<https://www.ncbi.nlm.nih.gov/pubmed/21559498>

A strong association between rs12914385 and rs8042374, and lung cancer risk was shown, odds ratios (OR) were 1.44, (95% confidence interval (CI): 1.29–1.62, P = 3.69×10−10) and 1.35 (95% CI: 1.18–1.55, P = 9.99×10−6) respectively. Each copy of risk alleles at rs12914385 and rs8042374 was associated with increased cigarette consumption of 1.0 and 0.9 cigarettes per day (CPD) (P = 5.18×10−5 and P = 5.65×10−3).

<https://www.ncbi.nlm.nih.gov/pubmed/21436384>

while the major C allele of rs12914385 in CHRNA3 was associated with a decrease of 3.25 (SE=0.82; p=7.62×10−5) pack years per allele.

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

Results show that nicotine dependence is a mediator of the association between lung adenocarcinoma and gene variations in the regions of CHRNA5/A3/B4 and accounts for approximately 15% of this relationship. The top two CHRNA3 SNPs associated with the risk for lung adenocarcinoma were rs1051730 and rs12914385 (p-value = 1.9×10−10 and 1.1×10−10, respectively). Also, these two SNPs had significant indirect effects on lung adenocarcinoma risk through nicotine dependence (p = 0.003 and 0.007).

<https://www.ncbi.nlm.nih.gov/pubmed/19654303>

the strongest associations identified were defined by SNPs mapping to 15q25.1 (rs12914385; P = 3.19 x 10(-16)), 5p15.33 (rs4975616; P = 6.66 x 10(-7)), and 6p21.33 (rs3117582; P = 9.13 x 10(-7)). Variation at 15q25.1, but not 5p15.33 or 6p21.33,

ecently genome-wide association (GWA) studies of lung cancer have shown common variation at 15q24−25.1 as a determinant of risk([1](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754318/#R1)–[3](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754318/#R3)). Two studies found that the same alleles at this locus increased risk of lung cancer and influenced tobacco smoking behaviour. Genes mapping to this region of association include CHRNA3, CHRNA4, CHRNA5, PSM4, LOC123688, and IREB2. The CHRNA genes encode the nicotinic receptor subunits; in addition to playing a role in development of nicotine dependence, nicotine receptors also influence cell proliferation and apoptosis. Hence these genes represent strong candidates for combined lung cancer susceptibility and predilection to smoking. PSMA4 encodes the fourth component of the proteasome which plays a role in protein degradation and IREB2 is involved in iron metabolism which may thus impact on oxidative damage. A second lung cancer locus identified through the GWA studies maps to 5p and includes the genes encoding TERT and CLMPTL1. In addition to these loci we and others have found statistically significant evidence implicating a third locus at 6p as a risk factor for lung cancer([4](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754318/#R4), [5](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2754318/#R5)).

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **rs12914385** | | |  | **Per Allele** | | |  | **Heterozygous** | | |  | | **Homozygous** | | | |
| **Study** | **Cases** | **Controls** |  | **OR** | **95% CI** | ***P*-value** |  | **OR** | **95% CI** | ***P*-value** | |  | | **OR** | **95% CI** | ***P*-value** | |
| UK GWAs P1 | 1952 | 1438 |  | 1.32 | (1.19-1.45) | 4.47 x 10-8 |  | 1.31 | (1.12-1.53) | 5.84 x 10-4 | |  | | 1.74 | (1.43-2.12) | 9.48 x 10-8 | |
| UK GWAs P2 | 2465 | 3005 |  | 1.27 | (1.18-1.37) | 1.08 x 10-9 |  | 1.25 | (1.11-1.41) | 2.35 x 10-4 | |  | | 1.62 | (1.38-1.90) | 2.88 x 10-9 | |
| **Combined** | **4417** | **4443** |  | **1.29** | **(1.21-1.37)** | **3.19 x 10-6** |  | **1.27** | **(1.16-1.4)** | **5.51 x 10-7** | |  | | **1.66** | **(1.47-1.88)** | **1.98 x 10-15** | |

<https://www.ncbi.nlm.nih.gov/pubmed/24621683>

| **Locus** | **Nearest gene(s)** | **SNP** | **Risk Allele** | **Frequency** | | **Meta-Analysis** | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Nhw** | **Aa** | **OR (CI)** | **P** | **I2** | **Q** |
| 15q25 | *CHRNA3* | rs12914385 | T | 0•42 | 0•19 | 1•39 (1•29-1•51) | 2•70×10−16 | 0 | 0•76 |

<https://www.ncbi.nlm.nih.gov/pubmed/22290489>

CHRNA5SNP rs12915366 and CHRNA3 SNP rs12914385 were found to be associated with smoking persistence ([Hamidovic et al. 2011](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3864572/" \l "R78)). Both SNPs are located in regions that have been associated with smoking and nicotine dependence in European Americans ([Liu et al. 2010](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3864572/#R131); [Saccone et al. 2009](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3864572/" \l "R190); [TAG 2010](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3864572/#R212)), suggesting that there may be distinct variants which modulate smoking behavior phenotypes in African-Americans.

<https://www.ncbi.nlm.nih.gov/pubmed/20418890>

A total of 130 SNPs in the 15q25.1 nicotinic receptor gene cluster were significantly associated with Cigarettes smoked per day (n = 38,181, minimum P = 4.2 × 10−35 at rs12914385 in CHRNA3).

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

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **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** |
| **rs12914385** | CHRNA3 intronic | 0.4 | **(2.35, 2.55)** | -0.39 | 0.32 | (1.85, 2.01) | 0.36 | 0.2 | (1.13, 1.35) | 0.39 |

<https://www.ncbi.nlm.nih.gov/pubmed/28827732>

| **enes** | **Variants\*** | | **Frequency (%)†** | | **Ethnicity** | | | **Number evaluated** | | | **Genetic associations with lung cancer** | | | | | **Heterogeneity** | | | | **Begg *P*** | | **Venice criteria grades∫** | | | **Credibility of evidence§** | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | |  |  | |  | |  |  | |  | |
| *CHRNA3* | | rs12914385(T/C) | | 35.09 | | All | 4 | | 5356/2873 | | | T vs C | | 1.20(1.01–1.44) | | | 0.044 | | 76 | | 0.007 | | 0.734 | ACA | | Weak |

<https://www.ncbi.nlm.nih.gov/pubmed/29030599>

| **Exposure** | **SNPs in the IV** | **Beta** | **SE** | ***P* -value** | **Egger pleiotropy P** | **SD** | **Years per exposure unit** | **Interquartile effect in years** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Cigarettes smoked per day | rs12914385 | 0.034 | 0.005 | 6.47 × 10−10 | − | 11.7 | 0.338 | 5.3 |

<https://www.ncbi.nlm.nih.gov/pubmed/23094028>

In the meta-analysis, this region became very significant with the strongest signal at rs12914385 with a p-value 1.98×10−9. This result confirmed that the CHRNA3-A5 region on 15q24–25.1 is associated with both lung cancer development and smoking behavior, which several other independent studies have already proven [[https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3477105/#pone.0046612-Liu1]](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3477105/#pone.0046612-Liu1)–[[ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3477105/#pone.0046612-Hung1]](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3477105/#pone.0046612-Hung1), and that CPD is an intermediate phenotype for lung cancer.

<https://www.ncbi.nlm.nih.gov/pubmed/23870182>

Wang et al. [https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3717087/#B17] demonstrated that each copy of chromosome 15q risk alleles was associated with increased cigarette consumption of 1.0 cigarette per day at rs12914385

<https://www.ncbi.nlm.nih.gov/pubmed/19836008>

The strongest evidence for association with lung cancer risk overall and with each histology group was observed for the 15q25.1 locus.[1–3](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2775843/#bib1) (nicotinic acetylcholine receptor genes), beginning with rs12914385 in CHRNA3 (MIM https://www.ncbi.nlm.nih.gov/omim/118503) (OR = 1.34, 95% CI = 1.27–1.42, p = 5.24 × 10−27 rs12914385 had an OR = 1.30, 95% CI = 1.25–1.36, p = 2.75 × 10−38

<https://www.ncbi.nlm.nih.gov/pubmed/20485328>

Cocaine dependence was nominally associated with two CHRNA3 SNPs, rs12914385 (OR=0.64, P=0.004,

<https://www.ncbi.nlm.nih.gov/pubmed/27099524>

Analysis of genotype, ORs, and significance of SNPs in genes for TRP ion channels and AChRs in ME/CFS patients and unfatigued controls in rank order of significance

| **Gene** | **CL** | **SNP** | **Genotype** | **ME/CFS, n %)** | **Unfatigued controls, n (%)** | χ**2** | **OR** | P**-value** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| CHRNA3 | 15 | rs12914385 | TT | 12 (85.7) | 2 (14.3) | 6.09 | 6.22 | 0.014 |

<http://www.uniprot.org/uniprot/P32297>

**Neuronal acetylcholine receptor subunit alpha-3**

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.

#### GO - Molecular functioni

* [acetylcholine binding](https://www.ebi.ac.uk/QuickGO/term/GO:0042166) Source: UniProtKB
* [acetylcholine-gated cation-selective channel activity](https://www.ebi.ac.uk/QuickGO/term/GO:0022848) Source: UniProtKB
* [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) Source: DFLAT
* [serotonin-gated cation-selective channel activity](https://www.ebi.ac.uk/QuickGO/term/GO:0022850) Source: GO\_Central

[View the complete GO annotation on QuickGO ...](http://www.ebi.ac.uk/QuickGO/annotations?geneProductId=P32297)

#### GO - Biological processi

* [acetylcholine receptor signaling pathway](https://www.ebi.ac.uk/QuickGO/term/GO:0095500) Source: ARUK-UCL
* [activation of transmembrane receptor protein tyrosine kinase activity](https://www.ebi.ac.uk/QuickGO/term/GO:0007171) Source: UniProtKB
* [behavioral response to nicotine](https://www.ebi.ac.uk/QuickGO/term/GO:0035095) Source: UniProtKB
* [excitatory postsynaptic potential](https://www.ebi.ac.uk/QuickGO/term/GO:0060079) Source: UniProtKB
* [ion transport](https://www.ebi.ac.uk/QuickGO/term/GO:0006811) Source: UniProtKB
* [locomotory behavior](https://www.ebi.ac.uk/QuickGO/term/GO:0007626) Source: UniProtKB
* [nervous system development](https://www.ebi.ac.uk/QuickGO/term/GO:0007399) Source: UniProtKB
* [regulation of acetylcholine secretion, neurotransmission](https://www.ebi.ac.uk/QuickGO/term/GO:0014056) Source: UniProtKB
* [regulation of dendrite morphogenesis](https://www.ebi.ac.uk/QuickGO/term/GO:0048814) Source: UniProtKB
* [regulation of membrane potential](https://www.ebi.ac.uk/QuickGO/term/GO:0042391) Source: UniProtKB
* [regulation of smooth muscle contraction](https://www.ebi.ac.uk/QuickGO/term/GO:0006940) Source: UniProtKB
* [response to acetylcholine](https://www.ebi.ac.uk/QuickGO/term/GO:1905144) Source: ARUK-UCL
* [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: UniProtKB
* [synaptic transmission involved in micturition](https://www.ebi.ac.uk/QuickGO/term/GO:0060084) Source: UniProtKB

[View the complete GO annotation on QuickGO ...](http://www.ebi.ac.uk/QuickGO/annotations?geneProductId=P32297)

#### Keywordsi

|  |  |
| --- | --- |
| 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) |

[Nicotinic acetylcholine receptors](http://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=76)

|  |  |
| --- | --- |
| DrugBanki | [DB01156.](https://www.drugbank.ca/drugs/DB01156) Bupropion.  [DB09028.](https://www.drugbank.ca/drugs/DB09028) Cytisine.  [DB00514.](https://www.drugbank.ca/drugs/DB00514) Dextromethorphan.  [DB00898.](https://www.drugbank.ca/drugs/DB00898) Ethanol.  [DB00674.](https://www.drugbank.ca/drugs/DB00674) Galantamine.  [DB00848.](https://www.drugbank.ca/drugs/DB00848) Levamisole.  [DB01227.](https://www.drugbank.ca/drugs/DB01227) Levomethadyl Acetate.  [DB00184.](https://www.drugbank.ca/drugs/DB00184) Nicotine.  [DB01090.](https://www.drugbank.ca/drugs/DB01090) Pentolinium.  [DB01273.](https://www.drugbank.ca/drugs/DB01273) Varenicline. |

CHRNA3 (Neuronal acetylcholine receptor subunit alpha-3) encodes a nicotine neurotransmitter receptor protein called [acetylcholine](http://www.uniprot.org/citations/8906617). It also controls [ion](http://www.uniprot.org/citations/20438829) and [serotonin](https://www.ebi.ac.uk/QuickGO/term/GO:0022850) channels in the brain. Variants in this gene have been associated with [nicotine dependence](<https://www.ncbi.nlm.nih.gov/pubmed/22290489>), increased daily [cigarette consumption](<https://www.ncbi.nlm.nih.gov/pubmed/23870182>), [lung cancer](<https://www.ncbi.nlm.nih.gov/pubmed/19836008>), [COPD](https://www.ncbi.nlm.nih.gov/pubmed/24621683), [cocaine dependence](<https://www.ncbi.nlm.nih.gov/pubmed/20485328>), and [CFS](<https://www.ncbi.nlm.nih.gov/pubmed/27099524>).

Brain and nervous system, immune system,

The CHRNA3 protein plays a role in developing nicotine dependence and regulating nicotine receptor proliferation and destruction. Incorrect formation of the nicotine neurotransmitter receptor protein has a variety of effects. This heterozygous variant causes increased risk of [lung cancer](<https://www.ncbi.nlm.nih.gov/pubmed/23094028>), with an [odds ratio of 1.2]( <https://www.ncbi.nlm.nih.gov/pubmed/28827732>), and [COPD](<https://www.ncbi.nlm.nih.gov/pubmed/24621683>), with an [odds ratio of 1.39](<https://www.ncbi.nlm.nih.gov/pubmed/24621683>). It causes an [increase](<https://www.ncbi.nlm.nih.gov/pubmed/29030599>) of [one](<https://www.ncbi.nlm.nih.gov/pubmed/21559498>) [cigarette](<https://www.ncbi.nlm.nih.gov/pubmed/23870182>) [per day](<https://www.ncbi.nlm.nih.gov/pubmed/20418890>) and may also cause [smoking persistence]( <https://www.ncbi.nlm.nih.gov/pubmed/22290489>). However, the C allele is protective, with a [decrease of 3.25 packs per year per C allele](<https://www.ncbi.nlm.nih.gov/pubmed/21436384>). Finally, his variant may cause an increase in [cocaine dependence](<https://www.ncbi.nlm.nih.gov/pubmed/20485328>).

People also should not smoke or use cocaine. If you do smoke, be aware of your risk for dependency and increased difficulty of quitting smoking.

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

\* Avoid cigarette, cigar, 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/P32297>) indicated for use for CHRNA3 issues include: [Bupropion](<https://www.drugbank.ca/drugs/DB01156>), [Cytisine](<https://www.drugbank.ca/drugs/DB09028>), [Dextromethorphan](<https://www.drugbank.ca/drugs/DB00514>), [Ethanol](<https://www.drugbank.ca/drugs/DB00898>), [Galantamine](<https://www.drugbank.ca/drugs/DB00674>), [Levamisole](<https://www.drugbank.ca/drugs/DB00848>), [Levomethadyl Acetate](<https://www.drugbank.ca/drugs/DB01227>), [Nicotine](<https://www.drugbank.ca/drugs/DB00184>), [Pentolinium](<https://www.drugbank.ca/drugs/DB01090>), and [Varenicline](https://www.drugbank.ca/drugs/DB01273).

The CHRNA3 protein plays a role in developing nicotine dependence and regulating nicotine receptor proliferation and destruction. Incorrect formation of the nicotine neurotransmitter receptor protein has a variety of effects. This homozygous variant causes greatly increased risk of [lung cancer](<https://www.ncbi.nlm.nih.gov/pubmed/23094028>), with an [odds ratio of 1.44](<https://www.ncbi.nlm.nih.gov/pubmed/21559498>), and [COPD](<https://www.ncbi.nlm.nih.gov/pubmed/24621683>), with an [odds ratio of 1.39](<https://www.ncbi.nlm.nih.gov/pubmed/24621683>). It causes an [increase](<https://www.ncbi.nlm.nih.gov/pubmed/29030599>) of [two](<https://www.ncbi.nlm.nih.gov/pubmed/21559498>) [cigarettes](<https://www.ncbi.nlm.nih.gov/pubmed/23870182>) [per day](<https://www.ncbi.nlm.nih.gov/pubmed/20418890>) and may also cause greatly increased [smoking persistence]( <https://www.ncbi.nlm.nih.gov/pubmed/22290489>). This variant may cause an increase in [cocaine dependence](<https://www.ncbi.nlm.nih.gov/pubmed/20485328>).

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 C78606381T (T;T) variant decreases gene expression in both the DNA and RNA, causing significant reduction in NKC activity. This variant was five as common in [CFS patients at 85.7% with an odds ratio of 6.22.](<https://www.ncbi.nlm.nih.gov/pubmed/27099524>)

People also should not smoke or use cocaine. If you do smoke, be aware of your greatly increased risk for dependency and difficulty of quitting smoking, and 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 cigarette, cigar, 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/P32297>) indicated for use for CHRNA3 issues include: [Bupropion](<https://www.drugbank.ca/drugs/DB01156>), [Cytisine](<https://www.drugbank.ca/drugs/DB09028>), [Dextromethorphan](<https://www.drugbank.ca/drugs/DB00514>), [Ethanol](<https://www.drugbank.ca/drugs/DB00898>), [Galantamine](<https://www.drugbank.ca/drugs/DB00674>), [Levamisole](<https://www.drugbank.ca/drugs/DB00848>), [Levomethadyl Acetate](<https://www.drugbank.ca/drugs/DB01227>), [Nicotine](<https://www.drugbank.ca/drugs/DB00184>), [Pentolinium](<https://www.drugbank.ca/drugs/DB01090>), and [Varenicline](https://www.drugbank.ca/drugs/DB01273).

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 in increase 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.

<https://www.ncbi.nlm.nih.gov/pubmed/28474623>

The rs13180 (IREB2), rs16969968 (CHRNA5) and rs1051730 (CHRNA3) were significantly associated with COPD in additive model [Padj =0.00001, odds ratio (OR)=0.64; Padj =0.0001, OR=1.41 and Padj =0.0001, OR=1.47]. The C-G haplotype by rs13180 and rs1051730 was a protective factor for COPD in our population (Padj =0.0005, OR=0.61). These results were confirmed only in smokers. The rs16969968 and rs1051730 were associated with decrease of forced expiratory volume in 1 sec % predicted (Padj =0.005 and Padj =0.0019).

#### INTERPRETATION & CONCLUSIONS:

Our study showed the association of rs13180, rs16969968 and rs1051730 with COPD and lung function in Tatar population from Russia. Further studies need to be done in other ethnic populations.

<https://www.ncbi.nlm.nih.gov/pubmed/28049019>

 rs1051730 T alleles were associated with reduced risk of TJR among current smokers (HR 0.84, 95% CI 0.76-0.98, per T allele),

<https://www.ncbi.nlm.nih.gov/pubmed/27663783>

Variants at 15q25 were significantly associated with CPD after multiple testing correction rs1051730:

<https://www.ncbi.nlm.nih.gov/pubmed/27613883>

Self-reported amount of smoking was associated with all three dimensions of psychological distress. For instance among participants smoking 30 cigarettes/day or more, the odds ratio (OR) for stress was 1.67 (95% confidence interval [CI] 1.47-1.89) compared to never-smokers. Corresponding ORs for fatigue and hopelessness were 2.18 (95% CI 1.92-2.47) and 3.08 (95% CI 2.62-3.62). Among current smokers, homozygotes and heterozygotes for the CHRNA3 genotype had higher tobacco consumption than noncarriers.

<https://www.ncbi.nlm.nih.gov/pubmed/27127891>

We found a robust association between risk allele A of rs1051730 and CPD >10 (odds ratio (OR)=1.77, 95% confidence interval (CI): 1.20-2.59, p=0.004),

<https://www.ncbi.nlm.nih.gov/pubmed/27072204>

In summary, CHRNA3 rs1051730 (G > A) and AGPHD1 rs8034191 (A > G) were more susceptible to lung cancers than noncarriers.

<https://www.ncbi.nlm.nih.gov/pubmed/26508385>

We observed a significant association between lung cancer and rs1051730 in pooled population by using allele (OR = 1.30, 95% CI = 1.27-1.34, P <  0.0001), dominant (OR = 1.41, 95% CI = 1.29-1.55, P < 0.0001), recessive (OR = 1.53, 95% CI = 1.42-1.65, P < 0.0001) and additive (OR = 1.75, 95% CI = 1.61-1.90, P < 0.0001) models.

<https://www.ncbi.nlm.nih.gov/pubmed/26054357>

n smokers, heterozygotes (CT) and homozygotes (TT) for rs1051730 genotype had higher smoking intensity compared with non-carriers (CC). Furthermore, in ever-smokers homozygotes had increased risk of antipsychotic medication with an odds ratio (OR) of 1.16 compared with non-carriers, Correspondingly, ORs were 1.60 (0.74-3.47) for schizophrenia and 1.31 (1.16-1.47) and 0.89 (0.58-1.36) for chronic obstructive pulmonary disease (P-interaction: 0.16). Odds ratios per rs1051730 allele for schizophrenia and antipsychotic medication use in ever-smokers in the general population were 1.22 (95% CI: 0.84-1.79) and 1.06 (1.00-1.12). In the Psychiatric Genomics Consortium, the corresponding OR for schizophrenia was 1.06 (1.04-1.08) in ever- and never-smokers combined.

<https://www.ncbi.nlm.nih.gov/pubmed/25891233>

An association between rs1051730 genotype and both outcome measures was observed at 7-days after the quit date. Each copy of the minor allele corresponded to a 2.9% decrease in adherence to prescribed Nicotine replacement therapy dose (P = 0.044), and a 1.0mg decrease in daily NRT consumption (P = 0.026).

<https://www.ncbi.nlm.nih.gov/pubmed/25777141>

n contrast, the per-allele increase inCHRNA3 rs1051730 associated with high tobacco consumption was associated with 0.59 kg (0.96; 0.22) lower body weight, 0.23 kg/m(2) (0.33; 0.13) lower body mass index, 0.32 cm (0.74; 0.003) lower waist circumference and 0.45 cm (0.66; 0.24) lower hip circumference.

<https://www.ncbi.nlm.nih.gov/pubmed/25632390>

Further analysis revealed the association between rs16969868-1051730 (OR = 2.66; 95% CI: 1.30-5.42) and number of cigarettes smoked per day (CPD) with heaviness of nicotine addiction measured by the Fagerström Test for Nicotine Dependence (FTND) (OR = 2.60; 95% CI: 1.24-5.43).

This heterozygous variant causes increased risk of [adenocarcinoma](<https://www.ncbi.nlm.nih.gov/pubmed/27072204>) and [squamous cell lung cancer among Caucasians and African Americans](https://www.ncbi.nlm.nih.gov/pubmed/24254305), with an [odds ratio of 2.25](<https://www.ncbi.nlm.nih.gov/pubmed/24337855>), but not in East Asians or never-smokers. It causes an increase in [cigarettes smoked per day](<https://www.ncbi.nlm.nih.gov/pubmed/27663783>) [(odds ratio 2.66)](<https://www.ncbi.nlm.nih.gov/pubmed/25632390>) and [severity of nicotine addiction (odds ratio 2.6)](<https://www.ncbi.nlm.nih.gov/pubmed/25632390>). There is a [2.9% decrease](<https://www.ncbi.nlm.nih.gov/pubmed/25891233>) in adherence to prescribed Nicotine replacement therapy (NRT) dose, and a [1.0mg decrease](<https://www.ncbi.nlm.nih.gov/pubmed/25891233>) in daily NRT consumption up to 28 days after beginning treatment. Physical changes associated with one T allele include [0.59 kg lower body weight, 0.23 kg/m(2) lower body mass index, 0.32 cm lower waist circumference, and 0.45 cm lower hip circumference](<https://www.ncbi.nlm.nih.gov/pubmed/25777141>). It also is associated with [higher resting heart rate, lower systolic blood pressure, and higher HDL cholesterol](<https://www.ncbi.nlm.nih.gov/pubmed/24867305>).

People also should not smoke. If you do smoke, be aware of your risk for dependency and increased difficulty of quitting smoking.

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

\* Avoid cigarette, cigar, 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/P32297>) indicated for use for CHRNA3 issues include: [Bupropion](<https://www.drugbank.ca/drugs/DB01156>), [Cytisine](<https://www.drugbank.ca/drugs/DB09028>), [Dextromethorphan](<https://www.drugbank.ca/drugs/DB00514>), [Ethanol](<https://www.drugbank.ca/drugs/DB00898>), [Galantamine](<https://www.drugbank.ca/drugs/DB00674>), [Levamisole](<https://www.drugbank.ca/drugs/DB00848>), [Levomethadyl Acetate](<https://www.drugbank.ca/drugs/DB01227>), [Nicotine](<https://www.drugbank.ca/drugs/DB00184>), [Pentolinium](<https://www.drugbank.ca/drugs/DB01090>), and [Varenicline](<https://www.drugbank.ca/drugs/DB01273>).

This homozygous variant causes increased risk of [adenocarcinoma and squamous cell lung cancer among Caucasians and African Americans](https://www.ncbi.nlm.nih.gov/pubmed/24254305), with an [odds ratio of 1.9](<https://www.ncbi.nlm.nih.gov/pubmed/25233467>), but not East Asians or never-smokers. It causes an increase in [cigarettes smoked per day](<https://www.ncbi.nlm.nih.gov/pubmed/27663783>) [(odds ratio 2.66)](<https://www.ncbi.nlm.nih.gov/pubmed/25632390>) and [severity of nicotine addiction (odds ratio 2.6)](<https://www.ncbi.nlm.nih.gov/pubmed/25632390>). There is a [5.8% decrease](<https://www.ncbi.nlm.nih.gov/pubmed/25891233>) in adherence to prescribed Nicotine replacement therapy (NRT) dose, and a [2.0mg decrease](<https://www.ncbi.nlm.nih.gov/pubmed/25891233>) in daily NRT consumption up to 28 days after beginning treatment. T alleles were associated with [1.18 kg lower body weight, 0.46 kg/m(2) lower body mass index, 0.64 cm lower waist circumference, and 0.90 cm lower hip circumference](<https://www.ncbi.nlm.nih.gov/pubmed/25777141>). It also causes [higher resting heart rate, lower systolic blood pressure, and higher HDL cholesterol](<https://www.ncbi.nlm.nih.gov/pubmed/24867305>). Among people who smoke more than 30 cigarettes per day, [fatigue and hopelessness](<https://www.ncbi.nlm.nih.gov/pubmed/27613883>) are also greatly increased. Homozygotes had increased risk of [antipsychotic medication and schizophrenia](<https://www.ncbi.nlm.nih.gov/pubmed/26054357>).

People also should not smoke. If you do smoke, be aware of your greatly increased risk for dependency and difficulty of quitting smoking, and consider regular checks for lung cancer. Monitor signs of schizophrenia and antipsychotic medication side effects.

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

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\* Have less than one alcoholic drink per day.

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