The CHRNA5 ([neuronal acetylcholine receptor subunit alpha-5](<http://www.uniprot.org/uniprot/P30532>)) gene creates a protein that operates [ion and cation channels](http://www.uniprot.org/citations/20438829) in the plasma membranes in neurons. These channels control [fast signal transmission at synapses](<https://www.ncbi.nlm.nih.gov/gene/1138>) and cause the body’s response to [nicotine](<http://www.uniprot.org/citations/18227835>) and [neuromuscular synaptic transmission](<http://www.uniprot.org/uniprot/P30532>). Variants in CHRNA5 cause [increased](https://www.ncbi.nlm.nih.gov/pubmed/19443489) [susceptibility](https://www.ncbi.nlm.nih.gov/pubmed/18385738) to [lung](https://www.ncbi.nlm.nih.gov/pubmed/20643934) [cancer](https://www.ncbi.nlm.nih.gov/pubmed/18385739) and [COPD](https://www.ncbi.nlm.nih.gov/pubmed/26771213). Variants that cause [increased](https://www.ncbi.nlm.nih.gov/pubmed/1944348) [risk](https://www.ncbi.nlm.nih.gov/pubmed/18385738) of [smoking](<https://www.ncbi.nlm.nih.gov/pubmed/18385739>) also causes greater [difficulty](https://www.ncbi.nlm.nih.gov/pubmed/20643934) in [cessation](https://www.ncbi.nlm.nih.gov/pubmed/28884473), greater numbers of [cigarettes smoked per day](https://www.ncbi.nlm.nih.gov/pubmed/27344179), and higher rates of [anxiety](<https://www.ncbi.nlm.nih.gov/pubmed/25826680>). Variants are also associated with [ME/CFS](<https://www.ncbi.nlm.nih.gov/pubmed/27099524>) due to natural killer cell (NKC) disfunction.

Smoking as a quantitative trait locus 3

<http://www.uniprot.org/uniprot/P30532>

Protein

**Neuronal acetylcholine receptor subunit alpha-5**

Gene

**CHRNA5**

After binding acetylcholine, the AChR responds by an extensive change in conformation that affects all subunits and leads to opening of an ion-conducting channel across the plasma membrane.

* [acetylcholine-gated cation-selective channel activity](https://www.ebi.ac.uk/QuickGO/term/GO:0022848) http://www.uniprot.org/citations/20438829
* [acetylcholine receptor activity](https://www.ebi.ac.uk/QuickGO/term/GO:0015464) Source: UniProtKB
* [ligand-gated ion channel activity](https://www.ebi.ac.uk/QuickGO/term/GO:0015276) http://www.uniprot.org/citations/20438829

[View the complete GO annotation on QuickGO ...](http://www.ebi.ac.uk/QuickGO/annotations?geneProductId=P30532)

#### GO - Biological process**i**

* [behavioral response to nicotine](https://www.ebi.ac.uk/QuickGO/term/GO:0035095) <http://www.uniprot.org/citations/18227835>
* [chemical synaptic transmission](https://www.ebi.ac.uk/QuickGO/term/GO:0007268) http://www.uniprot.org/citations/9009220

* [neuromuscular synaptic transmission](https://www.ebi.ac.uk/QuickGO/term/GO:0007274) Source: GO\_Central
* [signal transduction](https://www.ebi.ac.uk/QuickGO/term/GO:0007165) Source: UniProtKB
* [synaptic transmission, cholinergic](https://www.ebi.ac.uk/QuickGO/term/GO:0007271) Source: GO\_Central

#### Keywords**i**

|  |  |
| --- | --- |
| Molecular function | [Ion channel](http://www.uniprot.org/keywords/KW-0407), [Ligand-gated ion channel](http://www.uniprot.org/keywords/KW-1071), [Receptor](http://www.uniprot.org/keywords/KW-0675) |
| Biological process | [Ion transport](http://www.uniprot.org/keywords/KW-0406), [Transport](http://www.uniprot.org/keywords/KW-0813) |

[DB00898.](https://www.drugbank.ca/drugs/DB00898) [Ethanol](https://www.drugbank.ca/drugs/DB00898)  
[DB00674.](https://www.drugbank.ca/drugs/DB00674) Galantamine  
[DB00184.](https://www.drugbank.ca/drugs/DB00184) Nicotine

[Medications](http://www.uniprot.org/uniprot/P30532#pathology\_and\_biotech) used for treating CHRNA5 issues include [Ethanol](https://www.drugbank.ca/drugs/DB00898), [Galantamine](https://www.drugbank.ca/drugs/DB00674), and [nicotine](<https://www.drugbank.ca/drugs/DB00184>).

<https://www.ncbi.nlm.nih.gov/gene/1138>

The protein encoded by this gene is a nicotinic acetylcholine receptor subunit and a member of a superfamily of ligand-gated ion channels that mediate fast signal transmission at synapses. These receptors are thought to be heteropentamers composed of separate but similar subunits. Defects in this gene have been linked to susceptibility to lung cancer type 2 (LNCR2).[provided by RefSeq, Jun 2010]

<https://www.snpedia.com/index.php/Rs16969968>

<http://www.ncbi.nlm.nih.gov/omim/612052>

LUNG CANCER SUSCEPTIBILITY 2;

<http://www.ncbi.nlm.nih.gov/omim/118505>

CHOLINERGIC RECEPTOR, NEURONAL NICOTINIC, ALPHA POLYPEPTIDE 5; CHRNA5

|  |  |
| --- | --- |
| **isk** | [Rs16969968(A;A)](https://www.snpedia.com/index.php/Rs16969968(A;A)) |
| **Alt** | [Rs16969968(A;A)](https://www.snpedia.com/index.php/Rs16969968(A;A)) |
| **Reference** | [Rs16969968(G;G)](https://www.snpedia.com/index.php/Rs16969968(G;G)) |
| **Significance** | Other |
| **Disease** | [Lung cancer susceptibility 2](https://www.snpedia.com/index.php/Special:FormEdit/ClinVar_Disease/Lung_cancer_susceptibility_2) [Smoking as a quantitative trait locus 3](https://www.snpedia.com/index.php/Special:FormEdit/ClinVar_Disease/Smoking_as_a_quantitative_trait_locus_3) |
| **Variation** | [info](http://www.ncbi.nlm.nih.gov/variation/view/?q=rs16969968) |
| **Gene** | [CHRNA5](https://www.snpedia.com/index.php/CHRNA5) |
| **CLNDBN** | Lung cancer susceptibility 2 https://www.ncbi.nlm.nih.gov/medgen/C2677571 Smoking as a quantitative trait locus 3 https://www.ncbi.nlm.nih.gov/medgen/C3150168 |
| **Reversed** | 0 |
| **HGVS** | NC\_000015.9:g.78882925G>A |
| **CLNSRC** | [OMIM Allelic Variant](https://www.snpedia.com/index.php/OMIM_Allelic_Variant) [UniProtKB (protein)](https://www.snpedia.com/index.php?title=UniProtKB_(protein)&action=edit&redlink=1" \o "UniProtKB (protein) (page does not exist)) |
| **CLNACC** | [RCV000019049.3](http://www.ncbi.nlm.nih.gov/clinvar/RCV000019049.3), [RCV000033213.3](http://www.ncbi.nlm.nih.gov/clinvar/RCV000033213.3), |
|  |  |

<https://www.ncbi.nlm.nih.gov/clinvar/variation/17497/>

## NM\_000745.3(CHRNA5):c.1192G>A (p.Asp398Asn)

<https://www.ncbi.nlm.nih.gov/pubmed/>

Lung cancer susceptibility 2

https://www.ncbi.nlm.nih.gov/pubmed/[18385738](https://www.ncbi.nlm.nih.gov/clinvar/?LinkName=pubmed_clinvar&uid=18385738) https://www.ncbi.nlm.nih.gov/pubmed/[20643934](https://www.ncbi.nlm.nih.gov/clinvar/?LinkName=pubmed_clinvar&uid=20643934) https://www.ncbi.nlm.nih.gov/pubmed/[18385739](https://www.ncbi.nlm.nih.gov/clinvar/?LinkName=pubmed_clinvar&uid=18385739) https://www.ncbi.nlm.nih.gov/pubmed/[19443489](https://www.ncbi.nlm.nih.gov/clinvar/?LinkName=pubmed_clinvar&uid=19443489)

Smoking as a quantitative trait locus 3

https://www.ncbi.nlm.nih.gov/pubmed/[18385738](https://www.ncbi.nlm.nih.gov/clinvar/?LinkName=pubmed_clinvar&uid=18385738) https://www.ncbi.nlm.nih.gov/pubmed/[20643934](https://www.ncbi.nlm.nih.gov/clinvar/?LinkName=pubmed_clinvar&uid=20643934) https://www.ncbi.nlm.nih.gov/pubmed/[18385739](https://www.ncbi.nlm.nih.gov/clinvar/?LinkName=pubmed_clinvar&uid=18385739) https://www.ncbi.nlm.nih.gov/pubmed/[19443489](https://www.ncbi.nlm.nih.gov/clinvar/?LinkName=pubmed_clinvar&uid=19443489)

<https://www.ncbi.nlm.nih.gov/projects/SNP/snp_ref.cgi?rs=16969968>

<https://www.ncbi.nlm.nih.gov/pubmed/26757861>

However, there was an association among non-smoking subjects between the A allele of rs16969968 and high a BMI (p < 0.01).

#### CONCLUSIONS:

This last variant may be involved in food-addiction disorders.

<https://www.ncbi.nlm.nih.gov/pubmed/26434895>

We found the CHRNA5 rs16969968 polymorphism to be associated with the risk of lung cancer (AA vs GG: OR=1.60, 95%CI=1.51-1.71). On stratified analysis by smoking status, a statistically significant increased risk was observed in the smoking group (AA vs GG: OR=1.80, 95%CI=1.61-2.01). However, this polymorphism was not associated with lung cancer risk in Asians (AA vs GG: OR=0.95, 95%CI=0.35-2.59), whereas it was linked to increased risk of lung cancer among Caucasians (AA vs GG: OR=1.65, 95%CI=1.55-1.76).

<https://www.ncbi.nlm.nih.gov/pubmed/28884473>

For six-month abstinence, we found statistically significant heterogeneity between genotypes (rs16969968) for nicotine replacement therapy (NRT) versus placebo at six months for NHB participants (P = 0.03; n = 2 trials), but not for other biomarkers or treatment comparisons. Six-month abstinence was increased in the active NRT group as compared to placebo among participants with a GG genotype (risk ratio (RR) 1.47, 95% confidence interval (CI) 1.07 to 2.03), but not in the combined group of participants with a GA or AA genotype (RR 0.43, 95% CI 0.15 to 1.26; ratio of risk ratios (RRR) GG vs GA or AA of 3.51, 95% CI 1.19 to 10.3).

<https://www.ncbi.nlm.nih.gov/pubmed/28069549>

the strongest determinant of tobacco dependence was rs16969968 with OR (95%CI) 1.32 (1.08-1.62) for A allele carriers vs. GG comparison (P=0.003)

<https://www.ncbi.nlm.nih.gov/pubmed/27543155>

he CHRNA5 rs16969968 risk genotype (AA) was associated with increased risk and earlier diagnosis for lung cancer,

<https://www.ncbi.nlm.nih.gov/pubmed/27344179>

Further association with smoking behaviors indicating those three SNPs (rs16969968 [A], rs1051730 [A] and rs2036534 [C]) significantly associated with number of cigarettes smoked per day, CPD, with P = 0.009, 0.011 and 0.001 respectively.

Especially, rs16969968, a nonsynonymous variant, was indicated with functions of altering nicotinic receptor conductance in vitroby amino acid change in the CHRNA5 [[7](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5216947/#R7), [18](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5216947/#R18), [19](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5216947/#R19)]. Those two loci have been found to be associated with lung cancer, chronic obstructive pulmonary disease and body mass index in never smokers [[13](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5216947/#R13), [20](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5216947/#R20)–[23](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5216947/#R23)]. Based on our study, both rs1051730 allele (A) in CHRNA3 gene and rs16969968 allele (A) in CHRNA5 gene increased smoking quantity and delayed smoking cessation behaviors,

<https://www.ncbi.nlm.nih.gov/pubmed/26771213>

Our top result was rs16969968 (P = 1.7 × 10(-14)) in CHRNA5, a locus previously associated with COPD susceptibility and nicotine dependence.

<https://www.ncbi.nlm.nih.gov/pubmed/26239294>

The common nonsynonymous variant rs16969968 in the α5 nicotinic receptor subunit gene (CHRNA5) is the strongest genetic risk factor for nicotine dependence in European Americans and contributes to risk in African Americans.  Meta-analysis confirmed the risk effect of the only common variant (rs16969968, European ancestry: odds ratio (OR)=1.3, P=3.5 × 10(-11); African ancestry: OR=1.3, P=0.01) and demonstrated that three low frequency variants contributed an independent risk (aggregate term, European ancestry: OR=1.3, P=0.005; African ancestry: OR=1.4, P=0.0006).

<https://www.ncbi.nlm.nih.gov/pubmed/25948103>

 Following overnight abstinence from nicotine, participants completed a protocol that included an intravenous (IV) dose of saline and two escalating IV doses of nicotine. The outcomes evaluated were the aversive, pleasurable, and stimulatory ratings of nicotine's effects, cardiovascular reactivity to nicotine, withdrawal severity, and cognitive performance before and after the nicotine administration session. The heavy smoking risk allele (rs16969968\*A; frequency=28% (EA) and 6% (AA)) was associated with lower ratings of aversive effects (P<5 × 10(-8)) with marked specificity. This effect was evident in EA and AA subjects analyzed as separate groups and was most robust at the highest nicotine dose. Rs16969968\*A was also associated with greater improvement on a measure of cognitive control (Stroop Task) following nicotine administration.

<https://www.ncbi.nlm.nih.gov/pubmed/25941207>

Prevention intervention programs reduce substance use, including smoking, but not all individuals respond.   
There was a main effect of both the intervention (b = -0.24, P < .05) and genotype at rs16969968 (b = 0.14, P < .05) on high school smoking. Using dummy coding to allow for nonlinear effects, individuals with the A/A genotype smoked more often than those with G/G (b = 0.33, P < .05). A genotype × intervention effect was found with reduced smoking among those with A/A and G/A genotypes to levels similar to those with the G/G genotype (G/G vs. A/A: b = -0.67, P < .05; A/G vs. A/A: b = -0.61, P < .05; G/G vs. A/G ns). Results were nonsignificant for the other four markers.

<https://www.ncbi.nlm.nih.gov/pubmed/25826680>

rs16969968 and rs588765 were associated with the PANAS Nervous factor (p = 0.006 and 0.007 respectively).

<https://www.ncbi.nlm.nih.gov/pubmed/25674902>

Acetylcholine influences the speed of information processing. We examined the effect of the rs3841324 polymorphism (L/S) and the rs16969968 (G/A) polymorphism on response speed in the Stroop task and the Negative priming task. These polymorphisms are located in the gene that encodes the nicotinic acetylcholine receptor α5-subunit (CHRNA5). Male carriers of the rs3841324 S/S genotype and the rs16969968 G/G genotype were faster than male carriers of at least one L allele or one A allele. In contrast, female carriers of the rs3841324 S/S genotype and the rs16969968 G/G genotype were slower than female carriers of at least one L allele or one A allele. These results indicate that the minor alleles of both polymorphisms modulate response speed in a sex-dependent, diametrically opposed manner.

<https://www.ncbi.nlm.nih.gov/pubmed/24934182>

s16969968, predicted nicotine deprivation-induced reduction of P3a amplitude

P3b and P3a components of the event-related brain potential waveform evoked by a three-stimulus visual oddball task are widely viewed as positive indices of cognitive control-related processes. Cognitive control

<https://www.ncbi.nlm.nih.gov/pubmed/24838476>

The effect of maternal smoking on newborn lung function was associated with maternal genotype for the α5 nicotinic receptor (rs16969968) (P < .001 for interaction). Supplemental vitamin C taken by pregnant smokers improved newborn PFT results and decreased wheezing through 1 year in the offspring. Vitamin C in pregnant smokers may be an inexpensive and simple approach to decrease the effects of smoking in pregnancy on newborn pulmonary function and respiratory morbidities.

<https://www.ncbi.nlm.nih.gov/pubmed/24819610>

(CHRNA5, rs16969968) on both dorsolateral prefrontal cortex mediated behavior and physiology during working memory and on prefrontal gray matter volume.

CHNRA5 rs16969968 (G>A) on prefrontal phenotypes, including cognitive performance at the N-Back task, prefrontal physiology with BOLD fMRI during performance of the 2-Back working memory task, and prefrontal morphometry with structural MRI.

#### RESULTS:

We found that DRD2 rs1076560 and CHNRA5 rs16969968 interact to modulate cognitive function, prefrontal physiology during working memory, and prefrontal gray matter volume. More specifically, CHRNA5-AA/DRD2-GT subjects had greater behavioral performance, more efficient prefrontal cortex activity at 2Back working memory task, and greater prefrontal gray matter volume than the other genotype groups.

<https://www.ncbi.nlm.nih.gov/pubmed/24727484>

45.0% abstinence for A allele carriers vs. 51.7% for GG homozygotes decreased abstinence at 1 year (69.1% abstinence for A allele carriers vs. 76.0% for GG homozygotes Among patients who have smoked and who are hospitalized with acute myocardial infarction MI, the high-risk CHRNA5 allele was associated with lower likelihood of quitting before hospitalization and significantly less abstinence 1 year after hospitalization with MI. The CHRNA5 rs16969968 genotype may therefore identify patients who would benefit from aggressive, personalized smoking cessation intervention.

<https://www.ncbi.nlm.nih.gov/pubmed/23358500>

Genotype at rs16969968 predicted nicotine titration, with homozygotes for the major allele (G:G) displaying significantly reduced puff volume in response to nicotine, whereas minor allele carriers (A:G or A:A) produced equivalent puff volumes for placebo and nicotine cigarettes. The present results suggest that puff volume may be a more powerful objective phenotype of smoking behavior than self-reported cigarettes per day and nicotine dependence.

<https://www.ncbi.nlm.nih.gov/projects/SNP/snp_ref.cgi?rs=6495306>

<https://www.snpedia.com/index.php/Rs6495306>

<https://www.ncbi.nlm.nih.gov/pubmed/26270548>

CHRNA5 nicotinic receptor gene on chromosome 15, that is genome wide significant for risk for nicotine dependence.

| **SNP** | **Function** | **EUR Freq** | **Tajima’s D EUR** | **iHS EUR** | **ASN Freq** | **Tajima’s D ASN** | **iHS ASN** | **AFR Freq** | **Tajima’s D AFR** | **iHS AFR** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **rs6495306** | CHRNA5 intronic | 0.4 | **(2.07, 2.32)** | -0.32 | 0.15 | (-0.42, 0.06) | -0.2 | 0.26 | (-0.16, 0.31) | 0.41 |

<https://www.ncbi.nlm.nih.gov/pubmed/28132300>

We analyzed three single nucleotide polymorphisms (SNPs) known to be associated with nicotine addiction (rs16969968 and rs6495306 localized on CHRNA5 gene; rs578776 localized on CHRNA3 gene)

<https://www.ncbi.nlm.nih.gov/pubmed/21229299>

Furthermore, the two haplotypes of rs16969968, rs6495306 (or rs588765), and rs3743078 that were associated with lung cancer risk, each containing the major allele of rs6495306, were found to correlate with low CHRNA5 mRNA expression.

<https://www.ncbi.nlm.nih.gov/pubmed/25233467>

 adenocarcinoma (ADC) odds ratio 0.86 Three SNPs in CHRNA5 (rs6495306, in complete LD (r2 = 0.99), had a significant total effect (p = 0.03, FDR q = 0.023) and direct effects (p = 0.04, FDR q = 0.034)

<https://www.ncbi.nlm.nih.gov/pubmed/26220977>

| **SNP (major allele)** | **Frontal cortex (*N* = 132)** | | **Temporal cortex (*N* = 126)** | | **Cerebellum (*N* = 120)** | | **Pons (*N* = 124)** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| ***β*** | ***P*** | ***β*** | ***P*** | ***β*** | ***P*** | ***β*** | ***P*** |
| rs6495306 (A) | −0.027 | **1.4 × 10−4** | −0.030 | **8.7 × 10−7** | 0.017 | 0.33 | −0.055 | **9.0 × 10−1** |

<https://www.ncbi.nlm.nih.gov/pubmed/26981579>

SNPs analyzed for association with cigarettes per day in WHI SHARe.

| **SNP** | **Chromosome (base-pair) position** | **Nearby genes** | **Alleles** | **Coded Allele** | **Coded AF** | ***ß* (s.e.)** | ***P-*value** | ***P-*value (adjusted)\*** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| rs7180002 | 15:78581651 | *CHRNA5* | A/T | T | 0.11941 | 0.072 (0.034) | 0.00307 | 0.08597 |

| **Gene** | **SNP** | ***ß* (s.e.)** | ***P*** | ***Adj. P*⁎** |
| --- | --- | --- | --- | --- |
| *CHRNA5* | rs7180002 | 0.344 (0.088) | 9.57 × 10− 05 | 8.61 × 10− 4 |

Analysis of frequency, distribution, and significance of SNPs in genes for TRP ion channels and AChRs in ME/CFS patients and unfatigued controls in rank order of significance (weak)

| **Gene** | **CL** | **SNP** | **BPs** | **A1** | **FMecfs** | **FControl** | **A2** | **χ2** | **OR** | **P-value** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| CHRNA5 | 15 | rs7180002 | 78,581,651 | T | 0.4342 | 0.2667 | A | 4.084 | 2.11 | 0.0433 |

<https://www.ncbi.nlm.nih.gov/pubmed/25233467>

 adenocarcinoma (ADC) odds ratio 0.86 Three SNPs in CHRNA5 (rs6495306, in complete LD (r2 = 0.99), had a significant total effect (p = 0.03, FDR q = 0.023) and direct effects (p = 0.04, FDR q = 0.034)

<https://www.ncbi.nlm.nih.gov/pubmed/26220977>

| **SNP (major allele)** | **Frontal cortex (*N* = 132)** | | **Temporal cortex (*N* = 126)** | | **Cerebellum (*N* = 120)** | | **Pons (*N* = 124)** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| ***β*** | ***P*** | ***β*** | ***P*** | ***β*** | ***P*** | ***β*** | ***P*** |
| rs6495306 (A) | −0.027 | **1.4 × 10−4** | −0.030 | **8.7 × 10−7** | 0.017 | 0.33 | −0.055 | **9.0 × 10−1** |

<https://www.ncbi.nlm.nih.gov/pubmed/26981579>

SNPs analyzed for association with cigarettes per day in WHI SHARe.

| **SNP** | **Chromosome (base-pair) position** | **Nearby genes** | **Alleles** | **Coded Allele** | **Coded AF** | ***ß* (s.e.)** | ***P-*value** | ***P-*value (adjusted)\*** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| rs7180002 | 15:78581651 | *CHRNA5* | A/T | T | 0.11941 | 0.072 (0.034) | 0.00307 | 0.08597 |

| **Gene** | **SNP** | ***ß* (s.e.)** | ***P*** | ***Adj. P*⁎** |
| --- | --- | --- | --- | --- |
| *CHRNA5* | rs7180002 | 0.344 (0.088) | 9.57 × 10− 05 | 8.61 × 10− 4 |

A78581651T (A;T) A78581651T (T;T)

This variant acts in the brain in the [frontal cortex, temporal cortex, and pons](<https://www.ncbi.nlm.nih.gov/pubmed/26220977>), controlling message transmission between the cortex and cerebellum, motor function, problem solving, memory formation and processing, language, judgement, impulse control, and sexual behavior. This variant also is associated with increased likelihood of [adenocarcinoma (ADC)](<https://www.ncbi.nlm.nih.gov/pubmed/25233467>) and an [increased number of cigarettes smoked per day](<https://www.ncbi.nlm.nih.gov/pubmed/26981579>).

Additionally, it affects the immune system. Natural killer cells (NKC) are a type of white blood cells found in the blood, bone marrow, spleen, and lymph nodes.  They kill viral infected cells and tumorous cells.  CFS patients have half the cellular efficiency of the normal population with a [17% cellular death rate](https://www.ncbi.nlm.nih.gov/pubmed/27099524).  The A78581651T variant may decrease gene expression in both the DNA and RNA, causing significant reduction in NKC activity.  This variant was 2X as common in [CFS patients with an odds ratio of 2.11](<https://www.ncbi.nlm.nih.gov/pubmed/27099524>).

People should avoid smoking, and proactively check for lung cancer if they smoke.

Many dietary supplements have been found to increase or decrease natural killer cell function.

\* [Resveratrol](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4855330/) stimulates the immune system by increasing NKC activity, but

sufficient body concentration can only be achieved through supplementation.

\* [Myricetin](https://www.ncbi.nlm.nih.gov/pubmed/25075019), a flavonoid found in food and red wine, can increase NKC activity.

\* [Quercetin](https://www.ncbi.nlm.nih.gov/pubmed/19449452), a flavonoid in onions and fruits, may improve NKC and T cell function.

\* [Histone deacetylase inhibitors (HDACi), including suberoylanilide hydroxamic acid and valproric acid,](https://www.ncbi.nlm.nih.gov/pubmed/17349632/) impair NKC function, and should be avoided.

[Other medications](http://www.uniprot.org/uniprot/P30532#pathology\_and\_biotech) used for treating CHRNA5 issues include [Ethanol](https://www.drugbank.ca/drugs/DB00898), [Galantamine](https://www.drugbank.ca/drugs/DB00674), and [nicotine](<https://www.drugbank.ca/drugs/DB00184>).

<# #>

| Variant |Population % |   
| :-------------: |:-------------:|  
| G1376C (G;G) | right-aligned |  
| G2691A (A;A) | centered |  
| C829T (T;T) | are neat |

| C984A (A;A)| are neat |

| C984A (A;A)| are neat |

People should not smoke. If you do smoke, be aware of your risk for dependency and increased difficulty of quitting smoking. Consider regular checks for lung cancer.

[Many factors may decrease your risk of lung cancer](https://www.cancer.gov/types/lung/patient/lung-prevention-pdq#section/all):

\* Avoid cigarettes, cigars, pipe smoking, and secondhand smoke.

\* Have less than one alcoholic drink per day.

\* Practice safe sex, and avoid HIV infection.

\* Avoid radiation exposure, including atomic bomb radiation, radiation therapy, imaging tests, and radon.

\* Avoid environmental toxins, such as asbestos, arsenic, chromium, nickel, beryllium, cadmium, tar, soot, and sir pollution.

\* [Beta carotene supplements, made from yellow and orange fruits and vegetables and dark green, leafy vegetables,](https://www.cancer.gov/types/lung/patient/lung-prevention-pdq#section/all) may help reduce risk for heavy smokers.

[Medications](http://www.uniprot.org/uniprot/P30532#pathology\_and\_biotech) used for treating CHRNA5 issues include [Ethanol](https://www.drugbank.ca/drugs/DB00898), [Galantamine](https://www.drugbank.ca/drugs/DB00674), and [nicotine](<https://www.drugbank.ca/drugs/DB00184>).

This variant acts in the brain in the [frontal cortex, temporal cortex, and pons](<https://www.ncbi.nlm.nih.gov/pubmed/26220977>), controlling message transmission between the cortex and cerebellum, motor function, problem solving, memory formation and processing, language, judgement, impulse control, and sexual behavior. Each recessive A allele [increases mRNA expression](<https://www.ncbi.nlm.nih.gov/pubmed/21229299>) in the brain, which in turn impacts body’s the response to nicotine. This variant is associated with increased [risk of adenocarcinoma (ADC)](<https://www.ncbi.nlm.nih.gov/pubmed/25233467>) [(lung cancer)](<https://www.ncbi.nlm.nih.gov/pubmed/21229299>) with an odds ratio of 0.86 and [nicotine addiction](<https://www.ncbi.nlm.nih.gov/pubmed/28132300>) or dependence, especially in Caucasians with an [odds ratio of 2.07](<https://www.ncbi.nlm.nih.gov/pubmed/26270548>).

This variant controls [cognitive function, working memory, and gray matter volume in the brain](<https://www.ncbi.nlm.nih.gov/pubmed/24819610>). Males have much faster [information processing](<https://www.ncbi.nlm.nih.gov/pubmed/25674902>), including [much better behavioral performance, more efficient cortex activity, and the largest gray matter volume](https://www.ncbi.nlm.nih.gov/pubmed/24819610), while women have much slower information processing. In general, [visual cognitive control is impaired](<https://www.ncbi.nlm.nih.gov/pubmed/24934182>). The brain changes caused by this variant is the [strongest genetic risk factor for developing nicotine dependence in African Americans and Caucasians, with an odds ratio of 1.3](<https://www.ncbi.nlm.nih.gov/pubmed/26239294>), causes difficulties with smoking cessation, and greatly increases the number of [cigarettes smoked per day](<https://www.ncbi.nlm.nih.gov/pubmed/27344179>). People are [15% less likely](<https://www.ncbi.nlm.nih.gov/pubmed/24727484>) to be able to quit smoking, and they respond much less well to [nicotine replacement therapy(NRT)](<https://www.ncbi.nlm.nih.gov/pubmed/28884473>). This may be caused due to the variant [greatly increasing the pleasure and mental stimulation experienced after smoking, as well as withdrawal severity](<https://www.ncbi.nlm.nih.gov/pubmed/25948103>). The AA homozygous variant is associated with greatly elevated risk and earlier diagnosis of [lung cancer with an odds ratio of 1.65](<https://www.ncbi.nlm.nih.gov/pubmed/27543155>), but not in [Asians](<https://www.ncbi.nlm.nih.gov/pubmed/26434895>). It is also associated with [COPD](<https://www.ncbi.nlm.nih.gov/pubmed/26771213>) and [newborn pulmonary disfunction and respiratory morbidities](<https://www.ncbi.nlm.nih.gov/pubmed/24838476>) in the children of smoking mothers.

People should not smoke. If you do smoke, be aware of your risk for dependency and increased difficulty of quitting smoking. Consider regular checks for lung cancer. Pregnant women should consider [supplemental vitamin C](<https://www.ncbi.nlm.nih.gov/pubmed/24838476>).

[Many factors may decrease your risk of lung cancer](https://www.cancer.gov/types/lung/patient/lung-prevention-pdq#section/all):

\* Avoid cigarettes, cigars, pipe smoking, and secondhand smoke.

\* Have less than one alcoholic drink per day.

\* Practice safe sex, and avoid HIV infection.

\* Avoid radiation exposure, including atomic bomb radiation, radiation therapy, imaging tests, and radon.

\* Avoid environmental toxins, such as asbestos, arsenic, chromium, nickel, beryllium, cadmium, tar, soot, and sir pollution.

\* [Beta carotene supplements, made from yellow and orange fruits and vegetables and dark green, leafy vegetables,](https://www.cancer.gov/types/lung/patient/lung-prevention-pdq#section/all) may help reduce risk for heavy smokers.

[Medications](http://www.uniprot.org/uniprot/P30532#pathology\_and\_biotech) used for treating CHRNA5 issues include [Ethanol](https://www.drugbank.ca/drugs/DB00898), [Galantamine](https://www.drugbank.ca/drugs/DB00674), and [nicotine](<https://www.drugbank.ca/drugs/DB00184>).

This heterozygous variant affects the brain in a variety of ways. This variant controls [cognitive function, working memory, and gray matter volume in the brain](<https://www.ncbi.nlm.nih.gov/pubmed/24819610>). Males have faster [information processing](<https://www.ncbi.nlm.nih.gov/pubmed/25674902>), including [better behavioral performance, more efficient cortex activity, and larger gray matter volume](https://www.ncbi.nlm.nih.gov/pubmed/24819610), while women have slower information processing. In general, people have worse [visual cognitive control](<https://www.ncbi.nlm.nih.gov/pubmed/24934182>). The brain changes caused by this variant is the [strongest genetic risk factor for developing nicotine dependence in African Americans and Caucasians, with an odds ratio of 1.3](<https://www.ncbi.nlm.nih.gov/pubmed/26239294>), causes difficulties with smoking cessation, and increases the number of [cigarettes smoked per day](<https://www.ncbi.nlm.nih.gov/pubmed/27344179>). People are [15% less likely](<https://www.ncbi.nlm.nih.gov/pubmed/24727484>) to be able to quit smoking, and they respond less well to [nicotine replacement therapy(NRT)](<https://www.ncbi.nlm.nih.gov/pubmed/28884473>). This may be caused due to the variant [increasing the pleasure and mental stimulation experienced after smoking, as well as withdrawal severity](<https://www.ncbi.nlm.nih.gov/pubmed/25948103>). This variant is also associated with a greater risk for [lung cancer and COPD](<https://www.ncbi.nlm.nih.gov/pubmed/27344179>).

People should not smoke. If you do smoke, be aware of your risk for dependency and increased difficulty of quitting smoking. Consider regular checks for lung cancer.

[Many factors may decrease your risk of lung cancer](https://www.cancer.gov/types/lung/patient/lung-prevention-pdq#section/all):

\* Avoid cigarettes, cigars, pipe smoking, and secondhand smoke.

\* Have less than one alcoholic drink per day.

\* Practice safe sex, and avoid HIV infection.

\* Avoid radiation exposure, including atomic bomb radiation, radiation therapy, imaging tests, and radon.

\* Avoid environmental toxins, such as asbestos, arsenic, chromium, nickel, beryllium, cadmium, tar, soot, and sir pollution.

\* [Beta carotene supplements, made from yellow and orange fruits and vegetables and dark green, leafy vegetables,](https://www.cancer.gov/types/lung/patient/lung-prevention-pdq#section/all) may help reduce risk for heavy smokers.

[Medications](http://www.uniprot.org/uniprot/P30532#pathology\_and\_biotech) used for treating CHRNA5 issues include [Ethanol](https://www.drugbank.ca/drugs/DB00898), [Galantamine](https://www.drugbank.ca/drugs/DB00674), and [nicotine](<https://www.drugbank.ca/drugs/DB00184>).

# What does the CHRNA5 gene do?

The CHRNA5 ([neuronal acetylcholine receptor subunit alpha-5](http://www.uniprot.org/uniprot/P30532)) gene creates a protein that operates [ion and cation channels](http://www.uniprot.org/citations/20438829) in the plasma membranes in neurons. These channels control [fast signal transmission at synapses](https://www.ncbi.nlm.nih.gov/gene/1138) and cause the body’s response to [nicotine](http://www.uniprot.org/citations/18227835) and [neuromuscular synaptic transmission](http://www.uniprot.org/uniprot/P30532). Variants in CHRNA5 cause [increased](https://www.ncbi.nlm.nih.gov/pubmed/19443489) [susceptibility](https://www.ncbi.nlm.nih.gov/pubmed/18385738) to [lung](https://www.ncbi.nlm.nih.gov/pubmed/20643934) [cancer](https://www.ncbi.nlm.nih.gov/pubmed/18385739) and [COPD](https://www.ncbi.nlm.nih.gov/pubmed/26771213). Variants that cause [increased](https://www.ncbi.nlm.nih.gov/pubmed/1944348) [risk](https://www.ncbi.nlm.nih.gov/pubmed/18385738) of [smoking](https://www.ncbi.nlm.nih.gov/pubmed/18385739) also causes greater [difficulty](https://www.ncbi.nlm.nih.gov/pubmed/20643934) in [cessation](https://www.ncbi.nlm.nih.gov/pubmed/28884473), greater numbers of [cigarettes smoked per day](https://www.ncbi.nlm.nih.gov/pubmed/27344179), and higher rates of [anxiety](https://www.ncbi.nlm.nih.gov/pubmed/25826680). Variants are also associated with [ME/CFS](https://www.ncbi.nlm.nih.gov/pubmed/27099524) due to natural killer cell (NKC) disfunction.

This gene is located on chromosome 15. The protein it creates acts in your lungs, immune system, nervous system, and brain.

# What are some common mutations of CHRNA5?

There are three well-known variants in CHRNA5: [G1192A (Asp398Asn)](https://www.ncbi.nlm.nih.gov/clinvar/variation/17497/), [A78573551G](https://www.ncbi.nlm.nih.gov/projects/SNP/snp_ref.cgi?rs=6495306), and [A78581651T](https://www.ncbi.nlm.nih.gov/projects/SNP/snp_ref.cgi?rs=7180002).

<# G1192A #>

This variant is a change at a specific point in the CHRNA5 gene from guanine (G) to adenine (A) resulting in incorrect protein function. This substitution of a single nucleotide is known as a missense variant.

<# A78573551G #>

This variant is a change at a specific point in the CHRNA5 gene from adenine (A) to guanine (G) resulting in incorrect protein function. This substitution of a single nucleotide is known as a missense variant.

<# A78581651T #>

This variant is a change at a specific point in the gene from adenine (A) to thymine (T) resulting in incorrect three function. This substitution of a single nucleotide is known as a missense variant.

<# G1192A #>

# What does this mean?

People with this variant have one copy of the [G1192A (Asp398Asn)](https://www.ncbi.nlm.nih.gov/clinvar/variation/17497/) variant. This substitution of a single nucleotide is known as a missense mutation.

# What is the effect of this variant?

You are in the Mild Loss of Function category. See below for more information.

# How common is this genotype in the general population?

<piechart percentage=39.2 />

# What does this mean?

People with this variant have two copies of the [C78606381T](https://www.ncbi.nlm.nih.gov/projects/SNP/snp\_ref.cgi?rs=12914385) variant. This substitution of a single nucleotide is known as a missense mutation.

# What is the effect of this variant?

You are in the Moderate Loss of Function category. See below for more information.

# How common is this genotype in the general population?

<piechart percentage=5.2 />

# What does this mean?

Your CHRNA5 gene has no variants. A normal gene is referred to as a "wild-type" gene.

# What is the effect of this variant?

This variant is not associated with increased risk.

# How common is this genotype in the general population?

<piechart percentage=55.6 />

<# A78573551G #>

# What does this mean?

People with this variant have one copy of the [A78573551G](https://www.ncbi.nlm.nih.gov/projects/SNP/snp\_ref.cgi?rs=6495306) variant. This substitution of a single nucleotide is known as a missense mutation.

# What is the effect of this variant?

You are in the Mild Loss of Function category. See below for more information.

# How common is this genotype in the general population?

<piechart percentage=39.2 />

# What does this mean?

People with this variant have two copies of the [A78573551G](https://www.ncbi.nlm.nih.gov/projects/SNP/snp\_ref.cgi?rs=6495306) variant. This substitution of a single nucleotide is known as a missense mutation.

# What is the effect of this variant?

You are in the Moderate Loss of Function category. See below for more information.

# How common is this genotype in the general population?

<piechart percentage=17.9 />

# What does this mean?

Your CHRNA5 gene has no variants. A normal gene is referred to as a "wild-type" gene.

# What is the effect of this variant?

This variant is not associated with increased risk.

# How common is this genotype in the general population?

<piechart percentage=42.9 />

<# A78581651T #>

# What does this mean?

People with this variant have one copy of the [A78581651T](https://www.ncbi.nlm.nih.gov/projects/SNP/snp\_ref.cgi?rs=7180002) variant. This substitution of a single nucleotide is known as a missense mutation.

# What is the effect of this variant?

You are in the Mild Loss of Function category. See below for more information.

# How common is this genotype in the general population?

<piechart percentage=27.3 />

# What does this mean?

People with this variant have two copies of the [A78581651T](https://www.ncbi.nlm.nih.gov/projects/SNP/snp\_ref.cgi?rs=7180002) variant. This substitution of a single nucleotide is known as a missense mutation.

# What is the effect of this variant?

You are in the Mild Loss of Function category. See below for more information.

# How common is this genotype in the general population?

<piechart percentage=9.5 />

# What does this mean?

Your gene has no variants. A normal gene is referred to as a "wild-type" gene.

# What is the effect of this variant?

This variant is not associated with increased risk.

# How common is this genotype in the general population?

<piechart percentage=63.2 />

<# unknown #>

# What does this mean?

Your CHRNA5 gene has an unknown variant.

# What is the effect of this variant?

The effect is unknown.

# How common is this genotype in the general population?

<piechart percentage= />

<# wildtype #>

# What does this mean?

Your CHRNA5 gene has no variants. A normal gene is referred to as a "wild-type" gene.

# What is the effect of this variant?

Your variant is not associated with any loss of function.

# How common is this genotype in the general population?

<piechart percentage= />

# How do changes in CHRNA5 affect people?

For the vast majority of people, the overall risk associated with the common CHRNA5 variants is small and does not impact treatment. It is possible that variants in this gene interact with other gene variants, which is the reason for our inclusion of this gene.

<# G1192A (G;A) #>

| **Variant** | **Population %** |
| --- | --- |
| G1192A (G;A) | 39.2% |

# Mild Risk

This heterozygous variant affects the brain in a variety of ways. This variant controls [cognitive function, working memory, and gray matter volume in the brain](https://www.ncbi.nlm.nih.gov/pubmed/24819610). Males have faster [information processing](https://www.ncbi.nlm.nih.gov/pubmed/25674902), including [better behavioral performance, more efficient cortex activity, and larger gray matter volume](https://www.ncbi.nlm.nih.gov/pubmed/24819610), while women have slower information processing. In general, people have worse [visual cognitive control](https://www.ncbi.nlm.nih.gov/pubmed/24934182). The brain changes caused by this variant is the [strongest genetic risk factor for developing nicotine dependence in African Americans and Caucasians, with an odds ratio of 1.3](https://www.ncbi.nlm.nih.gov/pubmed/26239294), causes difficulties with smoking cessation, and increases the number of [cigarettes smoked per day](https://www.ncbi.nlm.nih.gov/pubmed/27344179). People are [15% less likely](https://www.ncbi.nlm.nih.gov/pubmed/24727484) to be able to quit smoking, and they respond less well to [nicotine replacement therapy(NRT)](https://www.ncbi.nlm.nih.gov/pubmed/28884473). This may be caused due to the variant [increasing the pleasure and mental stimulation experienced after smoking, as well as withdrawal severity](https://www.ncbi.nlm.nih.gov/pubmed/25948103). This variant is also associated with a greater risk for [lung cancer and COPD](https://www.ncbi.nlm.nih.gov/pubmed/27344179).

# What should I do about this?

People should not smoke. If you do smoke, be aware of your risk for dependency and increased difficulty of quitting smoking. Consider regular checks for lung cancer.

[Many factors may decrease your risk of lung cancer](https://www.cancer.gov/types/lung/patient/lung-prevention-pdq#section/all):

* Avoid cigarettes, cigars, pipe smoking, and secondhand smoke.
* Have less than one alcoholic drink per day.
* Practice safe sex, and avoid HIV infection.
* Avoid radiation exposure, including atomic bomb radiation, radiation therapy, imaging tests, and radon.
* Avoid environmental toxins, such as asbestos, arsenic, chromium, nickel, beryllium, cadmium, tar, soot, and sir pollution.
* [Beta carotene supplements, made from yellow and orange fruits and vegetables and dark green, leafy vegetables,](https://www.cancer.gov/types/lung/patient/lung-prevention-pdq#section/all) may help reduce risk for heavy smokers.

[Medications](http://www.uniprot.org/uniprot/P30532#pathology_and_biotech) used for treating CHRNA5 issues include [Ethanol](https://www.drugbank.ca/drugs/DB00898), [Galantamine](https://www.drugbank.ca/drugs/DB00674), and [nicotine](https://www.drugbank.ca/drugs/DB00184).

<# G1192A (G;G) #>

| **Variant** | **Population %** |
| --- | --- |
| G1192A (A;A) | 5.2% |

# Moderate Risk

This variant controls [cognitive function, working memory, and gray matter volume in the brain](https://www.ncbi.nlm.nih.gov/pubmed/24819610). Males have much faster [information processing](https://www.ncbi.nlm.nih.gov/pubmed/25674902), including [much better behavioral performance, more efficient cortex activity, and the largest gray matter volume](https://www.ncbi.nlm.nih.gov/pubmed/24819610), while women have much slower information processing. In general, [visual cognitive control is impaired](https://www.ncbi.nlm.nih.gov/pubmed/24934182). The brain changes caused by this variant is the [strongest genetic risk factor for developing nicotine dependence in African Americans and Caucasians, with an odds ratio of 1.3](https://www.ncbi.nlm.nih.gov/pubmed/26239294), causes difficulties with smoking cessation, and greatly increases the number of [cigarettes smoked per day](https://www.ncbi.nlm.nih.gov/pubmed/27344179). People are [15% less likely](https://www.ncbi.nlm.nih.gov/pubmed/24727484) to be able to quit smoking, and they respond much less well to [nicotine replacement therapy(NRT)](https://www.ncbi.nlm.nih.gov/pubmed/28884473). This may be caused due to the variant [greatly increasing the pleasure and mental stimulation experienced after smoking, as well as withdrawal severity](https://www.ncbi.nlm.nih.gov/pubmed/25948103). The AA homozygous variant is associated with greatly elevated risk and earlier diagnosis of [lung cancer with an odds ratio of 1.65](https://www.ncbi.nlm.nih.gov/pubmed/27543155), but not in [Asians](https://www.ncbi.nlm.nih.gov/pubmed/26434895). It is also associated with [COPD](https://www.ncbi.nlm.nih.gov/pubmed/26771213) and [newborn pulmonary disfunction and respiratory morbidities](https://www.ncbi.nlm.nih.gov/pubmed/24838476) in the children of smoking mothers.

# What should I do about this?

People should not smoke. If you do smoke, be aware of your risk for dependency and increased difficulty of quitting smoking. Consider regular checks for lung cancer. Pregnant women should consider [supplemental vitamin C](https://www.ncbi.nlm.nih.gov/pubmed/24838476).

[Many factors may decrease your risk of lung cancer](https://www.cancer.gov/types/lung/patient/lung-prevention-pdq#section/all):

* Avoid cigarettes, cigars, pipe smoking, and secondhand smoke.
* Have less than one alcoholic drink per day.
* Practice safe sex, and avoid HIV infection.
* Avoid radiation exposure, including atomic bomb radiation, radiation therapy, imaging tests, and radon.
* Avoid environmental toxins, such as asbestos, arsenic, chromium, nickel, beryllium, cadmium, tar, soot, and sir pollution.
* [Beta carotene supplements, made from yellow and orange fruits and vegetables and dark green, leafy vegetables,](https://www.cancer.gov/types/lung/patient/lung-prevention-pdq#section/all) may help reduce risk for heavy smokers.

[Medications](http://www.uniprot.org/uniprot/P30532#pathology_and_biotech) used for treating CHRNA5 issues include [Ethanol](https://www.drugbank.ca/drugs/DB00898), [Galantamine](https://www.drugbank.ca/drugs/DB00674), and [nicotine](https://www.drugbank.ca/drugs/DB00184).

<# A78573551G (A;G) A78573551G (G;G) #>

| **Variant** | **Population %** |
| --- | --- |
| A78573551G (A;G) | 39.2% |
| A78573551G (G;G) | 17.9% |

# Moderate Risk

This variant acts in the brain in the [frontal cortex, temporal cortex, and pons](https://www.ncbi.nlm.nih.gov/pubmed/26220977), controlling message transmission between the cortex and cerebellum, motor function, problem solving, memory formation and processing, language, judgement, impulse control, and sexual behavior. Each recessive A allele [increases mRNA expression](https://www.ncbi.nlm.nih.gov/pubmed/21229299) in the brain, which in turn impacts body’s the response to nicotine. This variant is associated with increased [risk of adenocarcinoma (ADC)](https://www.ncbi.nlm.nih.gov/pubmed/25233467) [(lung cancer)](https://www.ncbi.nlm.nih.gov/pubmed/21229299) with an odds ratio of 0.86 and [nicotine addiction](https://www.ncbi.nlm.nih.gov/pubmed/28132300) or dependence, especially in Caucasians with an [odds ratio of 2.07](https://www.ncbi.nlm.nih.gov/pubmed/26270548).

# What should I do about this?

People should not smoke. If you do smoke, be aware of your risk for dependency and increased difficulty of quitting smoking. Consider regular checks for lung cancer.

[Many factors may decrease your risk of lung cancer](https://www.cancer.gov/types/lung/patient/lung-prevention-pdq#section/all):

* Avoid cigarettes, cigars, pipe smoking, and secondhand smoke.
* Have less than one alcoholic drink per day.
* Practice safe sex, and avoid HIV infection.
* Avoid radiation exposure, including atomic bomb radiation, radiation therapy, imaging tests, and radon.
* Avoid environmental toxins, such as asbestos, arsenic, chromium, nickel, beryllium, cadmium, tar, soot, and sir pollution.
* [Beta carotene supplements, made from yellow and orange fruits and vegetables and dark green, leafy vegetables,](https://www.cancer.gov/types/lung/patient/lung-prevention-pdq#section/all) may help reduce risk for heavy smokers.

[Medications](http://www.uniprot.org/uniprot/P30532#pathology_and_biotech) used for treating CHRNA5 issues include [Ethanol](https://www.drugbank.ca/drugs/DB00898), [Galantamine](https://www.drugbank.ca/drugs/DB00674), and [nicotine](https://www.drugbank.ca/drugs/DB00184).

<# A78581651T (A;T) A78581651T (T;T) #>

| **Variant** | **Population %** |
| --- | --- |
| A78581651T (A;T) | 27.3% |
| A78581651T (T;T) | 9.5% |

# Mild Risk

This variant acts in the brain in the [frontal cortex, temporal cortex, and pons](https://www.ncbi.nlm.nih.gov/pubmed/26220977), controlling message transmission between the cortex and cerebellum, motor function, problem solving, memory formation and processing, language, judgement, impulse control, and sexual behavior. This variant also is associated with increased likelihood of [adenocarcinoma (ADC)](https://www.ncbi.nlm.nih.gov/pubmed/25233467) and an [increased number of cigarettes smoked per day](https://www.ncbi.nlm.nih.gov/pubmed/26981579).

Additionally, it affects the immune system. Natural killer cells (NKC) are a type of white blood cells found in the blood, bone marrow, spleen, and lymph nodes. They kill viral infected cells and tumorous cells. CFS patients have half the cellular efficiency of the normal population with a [17% cellular death rate](https://www.ncbi.nlm.nih.gov/pubmed/27099524). The A78581651T variant may decrease gene expression in both the DNA and RNA, causing significant reduction in NKC activity. This variant was 2X as common in [CFS patients with an odds ratio of 2.11](https://www.ncbi.nlm.nih.gov/pubmed/27099524).

# What should I do about this?

People should avoid smoking, and proactively check for lung cancer if they smoke.

Many dietary supplements have been found to increase or decrease natural killer cell function.

* [Resveratrol](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4855330/) stimulates the immune system by increasing NKC activity, but sufficient body concentration can only be achieved through supplementation.
* [Myricetin](https://www.ncbi.nlm.nih.gov/pubmed/25075019), a flavonoid found in food and red wine, can increase NKC activity.
* [Quercetin](https://www.ncbi.nlm.nih.gov/pubmed/19449452), a flavonoid in onions and fruits, may improve NKC and T cell function.
* [Histone deacetylase inhibitors (HDACi), including suberoylanilide hydroxamic acid and valproric acid,](https://www.ncbi.nlm.nih.gov/pubmed/17349632/) impair NKC function, and should be avoided.