabis dependence.

Genetic variation in cannabinoid receptor 1 (CNR1) is associated with derangements in lipid homeostasis, independent of body mass index.

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Interaction between two independent CNR1 variants increases risk for cocaine dependence in European Americans: a replication study in family-based sample and population-based sample.

CB1 expression is attenuated in Fallopian tube and decidua of women with ectopic pregnancy.

Candidate genes for cannabis use disorders: findings, challenges and directions.

Association of CNR1 and FAAH endocannabinoid gene polymorphisms with anorexia nervosa and bulimia nervosa: evidence for synergistic effects.

The implication of CNR1 gene's polymorphisms in the modulation of endocannabinoid system effects.

Eating disorders: the current status of molecular genetic research.

Investigation of CNR1 and FAAH endocannabinoid gene polymorphisms in bipolar disorder and major depression.

CNR1 gene polymorphisms in addictive disorders: a systematic review and a meta-analysis.

G1359A polymorphism of the cannabinoid receptor gene (CNR1) and insulin resistance in patients with diabetes mellitus type 2.

Role of genetic variation in the cannabinoid type 1 receptor gene (CNR1) in the pathophysiology of human obesity.

Endocannabinoid Pro129Thr FAAH functional polymorphism but not 1359G/A CNR1 polymorphism is associated with antipsychotic-induced weight gain.

Are endocannabinoid type 1 receptor gene (CNR1) polymorphisms associated with obesity and metabolic syndrome in postmenopausal Polish women?

A common variation in the cannabinoid 1 receptor (CNR1) gene is associated with pre-eclampsia in the Central European population.

Cannabinoid type 1 receptor gene polymorphisms are not associated with olanzapine-induced weight gain.

Cannabinoid Receptor Genotype Moderation of the Effects of Childhood Physical Abuse on Anhedonia and Depression.

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Gene related topics:

depression(5.00) · bipolar disorder(1.00) · anxiety(1.00) · eating disorder(1.00) · insulin resistance(1.00) · cognitive impairment(1.00) · diabetes mellitus type 2(1.00) · body mass(1.00) · olanzapine(1.00) · multiple sclerosis(1.00) · anorexia nervosa(1.00) · diabetes mellitus(1.00) · metabolic syndrome(1.00) · nicotine(1.00) · weight(1.00) · eating disorders(1.00) · schizophrenia(1.00) · METABOLIC(1.00) · adiposity(1.00) · major depression(1.00) · body mass index(1.00) · obesity(1.00) · bulimia(1.00) · insulin(1.00) · impulsivity(1.00) · nicotine dependence(1.00) · cocaine dependence(1.00) · weight gain(1.00) · CHEMDEPENDENCY(0.67) · marijuana abuse(0.67)

Relevant papers and external links:

PMID 18579347
PMID 18213623
PMID 16917946
PMID 17292652
PMID 17873324
PMID 17881126
PMID 17942526
PMID 18179391
PMID 18606954
PMID 18776593
PMID 19014633
PMID 19016476
PMID 19018721
PMID 19052543
PMID 19093002
PMID 19335651
PMID 19659925
PMID 19886064
PMID 20033240
PMID 20080186
PMID 20192949
PMID 20204253
PMID 20415562
PMID 20631561
PMID 20838400
PMID 21129839
PMID 21695734
PMID 22393204

dbSNP: rs1049353 Genecard: CNR1 chromosome 6 SNPedia: rs1049353(G;G)

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★ rs6277(T;T) good:1.66 5.95% **normal schizophrenia risk, learns NoGo faster**

According to 23andMe blog this genotype is better for a particular learning task.
rs6277 (957C>T, Pro319Pro) is one of several SNPs in the dopamine receptor DRD2 gene.

In a study of 300+ Russian patients with schizophrenia, the rs6277(C) allele was associated with higher risk. From a pooled meta-study (total of 4 other reports plus this one) the allelic odds ratio is 1.42 (CI: 1.26-1.61, p<0.00005), and the genotypic odds ratio for the (C;C) genotype was 1.6 (CI: 1.32-1.95, p<0.00005).

Note that rs6275 and rs6277 are only 18bp apart, hence their very tight linkage (r2=1).

gs278 reflects a gene-gene interaction between this SNP and a NR3A SNP, rs10989591, in which older adults with a particular combination of genotypes at these two (independent) loci are reported to exhibit better episodic memory.

C allele associated significantly (p = 0.021) with post-traumatic stress disorder in a sample of (assumedly Australian) 127 war veterans w/ 228 controls

23andMe blog people with two As at rs6277(T;T) were better at NoGo learning.

[pharmgkb] T allele associated with decrease in mRNA levels

Gene related topics:

CHEMDEPENDENCY(6.04) · alcoholism(6.04) · alcoholism substance related disorders(4.00) · PSYCH(2.30) · schizophrenia(2.30) · METABOLIC(2.00) · NEUROLOGICAL(2.00) · hyperprolactinaemia hyperprolactinemia(2.00) · nervous system diseases(2.00) · substance withdrawal syndrome(2.00) · substance withdrawal syndrome tobacco use disorder(2.00) · tic combined vocal and multiple motor tourette syndrome(2.00) · smoking behavior(1.74) · UNKNOWN(1.29) · neuroleptic malignant syndrome(1.29) · heroin dependence(1.00) · methamphetamine abuse(1.00) · memory(1.00) · stress(1.00) · OTHER(1.00) · tardive dyskinesia(0.95) · heroin abuse(0.83) · cocaine dependence(0.80) · cocaine related disorders(0.67) · delirium(0.57) · impulsivity(0.57) · alcohol abuse(0.52) · tobacco use disorder(0.44) · adhd(0.40) · mood disorders(0.40) · parkinson s disease(0.40) · smoking(0.33) · alcohol(0.32) · mood disorder(0.27) · substance related disorders(0.27) · CARDIOVASCULAR(0.25) · atrial natriuretic factor(0.25) · alcohol dependence(0.22) · personality traits(0.21) · tourette syndrome(0.21) · dyslexia(0.19) · migraine disorders(0.17) · adhd attention deficit hyperactivity disorder(0.15) · personality(0.14) · personality disorders(0.12) · depressive disorder major(0.10) · bipolar disorder(0.07) · attention deficit hyperactivity disorder(0.05) · autism(0.03)

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Relevant papers and external links:

PMID 18255274

PMID 18833581

PHARMGKB PA165374657
Evidence: PubMed ID:20714340Risk or phenotype-associated allele: CC. Phenotype: The CC genotype was associated with weight gain of at least 7% in schizophrenia patients treatment with clozapine or olanzapine. Study size: 206. Study population/ethnicity: European american; African American; German; Schizophrenia. Significance metric(s): OR = 3.37 (CI = 1.00-11.36). Type of association: PD.

PHARMGKB PA161145172
Evidence: Web Resource:External Link allele led to a decrease in mRNA levels, C/C genotype was reported to be associated with schizophrenia.

PHARMGKB PA165291683
Evidence: PubMed ID:18687376Phenotype: The 957CC carriers were more frequently non-responders to methadone treatment (OR=2.4; p=0.02). The 957CC carriers were 25% (95% CI = 15-36%) in the non-responder group (n = 73) whereas they were only 12% (95% CI = 8-18%) in the responder group (n = 165; $\chi 2 = 5.9$; p = 0.015). No significant difference was observed for the TaqI A genotype frequency in responder and non-responder groups (p = 0.9). Study size: 238 patients. Study population: Caucasian.

PHARMGKB PA165291681

Evidence: PubMed ID:15567074The T allele led to a decrease in mRNA levels and stability whereas the C allele was not found to be associated with any mRNA changes, which led to a relative increase in the expression of DRD2 in carriers of the C allele.

PHARMGKB PA165291682
Evidence: PubMed ID:19582781Results of an in vivo study with [11C]raclopride indicated that this variant increased binding potential by decreasing DRD2 KD (C/C>C/T>T/T), while Bmax was not significantly altered.

PHARMGKB PA165291689
Evidence: PubMed ID:16973280Risk or phenotype-associated allele: C. Phenotype: A greater proportion of patients with schizophrenia than healthy controls were C-allele carriers. Study size: 188 schizophrenia patients and 384 healthy controls. Study population: Finnish. Metric(s): OR =1.5, 95% confidence interval (CI) 1.0-2.3, p=0.05.

PHARMGKB PA165291685
Evidence: PubMed ID:19603545Phenotype: In this case-control study the polymorphisms -141C Ins/Del (rs1799732); C957T (rs6277); A1385G (rs6276); and TaqIA (rs1800497) were genotyped. The haplotypes I-C-G-A2 and I-C-A-A1 occurred with a higher frequency in alcoholics [P=0.026, odds ratio (OR): 1.340; P=0.010, OR: 1.521, respectively]. Study size: 360 alcoholics and 368 controls. Study population:Caucasian individuals of German origin.

PHARMGKB PA165291676
Evidence: PubMed ID:18926547Phenotype: Patients with C/C genotype were associated with poor aripiprazole response for excitement symptoms (measured on the positive and negative syndrome scale, PANSS - excitement subscale) when compared with T/T patients. Study size: 128 schizophrenic patients. Study population: Chinese.

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dbSNP: rs6277 Genecard: DRD2 chromosome 11 SNPedia: rs6277(T;T)

★ **rs11146020(G;G)** **info:0.41** **79.74%**

located in 5' UTR of GRIN1

significant (p = .0000013) assoc. w/ schizophrenia in a sample of 2455 Han Chinese

mentioned w/ possible schizophrenia association in a sample of 677 Germans (354 patients, 323 controls), but the initial association did not survive multiple correction

Gene related topics:

schizophrenia(1.00)

Relevant papers and external links:

PMID 16476413
PMID 17728671
OMIM 138249

dbSNP: rs11146020 Genecard: GRIN1 chromosome 9 SNPedia: rs11146020(G;G)

★ rs6311(C;T) good:2.42 49.36% **Normal risk of sexual dysfunction when taking SSRI Antidepressants.**

rs6311 (-1438A>G / A-1438G or -1438G>A / G-1438A) is a SNP located upstream (and within the promoter region of) HTR2A.

Multiple Regulatory Variants Modulate Expression of 5-Hydroxytryptamine 2A Receptors in Human Cortex. The minor A allele of rs6311 reduces expression of a previously unannotated extension of the 5' untranslated region of HTR2A mRNA. rs6311 together with rs6314 have a modest effect on depression severity, when examined in the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study.

Three (rs643627-rs594242-rs6311: A-C-T), two (rs594242-rs6311: C-T) and a single functional (rs6311: T) marker were protective against suicidal behavior.
The complementary markers (rs594242-rs6311: G-C and rs6311: C) were associated with increased risk for non-violent and impulsive suicidal behavior.
Furthermore, CC-homozygotes for the functional SNP rs6311 reported more anger- and aggression-related behavior.

This SNP has also been reported to be part of a haplotype associated with risk for rheumatoid arthritis. In this report, the risk allele is rs6311(C).

may effect promoter activity (in the presence of a SV40 enhancer, promoter activity was significantly higher with the A allele than a G allele, but only in cell lines expressing endogenous HTR2A)

-1438 A allele creates a consensus binding site for Th1/E47, a transcription factor implicated in development of the nervous system

Polymorphisms in the serotonin receptor gene HTR2A are associated with quantitative traits in panic disorder.

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Gene related topics:

PSYCH(3.00) · anorexia nervosa(3.00) · anorexia nervosa bulimia(3.00) · PHARMACOGENOMIC(2.00) · impulsive behavior(2.00) · olanzapine(2.00) · response to clozapine(2.00) · schizophrenia affective disorder(2.00) · schizophrenia(1.64) · arthritis(1.00) · rheumatoid arthritis(1.00) · quantitative traits(1.00) · bulimia(0.94) · major depression(0.80) · suicidal behavior(0.69) · major depressive disorder(0.68) · depression(0.67) · obsessive compulsive disorder(0.58) · neuroleptic malignant syndrome(0.57) · schizophrenia tardive dyskinesia(0.57) · suicide(0.56) · personality disorders(0.50) · personality traits(0.47) ·

cognitive function(0.33) · depressive disorder major(0.29) · autism(0.28) · adhd(0.26) · mood disorders(0.23) · panic disorder(0.21) · adhd attention deficit hyperactivity disorder(0.21) · attention deficit hyperactivity disorder(0.21) · tourette syndrome(0.21) · bipolar disorder(0.20) · personality(0.14) · CHEMDEPENDENCY(0.13) · heroin abuse(0.13) · NEUROLOGICAL(0.11) · migraine(0.11) · tardive dyskinesia(0.11) · smoking behavior(0.09) · CARDIOVASCULAR(0.05) · blood pressure determination(0.05) · alcohol abuse(0.04)

Relevant papers and external links:

PMID 23158458

PMID 16814396

PMID 18006541

PMID 15364038

PMID 18079067

PHARMGKB PA165111369
Evidence: PubMed ID:19997080Risk or phenotype-associated allele: A Phenotype: Carriers of the A variant of HTR2A:(-1438)G>A had lower Autism Treatment Evaluation Checklist (ATEC) scores than GG homozygotes, indicating improved symptoms and response to risperidone. Study size: 45 Study population/ethnicity: Children with Autism receiving risperidone Significance metric(s): p = 0.019 Type of association: PD

PMID 17440930

PHARMGKB PA161145082
Evidence: PubMed ID:17688403; PubMed ID:17804117Associated with anorexia and bulimia. The AA genotype was found to be a risk factor for tardive dyskinesia (TD).

PHARMGKB PA162190493
Evidence: PubMed ID:15364038; PubMed ID:18079067The A allele of -1438G/A is suggested to have increased promoter activity in functional in vitro studies. In silico analysis revealed that the -1438 A allele creates a consensus binding site for Th1/E47, a transcription factor implicated in the development of the nervous system. The SNP was also associated with Chronic fatigue syndrome together with rs 6313 and rs1923884.

dbSNP: rs6311 Genecard: HTR2A chromosome 13 SNPedia: rs6311(C;T)

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★ rs4680(G;G) good:1.99 39.79% **(warrior) multiple associations, see details**

You have the VAL/VAL version of the snp discussed in this news article. It is able to perform better in a test where the optimal strategy changes.

Placebo is less effective for you

External Link
rs4680 (Val158Met) is a well studied SNP in the COMT gene. 23andMe blog summarizes them as rs4680(A) = Worrier. Met, more exploratory, lower COMT enzymatic activity, therefore higher dopamine levels; lower pain threshold, enhanced vulnerability to stress, yet also more efficient at processing

information under most conditions
rs4680(G) = Warrior. Val, less exploratory, higher COMT enzymatic activity, therefore lower dopamine levels; higher pain threshold, better stress resiliency, albeit with a modest reduction in executive cognition performance under most conditions

Roughly speaking, the predominant wisdom (known colloquially as the warrior/worrier hypothesis; summary at) posits that people with Val alleles have increased COMT activity and lower prefrontal extracellular dopamine compared with those with the Met substitution. Val158 alleles may be associated with an advantage in the processing of aversive stimuli (warrior strategy), while Met158 alleles may be associated with an advantage in memory and attention tasks (worrier strategy). Under conditions of increased dopamine release (eg, stress), individuals with Val158 alleles may have improved dopaminergic transmission and better performance, while individuals with Met158 alleles may have less efficient neurotransmission and worse performance. Some evidence suggests that Val158 alleles are associated with schizophrenia, while Met158 alleles are associated with anxiety.

Specific studies include:

rs4680, a functional Val/Met polymorphism, showed modest association with Irish familial schizophrenia. Haplotype A-G-A for SNPs rs737865-rs4680-rs165599 was preferentially transmitted to the affected subjects.

A study of 400 individuals reported that an increase in plasma total homocysteine (tHcy) of 10.4% (CI: 0.01-0.21, p=0.03) for associated with rs4680(A;A) homozygotes compared with rs4680(G;G) subjects. The (A;A) genotype was also more common, but statistically not that significantly, in venous thrombosis patients (OR 1.61, CI: 0.97-2.65], p=0.06) compared to control subjects.

And from :
"Adolescent cannabis use was associated with increased risk of schizophreniform disorder in adulthood among Val/Val (i.e. rs4680(G;G)) individuals (OR = 10.9, 95% CI: 2.2â€“54.1) and, to a lesser extent, among Met/Val individuals (rs4680(A;G)); OR = 2.5, 95% CI: .78 â€“ 8.2), but not among Met/Met (rs4680 (A;A)) individuals (OR = 1.1, 95% CI: .21â€“5.4)."

Also potentially associated with schizophrenia

As part of a haplotype with rs4633, the (G) allele is also associated with endometrial cancer

In a study of 2 populations of breast cancer patients (2,000+ patients), increased risk was associated with rs4680(G;G) genotypes in both the Ontario [odds ratio 2.22, CI: 1.49-3.28] and Finland [OR 1.73, CI: 1.08-2.78] populations.

23andMe blog The A version of rs4680 appears to boost working memory and cognitive function compared to G â€” but it also hampers emotional control.

A study of 330 cocaine-dependent individuals, all of African descent, concluded that there was a slight (odds ratio 1.44, CI: 1.12-1.86, p = 0.014) association between the rs4680(A) allele, in other words the Met encoding allele, and cocaine dependence.

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A study of the antidepressant paroxetine found better response in Met/Met homozygotes, worse effects in Val/Val homozygotes and intermediate effects in heterozygotes. The effect became significant at the third week of treatment. Paroxetine daily dose was proportional to baseline severity, but did not influence outcome.

g2b2mh (A;A) subjects deploy more attentional focus when they realize they have made an error.

A meta-analysis of neuroimaging studies found a significant association between the COMT genotype and prefrontal activation; strong and opposing effects were found for executive cognition paradigms (favoring Met allele carriers) and emotional paradigms (favoring Val).

gray matter volume and interacts with rs2097603 related to extracellular dopamine

rs6275/DRD2 and rs4680/COMT useful in predicting disease risk among schizophrenia patients

rs4680(G;G) carriers deprived of sleep respond quite well to 2x 100mg modafinil in terms of improved vigor and well-being, and maintained baseline performance with respect to executive functioning, whereas rs4680 (A;A) individuals barely responded to the drug at all.

Met158 allele carriers had "a more focused response...during a working memory task." "The met158 allele seems to be beneficial during the performance of working memory and attention-related tasks, whereas the val158 allele appears to be advantageous during the processing of aversive emotional stimuli."

"Increased limbic and prefrontal activation elicited by unpleasant stimuli in subjects with more met158 alleles might contribute to the observed lower emotional resilience against negative mood states."

In response to pain Met/Met allele carriers showed greater "sensory and affective ratings of pain and a more negative internal affective state. Opposite effects were observed in val158 homozygotes. The COMT val158met polymorphism thus influences the human experience of pain and may underlie interindividual differences in the adaptation and responses to pain and other stressful stimuli."

Reports that ease of entering hypnosis correlates with number of rs4680(G) alleles.

see gs226 for a report related to impulsiveness

External Link and blog discussion of data about rs4680 thinking about nothing in an fmri.

Breast Cancer Risk Modifiers

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Established associations:

blood metabolite measurement **you have 0 copies of the risk allele A**

(risk allele=A, X-01911 odds ratio/beta 0.044 [0.032-0.056] unit decrease with pval 1E-13, pubmedid=24816252; risk allele=A, X-11593--O-methylascorbate odds ratio/beta 0.049 [0.045-0.053] unit decrease with pval 5E-178, pubmedid=24816252)

Gene related topics:

UNKNOWN(6.00) · digeorge syndrome pharyngeal pouch syndrome(6.00) · PSYCH(5.72) · schizophrenia(5.72) · CANCER(3.00) · neoplasms pain(3.00) · fibromyalgia(2.67) · NEUROLOGICAL(2.00) · mamographic density(2.00) · pain temporomandibular joint disorders(2.00) · psychosis(1.67) · obsessive compulsive disorder(1.31) · CHEMDEPENDENCY(1.07) · substance related disorders(1.07) · panic disorder(1.03) · adhd attention deficit hyperactivity disorder(1.00) · eating disorders(1.00) · sleep(1.00) · cognitive function(1.00) · anxiety(1.00) · homocysteine(1.00) · memory(1.00) · stress(1.00) · cancer(1.00) · thrombosis(1.00) · venous thrombosis(1.00) · cocaine dependence(1.00) · pain(0.94) · breast cancer(0.83) · marijuana abuse(0.67) · mood disorders(0.62) · parkinson s disease(0.62) · DEVELOPMENTAL(0.60) · leiomyoma uterine neoplasms(0.60) · mental retardation(0.60) · schizophrenia bipolar disorder(0.60) · OTHER(0.57) · sleep deprivation(0.57) · bipolar disorder(0.50) · depression(0.50) · fractures bone(0.50) · personality(0.38) · mammographic density(0.36) · personality traits(0.33) · heroin abuse(0.30) · alcoholism(0.29) · adhd(0.26) · cognitive ability(0.25) · heroin dependence(0.25) · bulimia(0.24) · endometrial cancer(0.23) · smoking(0.21) · anorexia nervosa(0.15) · suicide(0.14) · liver cancer(0.13) · tobacco use disorder(0.11) · narcolepsy(0.11) · METABOLIC(0.10) · weight gain(0.10) · smoking behavior(0.09) · endometrial neoplasms(0.07) · attention deficit hyperactivity disorder(0.05) · IMMUNE(0.05) · vitiligo(0.05) · autism(0.03) · REPRODUCTION(0.02) · endometriosis(0.02)

Relevant papers and external links:

PMID 24816252
An atlas of genetic influences on human blood metabolites.

PMID 17008817

PMID 18064318

PMID 15866551

PMID 18194538

PMID 18704099

PMID 18989660

PMID 19417742

PMID 19071221

PMID 19207030

PMID 19037200

PMID 16878403

PMID 15673663

PMID 12595695

PMID 20509070

OMIM 116790

OMIM 104300

PHARMGKB PA162630417
Evidence: PubMed ID:19207030This variant (rs4680/COMT) along with rs6275/DRD2 are associated with risk for schizophrenia in a study consisting of 254 patients and 225 controls of southern indian origin.

PHARMGKB PA161145211
Evidence: Web Resource:External Link variant is responsible for low (Met) and high (Val) activity alleles that have been studied in relation to schizophrenia and other psychiatric/neurological disorders and in relation to breast cancer.

PHARMGKB PA161748325

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Evidence: PubMed ID:17156920In an study at 207 patients treated with morphine, carriers of COMT Val/Val and Val/Met genotype required 63% and 23%, respectively, higher morphine dose compared to carriers of Met/Met genotype (p=0.02).

PHARMGKB PA164944057
Evidence: PubMed ID:19365560The minor allele A of this 472G>A variant produces a valine to methionine substitution, resulting in a less thermostable COMT enzyme that exhibits a 3-fold reduction in activity.

PHARMGKB PA164944062
Evidence: PubMed ID:15537663On the basis of subjects' pain responsiveness, haplotypes involving rs6269 (A/G), rs4633 (C/T), rs4818 (C/G), and rs4680 (G/A) were designated as low (low pain sensitivity (LPS) haplotype; GCGG), average (average pain sensitivity (APS) haplotype; ATCA), or high (high pain sensitivity (HPS) haplotype; ACCG) pain sensitive.

dbSNP: rs4680 GWAS Catalog: rs4680 Genecard: COMT chromosome 22

SNPedia: rs4680(G;G)

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★ rs2283123(C;C) info:1.08 78.60% **normal risk of schizophrenia in limited study**

Associated with schizophrenia in a study of Croatians. Due to the limited number and diversity of the studied population, more study is needed to confirm any link. The T allele was associated with a decreased risk of schizophrenia.

Gene related topics:

schizophrenia(5.00) · PSYCH(2.00) · UNKNOWN(2.00) · dopamine beta hydroxylase activity(2.00) · interpersonal sensitivity paranoid ideation psychoticism(2.00) · perceptual disorders(1.00) · NEUROLOGICAL(0.33) · migraine with aura(0.33) · attention deficit hyperactivity disorder(0.21) · CHEMDEPENDENCY(0.16) · smoking behavior(0.16) · adhd attention deficit hyperactivity disorder(0.15) · personality(0.14) · migraine disorders(0.08) · adhd(0.06) · smoking(0.05) · autism(0.03)

Relevant papers and external links:

PMID 19673036

dbSNP: rs2283123 Genecard: DBH chromosome 9 SNPedia: rs2283123(C;C)

★ rs2870983(C;C) info:0.62 92.21%

plos The minor alleles of rs4819756 and rs2870983 were significantly negatively associated with schizophrenia

Gene related topics:

schizophrenia(1.00)

Relevant papers and external links:

dbSNP: rs2870983 Genecard: PRODH chromosome 22 SNPedia: rs2870983(C;C)

★ rs7294919(T;T) info:2.01 62.12% **Average hippocampal volume**

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rs7294919, showed a particularly strong link to a reduced hippocampus volume, suggesting that this gene is very important to hippocampus development or health. No associations for brain volume, but they did discover that intracranial volume was significantly associated with two loci: rs4273712, a known height locus on chromosome 6q22, and rs9915547, tagging the inversion on chromosome 17q21. The SNP is located between two genes, HRK and FBXW8 , but evidence suggests that it influences the expression level of a gene 3' to FBXW8, TESC . Each copy of the T allele was associated with a 107.8 mm3 decrease in hippocampal volume . In European populations, the effect allele (T) is found at frequency of 0.898 . The minor allele (C) is found at a frequency of 0.102.

Background
The hippocampus is a critical brain structure involved in learning and memory. In particular, it is associated with the ability to form long-term memories of facts and events . This is in contrast to short-term and working memory, which have been shown to be independent of the hippocampus . Hippocampal size decreases with age and is diminished in several disorders including Alzheimer's Disease , Major Depressive Disorder , Post-traumatic Stress Disorder , and Schizophrenia . Moreover, the size of the structure is heritable, with estimates of heritability ranging from 40-70% .

Studies
Two major studies were conducted which found an association between rs7294919 and hippocampal volume. They were published in the April 15th, 2012 issue of Nature Genetics . Though the P-values and regression slopes differ, both studies, together comprising tens of thousands of individuals, agree that the T allele is negatively associated with hippocampal volume.

The first study uses the CHARGE consortium (Cohorts for Heart and Aging Research in Genomic Epidemiology) as its discovery cohort . CHARGE comprises 8 sub-cohorts representing 9,232 people with an average age of 67.1 years. Most of the sub-cohorts were from Europe and hippocampal volume was determined using MRI. Second stage verification/replication was performed on two cohorts comprising 2,318 subjects. This study found that rs7294919 was associated with hippocampal volume with a meta-P value (combining the discovery and replication cohorts) of 2.9 x 10-11 and a regression slope (β) of -107.8 mm3 hippocampal volume. The authors provide some speculation about the SNP's mechanism of action by reviewing the neighboring two genes. HRK is involved in apoptosis of neurons and is thought to play a role in ischemia-induced apoptosis. FBXW8 targets an E3 ubiquitin ligase to protein aggregates and has been shown to be involved in hippocampal neuron dendrite growth. Potential pitfalls of this study include the older age of the participants, the mixture of both computerized and manual hippocampus tracing in MRIs, and the predominantly European ethnic makeup of the cohorts.
The second study's discovery cohort comprised 17 European-ancestry cohorts representing 5,775 healthy people with a mean age of 34.8 years . An additional 2,020 people with various neuropsychiatric disorders were also included to determine whether the SNPs had disease-specific effects. To verify/replicate their findings, they used several cohorts comprising both European ancestry and non-European populations (Yoruba and Los Angeles Mexican).

The study found that rs7294919 was associated with hippocampal volume with a combined P value of 1.99 x 10-7 with a regression slope of -42.74 mm3. The authors also examined the association of the SNP with IQ. While no association was found with full-scale IQ, a small association was found between having the C (minor) allele and an increase in verbal IQ (P = 0.043, β = 0.126). Using data from existing databases , rs7294919 (really rs4767492, a SNP used to impute rs7294919) was associated with expression of tescalin (TESC), a gene which lies 3' to FBXW8 in the brain. The T allele (associated with lower hippocampal volume) was associated with higher expression levels of TESC. TESC itself is expressed during brain development and is thought to regulate differentiation and proliferation. However, it is still not clear how increased TESC levels could be responsible for a decrease in hippocampal volume without additional studies.

References/Links
External Link
External Link
External Link
External Link

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Established associations:

hippocampal volume **you have 2 copies of the risk allele T**

(risk allele=T, odds ratio/beta 107.8 [76.05-139.55] mm3 decrease with pval 3E-11, pubmedid=22504421)

brain measurement **you have 0 copies of the risk allele C**

(risk allele=C, Mean bilateral hippocampal volume odds ratio/beta 47.58 [36.04-59.12] mm3 increase with pval 7E-16, pubmedid=22504417)

Gene related topics:

aging(1.00) · height(1.00) · memory(1.00) · stress(1.00) · brain(1.00) · schizophrenia(1.00) · hippocampus(1.00) · AGING(1.00) · major depressive disorder(1.00)

Relevant papers and external links:

PMID 22504417
Identification of common variants associated with human hippocampal and intracranial volumes.

PMID 22504421
Common variants at 12q14 and 12q24 are associated with hippocampal volume.

dbSNP: rs7294919 GWAS Catalog: rs7294919 Genecard: nan chromosome 12

SNPedia: rs7294919(T;T)

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★ rs1522305(G;G) info:3.02 70.07% **slightly increased risk for schizophrenia**

rs1522305 is a SNP in the phenylalanine hydroxylase (PAH) gene.

A study of Caucasian cohorts, Bulgarian families, and African American families concluded that the more common rs1522305(G) allele was associated in the first two populations with increased risk for schizophrenia.

Gene related topics:

METABOLIC(16.00) · phenylketonurias(16.00) · phenylketonuria pku(7.00) · schizophrenia(5.00) · phenylketonuria(4.00) · phenylalanine hydroxylase deficiency(2.00)

Relevant papers and external links:

PMID 18937293

dbSNP: rs1522305 Genecard: PAH chromosome 12 SNPedia: rs1522305(G;G)

★ rs1006615(C;C) good:1.03 42.84% **common in clinvar**

rs1006615 is associated with increased risk for schizophrenia in German and Scandinavian samples

Gene related topics:

schizophrenia(1.00)

Relevant papers and external links:

PMID 18936756

dbSNP: rs1006615 Genecard: HMCN2 chromosome 9 SNPedia: rs1006615(C;C)

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★ rs3132946(G;G) good:2.67

Established associations:

interstitial lung disease **you have 0 copies of the risk allele A**

(risk allele=A, odds ratio/beta 1.38 [1.21-1.57] with pval 8E-6, pubmedid=23583980)

Gene related topics:

PSYCH(0.38) · schizophrenia(0.38) · IMMUNE(0.34) · diabetes mellitus type 1(0.34) · scleroderma systemic(0.15) · lupus erythematosus systemic(0.14) · VISION(0.12) · macular degeneration(0.12) · CARDIOVASCULAR(0.04) · heart rate(0.04)

Relevant papers and external links:

PMID 23583980
Genome-wide association study identifies multiple susceptibility loci for pulmonary fibrosis.

dbSNP: rs3132946 GWAS Catalog: rs3132946 Genecard: NOTCH4 chromosome 6

SNPedia: rs3132946(G;G)

★ rs2071282(C;C) good:2.72

Gene related topics:

PSYCH(0.38) · schizophrenia(0.38) · IMMUNE(0.34) · diabetes mellitus type 1(0.34) · scleroderma systemic(0.15) · lupus erythematosus systemic(0.14) · VISION(0.12) · macular degeneration(0.12) · CARDIOVASCULAR(0.04) · heart rate(0.04)

Relevant papers and external links:

dbSNP: rs2071282 Genecard: NOTCH4 chromosome 6 SNPedia: rs2071282(C;C)

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★ rs3803300(G;G) info:1.27 45.04%

G allele associated with schizophrenia

among 120 (likely Japanese) first-episode neuroleptic-naive schizophrenics treated with risperidone genotyped for 30 variants in misc. dopamine and serotonin (receptors and otherwise) two SNPs in DRD2 (rs1799989 and rs1800497) and two SNPs in AKT1 (rs3803300 and rs2494732) were significant predictors of treatment response to risperidone

The ancestral allele is G in the dbSNP database.

Gene related topics:

schizophrenia(1.00)

Relevant papers and external links:

PMID 17915974

PMID 18855532

PHARMGKB PA162356248
Evidence: PubMed ID:18855532This SNP is significant predictor of treatment response to risperidone in first-episode schizophrenia.

dbSNP: rs3803300 Genecard: ZBTB42 chromosome 14 SNPedia: rs3803300(G;G)

★ rs2157249(T;T) good:1.49 68.21% **common in complete genomics**

rs9610449 schizophrenia (377 families, 1161 genotyped members and 647 genotyped affected in total) rs9610449 and rs6000200 associated with risk for schizophrenia in African-Americans. In the combined (AA and EA) sample, two SNPs, rs2003813 and rs2157249

Gene related topics:

schizophrenia(1.00)

Relevant papers and external links:

PMID 18632255

dbSNP: rs2157249 Genecard: APOL2 chromosome 22 SNPedia: rs2157249(T;T)

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★ rs6603272(T;-) good:1.75 **Normal risk of developing schizophrenia**

This snp is in the Pseudoautosomal region.

rs6603272, part of a haplotype block spanning introns 4, 5 and 6 of the IL3RA gene, has been reported in a whole genome association study to be associated with schizophrenia. (The other SNPs in this block are rs6422441 and rs17883192.)

The risk allele (oriented to the dbSNP entry) is (G); the odds ratio associated with this allele is 2.74.

Gene related topics:

schizophrenia(5.00) · OTHER(1.00)

Relevant papers and external links:

PMID 17522711

dbSNP: rs6603272 Genecard: IL3RA chromosome Y SNPedia: rs6603272(T;T)

★ rs1064395(G;G) good:2.61 56.67% **Normal risk of bipolar disorder or schizophrenia**

rs1064395 is a single nucleotide variant (SNV) found in the neurocan gene (NCAN) that has been implicated as a predictor of both bipolar disorder (BD) and schizophrenia. BD is characterized by a fluctuation between manic episodes and severe depression. Schizophrenia is characterized by hallucinations, both visual and auditory, paranoia, disorganized thinking and lack of normal social skills.

NCAN is a chondroitin sulfate proteoglycan that is involved in cell adhesion and migration. It contains 14 exons and spans 41 kb of the genome at the location 19p12. [OMIM] It has also been found that, in mice, this gene is expressed in a localized way in the cortical and hippocampal regions of the brain which are responsible for cognition and regulation of emotions.

In 2011, a study by Cichon et al identified rs1064395 in a genome-wide association study (GWAS) for Bipolar Disorder (BD). This study was done by analyzing around 500,000 autosomal SNPs and 12,000 X-chromosomal SNPS in 682 patients with BD and 1300 controls. The patients studied were from Europe, the USA, and Australia. The study then went forward to test the top 48 hits from their initial GWAS with an independent cohort of 1729 cases and 2313 controls, which narrowed down their significant hits to a list of eight. These eight were then used in a meta analysis. The rs1064395 was highly significant with a p-value of 3.02X10-8 and an odds ratio of 1.31, with A being the risk allele. The authors then further validated with a much larger sample size (6030 cases and 31,749 controls) and found a p-value of 2.74X10-4 and an odds ratio of 1.12 which, combined with their previous study lead to an overall p-value of 2.14X10-9 and an odds ratio of 1.17.

In 2012, a study by Mühleisen et al investigated this same SNP in case control studies involving schizophrenic patients. They designed a patient-control study using samples from patients with European ancestry. The initial study included a cohort of 5061 patients and 9655 controls. The risk A-allele was found more frequently in schizophrenic patients then in controls with a p-value of 2.28X10 -8 and an odds ratio of 1.11. They followed up this initial experiment using a independent cohort from the Schizophrenia Psychiatric GWAS Consortium that included 5537 patients and 8043 controls. This follow up inquiry yielded a p-value of 0.0239 and an odds ratio of 1.07. Thus, these authors concluded that, not only is rs1064395 predictive of BD, it is also predictive of schizophrenia.

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Established associations:

bipolar disorder **you have 0 copies of the risk allele A**

(risk allele=A, odds ratio/beta 1.17 with pval 2E-9, pubmedid=21353194)

Gene related topics:

bipolar disorder(5.00) · schizophrenia(5.00) · brain(1.00) · hallucinations(1.00) · depression(1.00) · METABOLIC(0.13) · ldl cholesterol(0.13)

Relevant papers and external links:

PMID 21353194

PMID 21353194

PMID 22497794

dbSNP: rs1064395 GWAS Catalog: rs1064395 Genecard: NCAN chromosome 19

SNPedia: rs1064395(G;G)

★ rs1800169(G;G) good:2.01 76.84% **greater relative benefit of iloperidone to schizophrenics**

rs1800169 is a SNP in the ciliary neurotrophic factor CNTF gene.

In a study of 417 patients with schizophrenia, 279 were treated with iloperidone while 138 were treated with placebo. Iloperidone significantly improved in 6 clinical scores versus placebo. rs1800169(G;G) homozygotes showed greater improvement with iloperidone compared to placebo for 3 of the clinical scores compared to carriers of a rs1800169(A) allele.

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Gene related topics:

schizophrenia(1.00)

Relevant papers and external links:

PMID 18303965

PHARMGKB PA161615729
Evidence: PubMed ID:18303965Schizophrenia patients with homozygous G/G for the rs1800169 show better response to iloperidone.

dbSNP: rs1800169 Genecard: CNTF chromosome 11 SNPedia: rs1800169(G;G)