SNPedia

# rs2736990

rs2736990 is a SNP associated with Parkinson's disease (PD), a neurodegenerative disorder characterized by the degradation of dopamine-producing neurons in the substantia nigra. Rs273990 is located on chromosome 4q22 in the synuclein-alpha SNCA locus. The function of SNCA is not fully understood, but it predominately found in the presynaptic terminals of neurons, and it is thought that it plays a role in maintaining adequate supplies of synaptic vesicles. SNCA is also a major component of Lewy Bodies (LB), protein accumulations often found in neurons in patients with PD.

The best evidence for the association of rs2736990 with PD was provided in a genome-wide association study (GWAS) that found an increased frequency of the minor C allele (T is the major allele) in position 90897564 among cases compared to controls. The study first identified this SNP in a pool of 1,713 cases and 3,978 controls of European ancestry. The researchers then successfully replicated this significant finding in a separate group of 3,361 cases and 4,573 controls, also of European ancestry. Estimates of effect size and statistical significance from the pooled dataset (which incorporates both groups) are as follows: OR = 1.23, p = 2.24 x 10-17 [PMID 19915575 (https://www.ncbi.nlm.nih.gov/pubmed/19915575?dopt=Abstract)].

Several other studies have also examined the relationship between rs2736990 and PD. A group of Japanese researchers conducting a GWAS on 2,011 cases and 18,381 controls of Japanese descent found a significant association of rs2736990 with PD that survived Bonferroni correction (p-value not reported) [PMID 19915576 (https://www.ncbi.nlm.nih.gov/pubmed/19915576?dopt=Abstract)]. Another group looked at only the rs2736990 SNP in 515 cases and 450 controls of Chinese descent and found the minor C allele was significantly more frequent in patients with PD (OR=1.26, p = 0.017)[PMID 24005725 (https://www.ncbi.nlm.nih.gov/pubmed/24005725?dopt=Abstract)]. Other studies have validated the association between rs2736990 and PD in European populations: The Harvard NeuroDiscovery Center tested rs2736990 only in 344 cases and 275 controls and found a significant association (OR = 1.40, p = 0.0032)[PMID 21953863 (https://www.ncbi.nlm.nih.gov/pubmed/21953863?dopt=Abstract)]; another group combined data from previous GWAS studies with their own data to create a GWAS dataset of 1752 cases and 1745 controls that yielded a significant association (OR = 1.29, p = 6.7 x 10-8)[PMID 20070850 (https://www.ncbi.nlm.nih.gov/pubmed/20070850?dopt=Abstract)] ; finally, a GWAS conducted on 772 cases and 2024 controls of Dutch descent found a significant association between rs2736990 and PD (OR = 1.325, p = 1.63 x 10-5)[PMID 21248740 (https://www.ncbi.nlm.nih.gov/pubmed/21248740?dopt=Abstract)].

It is not known with certainty how mutations in synuclein-alpha contribute to PD; however, mutations in this gene, both missense and copy number variants, have been linked to the development of PD. In addition, rs2736990 is one of several SNP's in the SNCA locus significantly associated with PD in GWAS studies, and the significant association of this SNP with PD has been replicated and validated in several subsequent studies. Moreover, estimates of effect size are similar across studies. As such, the biological plausibility of this mutation appears high. One candidate mechanism for development of PD due to SNCA hypothesizes that misfolded or excessively produced synuclein-alpha proteins accumulate in the neuron and interfere with normal function until they eventually cause death. This theory is supported by the abundance of synuclein-alpha proteins in LB's found in dopaminergic neurons in the substantia nigra. However, it is unclear if these LB's are a response to injury or themselves the cause of death.

[PMID 15637659 (https://www.ncbi.nlm.nih.gov/pubmed/15637659?dopt=Abstract)] Linkage disequilibrium patterns and tagSNP transferability among European populations.

[PMID 21248740 (https://www.ncbi.nlm.nih.gov/pubmed/21248740?dopt=Abstract)] Genome-wide association study confirms extant PD risk loci among the Dutch.

[PMID 21953863 (https://www.ncbi.nlm.nih.gov/pubmed/21953863?dopt=Abstract)] Association of SNCA with Parkinson: replication in the Harvard NeuroDiscovery Center Biomarker Study.

[PMID 22425546 (https://www.ncbi.nlm.nih.gov/pubmed/22425546?dopt=Abstract)] SNCA polymorphisms, smoking, and sporadic Parkinson's disease in Japanese.

[PMID 24005725 (https://www.ncbi.nlm.nih.gov/pubmed/24005725?dopt=Abstract)] Association of polymorphism in rs2736990 of the α-synuclein gene with Parkinson's disease in a Chinese population

[PMID 28676755 (https://www.ncbi.nlm.nih.gov/pubmed/28676755?dopt=Abstract)] Variants in SNCA Gene Are Associated with Parkinson's Disease Risk and Cognitive

| | |
|---|---|
| Orientation | minus |
| Stabilized | minus |

| Geno | Mag | Summary |
|---|---|---|
| (C;C) | 2 | Slightly increased risk of developing Parkinson's Disease |
| (C;T) | 1.5 | Slightly increased risk of developing Parkinson's Disease |
| (T;T) | 1 | Normal risk of developing Parkinson's Disease |

| | |
|---|---|
| Reference | GRCh38 38.1/141 |
| Chromosome | 4 |
| Position | 89757390 |
| Gene | SNCA |
| is a | snp |
| is | mentioned by |
| dbSNP | rs2736990 (https://www.ncbi.nlm.nih.gov/snp/rs2736990) |
| dbSNP (classic) | rs2736990 (https://www.ncbi.nlm.nih.gov/projects/SNP/snp_ref.cgi?do_not_redirect&rs=rs2736990) |
| ClinGen | rs2736990 (http://reg.clinicalgenome.org/redmine/projects/registry/genboree_registry/alleles?dbSNP.rs=2736990) |
| ebi | rs2736990 (https://www.ebi.ac.uk/gwas/search?query=rs2736990) |
| HLI | rs2736990 (https://search.hli.io/?q=rs2736990) |
| Exac | rs2736990 (http://exac.broadinstitute.org/awesome?query=rs2736990) |
| Gnomad | rs2736990 (http://gnomad.broadinstitute.org/awesome?query=rs2736990) |
| Varsome | rs2736990 (https://varsome.com/variant/hg19/rs2736990) |
| LitVar | rs2736990 (https://www.ncbi.nlm.nih.gov/CBBresearch/Lu/Demo/LitVar/#!?query=rs2736990) |
| Map | rs2736990 (http://popgen.uchicago.edu/ggv/?search=rs2736990) |
| PheGenI | rs2736990 (http://www.ncbi.nlm.nih.gov/gap/PheGenI?tab=2&rs=2736990) |
| Biobank | rs2736990 (https://biobankengine.stanford.edu/awesome?query=rs2736990) |

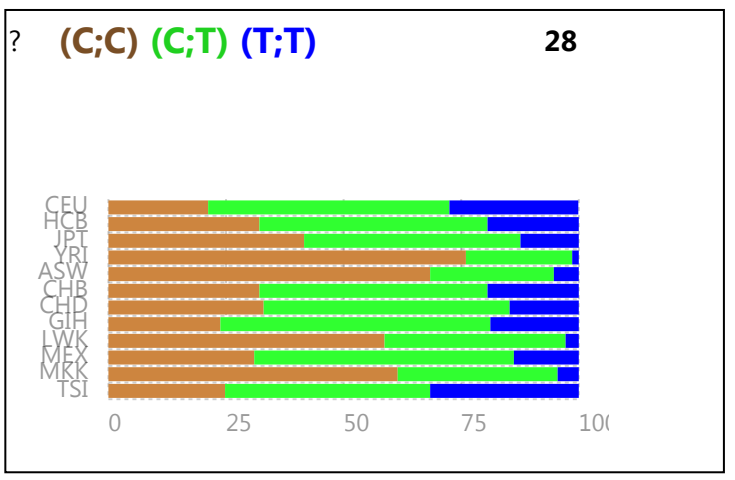
Symptoms in a Brazilian Sample.

[PMID 28844730 (https://www.ncbi.nlm.nih.gov/pubmed/28844730?dopt=Abstract)] Association between SNCA rs2736990 polymorphism and Parkinson's disease: a meta-analysis.

[PMID 30410434 (https://www.ncbi.nlm.nih.gov/pubmed/30410434?dopt=Abstract)] A Comprehensive Analysis of the Association Between SNCA Polymorphisms and the Risk of Parkinson's Disease.

Retrieved from "https://www.SNPedia.com/index.php?title=Rs2736990&oldid=1632689"

| | |
|---|---|
| 1000 genomes | rs2736990 (http://browser.1000genomes.org/Homo_sapiens/Variation/Population?v=rs2736990;vdb=variation) |
| hgdp | rs2736990 (http://hgdp.uchicago.edu/cgi-bin/gbrowse/HGDP/?name=SNP%3Ars2736990) |
| ensembl | rs2736990 (http://www.ensembl.org/Homo_sapiens/snpview?source=dbSNP;snp=rs2736990) |
| geneview | rs2736990 (http://bc3.informatik.hu-berlin.de/search?gv_search_query=RS:2736990) |
| scholar | rs2736990 (http://scholar.google.com/scholar?q=rs2736990&as_subj=bio) |
| google | rs2736990 (http://www.google.com/search?hl=en&q=rs2736990) |
| pharmgkb | rs2736990 (http://www.pharmgkb.org/rsid/rs2736990) |
| gwascentral | rs2736990 (http://www.gwascentral.org/marker/dbSNP:rs2736990) |
| openSNP | rs2736990 (https://opensnp.org/snps/rs2736990#users) |
| 23andMe | rs2736990 (https://www.23andme.com/tools/data/?query=rs2736990) |
| SNPshot | rs2736990 (http://bioai4core.fulton.asu.edu/snpshot/FactSheet?id=rs2736990&type=RSNO) |
| SNPdbe | rs2736990 (http://www.rostlab.org/services/snpdbe/dosearch.php?id=mutation&val=rs2736990) |
| MSV3d | rs2736990 (http://decryptho n.igbmc.fr/msv3d/cgi-bin/humsavar?rsid=rs2736990) |
| GWAS Ctlg | rs2736990 (https://www.ebi.ac.uk/gwas/search?query=rs2736990) |
| GMAF | 0.4045 |
| Max Magnitude | 2 |



| GWAS snp (http://www.genome.gov/26525384) | |
|---|---|
| **PMID** | [PMID 19915575 (https://www.ncbi.nlm.nih.gov/pubmed/19915575?dopt=Abstract)] |
| **Trait** | Parkinson's disease |
| **Title** | Genome-wide association study reveals genetic risk underlying Parkinson's disease |
| **Risk Allele** | C |
| **P-val** | 2E-16 |
| **Odds Ratio** | 1.23 [NR] |

| GWAS snp (http://www.genome.gov/26525384) | |
|---|---|
| **PMID** | [PMID 20070850 (https://www.ncbi.nlm.nih.gov/pubmed/20070850?dopt=Abstract)] |
| **Trait** | Parkinson's disease |
| **Title** | Genome-Wide Association Study Confirms SNPs in SNCA and the MAPT Region as Common Risk Factors for Parkinson Disease |
| **Risk Allele** | |
| **P-val** | 7E-8 |
| **Odds Ratio** | 1.29 [1.18-1.43] |

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|---|---|
| OMIM | 168601 (http://www.ncbi.nlm.nih.gov/omim/168601) |
| Desc | |
| Variant | |
| Related | also |

| | |
|---|---|
| OMIM | 613164 (http://www.ncbi.nlm.nih.gov/omim/613164) |
| Desc | |
| Variant | |
| Related | also |

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