rs2069718

<https://www.ncbi.nlm.nih.gov/pubmed/26063326>

Top 10 genetic markers associated with CFS based on weighted genetic variation (WGV) estimated by the Bayesian model

| **SNP ID** | **Proxy SNP** | **Gene symbola** | **SNP annotationa** | **WGV** | **SE of WGVb** |
| --- | --- | --- | --- | --- | --- |
| rs2288831 | rs3212227 | IL12B | Intron (UTR-3) | 3.95 | 0.0299 |
| rs2071376 |  | IL1A | Intron | 3.6 | 0.0296 |
| rs2069718 |  | IFNG | Intron | 3.34 | 0.0272 |

https://www.ncbi.nlm.nih.gov/pubmed/28867622

Spinal tuberculosis (STB) is an extrapulmonary form of tuberculosis (TB) caused by Mycobacterium tuberculosis (Mtb), which accounts for around 2% of all TB cases and can lead to spine degeneration. It is widely accepted that host genetic factors participate in the pathogenesis of active TB, but the factors controlling which TB form will manifest after Mtb infection remain unknown. We hypothesized that a genetic difference may exist between the development of STB and pulmonary tuberculosis (PTB). Here, three single nucleotide polymorphisms (SNPs) in the IFNG gene (rs2069718), IRGM gene (rs10065172), and MBL2 gene (rs11003125) were genotyped among 183 PTB patients, 177 STB patients, and 360 healthy controls from the Chinese Han population. We found that rs2069718genotypes were significantly associated with PTB (TT, p = 0.007; CT, p = 0.008) but not STB, and the TT genotype (p = 0.046) of rs2069718 were less common in PTB than in STB. In contrast, neither PTB nor STB were found to be associated with rs10065172 and rs11003125. Overall, we found a difference in the rs2069718 genetic distribution between the STB and PTB patients in a Chinese Han population. The rs2069718 TT genotype was associated with a protective role in PTB but not STB development during active Mtb infection.

<https://www.ncbi.nlm.nih.gov/pubmed/28651128>

Lumbar radicular pain after disc herniation may be associated with release of pro-inflammatory cytokines from nucleus pulposus (NP) tissue. In the present study we examined the role of interferon-γ (IFN-γ) and cluster of differentiation 68 (CD68) in the acute phase of this process. First, in an animal model mimicking the clinical situation after disc herniation, the role of IFN-γ close to the dorsal nerve roots was studied. Next, in patients with lumbar radicular pain due to disc herniation, we examined how two single nucleotide polymorphisms (SNPs; rs2069705 and rs2069718) are important for the IFN-γ expression influenced the pain behavior. The animal data demonstrated a significant increase in the nociceptive activity at the spinal level after local application of NP and IFN-γ onto the dorsal nerve roots. A positive correlation between IFN-γ and CD68 in the NP tissue was also demonstrated. In the patients, a significant increase in Oswestry Disability Index (ODI) score was observed in carriers of the IFN-γ SNPs; rs2069705 A and rs2069718 G alleles. The present data suggest that IFN-γ close to the dorsal nerve roots may contribute to the pathogenesis, the nociceptive activity and the pain behavior following lumbar disc herniation.

<https://www.ncbi.nlm.nih.gov/pubmed/26198819>

Intracranial aneurysm (IA) is often asymptomatic until the time of rupture resulting in subarachnoid hemorrhage (SAH).There is no precise biochemical or phenotype marker for diagnosis of aneurysm. Environmental risk factors that associate with IA can result in modifying the effect of inherited genetic factors and thereby increase the susceptibility to SAH. In addition subsequent to aneurismal rupture, the nature and quantum of inflammatory response might be critical for repair. Therefore, genetic liability to inflammatory response caused by polymorphisms in cytokine genes might be the common denominator for gene and environment in the development of aneurysm and complications associated with rupture.

Pro-inflammatory cytokines TNFA rs361525, IFNG rs2069718, and anti-inflammatory cytokine IL10 rs1800871 and rs1800872 were found to be significantly associated with IA, independent of epidemiological factors. TGFB1 rs1800469 polymorphism was observed to be associated with IA through co-modifying factors such as hypertension and gender. Functional prediction of all the associated SNPs of TNFA, IL10, and TGFB1 indicates their potential role in transcriptional regulation. Meta-analysis further reiterates that IL1 gene cluster and IL6 were not associated with IA.

<https://www.ncbi.nlm.nih.gov/pubmed/24529854>

Polymorphisms of the interferon gamma (IFN-γ) gene are associated with the risk of tuberculosis (TB) in different populations. However, the genetic susceptibility to TB in Han Chinese living in Taiwan is still unknown. The purpose of this study is to evaluate whether the polymorphisms of the IFN-γ gene are associated with TB in Han Taiwanese.

#### METHODS:

A total of 200 TB patients and 202 age-matched non-TB individuals were enrolled. Five tag single nucleotide polymorphisms (tSNPs) and rs2430561 (+874) of IFN-γ were selected from a public database. The genotypes were determined using polymerase chain reaction assays.

#### RESULTS:

Three IFN-γ polymorphisms in intron 3, rs1861494 and rs2069718, and rs2430561 in interon 1 were strongly associated with TB. The C carrier (CT+TT) of rs1861494, TT homozygous of rs2069718, and AA homozygous of rs2430561 were risk genotypes for susceptibility to TB.

#### CONCLUSION:

The IFN-γ polymorphisms, rs1861494, rs2069718, and rs2430561, may confer the risk of TB in Han Taiwanese.

<https://www.ncbi.nlm.nih.gov/pubmed/19919944>

# systemic lupus erythematosus.

#### OBJECTIVE:

Interferon-gamma (IFNG) is a type II interferon playing diverse roles in innate and adaptive immune systems. Elevated expression of IFNG has been associated with systemic lupus erythematosus (SLE). This study examined the association of IFNG polymorphisms with SLE susceptibility.

#### METHODS:

Five tag single-nucleotide polymorphisms (SNP) and eight variations in all known regulatory sequences affecting IFNG expression within and around IFNG were genotyped in 1759 unrelated Korean subjects. SLE susceptibility association was assessed by comparing 742 SLE patients and 1017 unaffected controls using multivariate logistic regression analysis with adjustment for age and gender.

#### RESULTS:

SLE susceptibility association was significant with rs2069705 in the promoter (adjusted OR 2.27, p=0.0024) and marginal with rs3181032 in the promoter (p=0.037), rs2430561 in intron 1 (p=0.022) and rs2069718 in intron 3 (p=0.026) in a recessive genetic model. F

<https://www.ncbi.nlm.nih.gov/pubmed/18385742>

Interferon-gamma (IFNgamma) is located on chromosome 12, and a number of studies have detected very strong linkage signals around this gene and asthma. The aim of this study was to analyze the association of a (CA)n repeat in intron 1 and six single nucleotide polymorphisms (((rs2069705, T/C) (promoter)), ((rs1861494, A/G), (rs1861493, T/C), (rs2069718, C/T) (intron 3)), ((rs2069727, A/G) and (rs2069728, G/A) (3' untranslated region))) spanning the whole gene with asthma. We report here the association of rs1861494 A/G with atopic asthma in a case-control cohort (n=189 and n=270 cases and controls, respectively) (P=0.0006), which was replicated (P=0.006) in a family study (n=137) as well. Allele G was found to be negatively associated (odds ratio=0.50, 95% confidence interval, P=0.0006). A five-locus haplotype also showed significant association with asthma in the case-control (P=0.002) and the family studies (P=0.0004). In our three-locus sliding window haplotypic analysis, we found the (CA)n repeat, rs1861494 A/G and rs2069718 C/T to be of high priority (P=0.0003). Using electrophoretic mobility shift assay, we provide evidence that the alleles of rs1861494 A/G have differential affinity to bind to putative nuclear factor(s). In conclusion, we report for the first time association of rs1861494 A/G polymorphism with asthma, which may regulate the IFNgamma levels and, hence, modulate asthma pathogenesis.

<http://www.uniprot.org/uniprot/P01579>

**Interferon gamma**

Produced by lymphocytes activated by specific antigens or mitogens. IFN-gamma, in addition to having antiviral activity, has important immunoregulatory functions. It is a potent activator of macrophages, it has antiproliferative effects on transformed cells and it can potentiate the antiviral and antitumor effects of the type I interferons.

* [cytokine activity](https://www.ebi.ac.uk/QuickGO/term/GO:0005125) Source: GO\_Central
* [interferon-gamma receptor binding](https://www.ebi.ac.uk/QuickGO/term/GO:0005133) Source: ProtInc

[View the complete GO annotation on QuickGO ...](http://www.ebi.ac.uk/QuickGO/annotations?geneProductId=P01579)

#### GO - Biological processi

* [adaptive immune response](https://www.ebi.ac.uk/QuickGO/term/GO:0002250) Source: GO\_Central
* [apoptotic process](https://www.ebi.ac.uk/QuickGO/term/GO:0006915) Source: MGI
* [cell cycle arrest](https://www.ebi.ac.uk/QuickGO/term/GO:0007050) Source: BHF-UCL
* [cell surface receptor signaling pathway](https://www.ebi.ac.uk/QuickGO/term/GO:0007166) Source: ProtInc
* [defense response to virus](https://www.ebi.ac.uk/QuickGO/term/GO:0051607) Source: UniProtKB-KW
* [extrinsic apoptotic signaling pathway](https://www.ebi.ac.uk/QuickGO/term/GO:0097191) Source: BHF-UCL
* [humoral immune response](https://www.ebi.ac.uk/QuickGO/term/GO:0006959) Source: GO\_Central
* [interferon-gamma-mediated signaling pathway](https://www.ebi.ac.uk/QuickGO/term/GO:0060333) Source: CAFA
* [interleukin-12-mediated signaling pathway](https://www.ebi.ac.uk/QuickGO/term/GO:0035722) Source: Reactome
* [negative regulation of epithelial cell differentiation](https://www.ebi.ac.uk/QuickGO/term/GO:0030857) Source: BHF-UCL
* [negative regulation of gene expression](https://www.ebi.ac.uk/QuickGO/term/GO:0010629) Source: UniProtKB
* [negative regulation of interleukin-17 production](https://www.ebi.ac.uk/QuickGO/term/GO:0032700) Source: BHF-UCL
* [negative regulation of smooth muscle cell proliferation](https://www.ebi.ac.uk/QuickGO/term/GO:0048662) Source: BHF-UCL
* [negative regulation of transcription, DNA-templated](https://www.ebi.ac.uk/QuickGO/term/GO:0045892) Source: CAFA
* [negative regulation of transcription by RNA polymerase II](https://www.ebi.ac.uk/QuickGO/term/GO:0000122) Source: BHF-UCL
* [positive regulation of autophagy](https://www.ebi.ac.uk/QuickGO/term/GO:0010508) Source: UniProtKB
* [positive regulation of calcidiol 1-monooxygenase activity](https://www.ebi.ac.uk/QuickGO/term/GO:0060559) Source: BHF-UCL
* [positive regulation of CD4-positive, CD25-positive, alpha-beta regulatory T cell differentiation involved in immune response](https://www.ebi.ac.uk/QuickGO/term/GO:0032834) Source: UniProtKB
* [positive regulation of cell proliferation](https://www.ebi.ac.uk/QuickGO/term/GO:0008284) Source: BHF-UCL
* [positive regulation of core promoter binding](https://www.ebi.ac.uk/QuickGO/term/GO:1904798) Source: CAFA
* [positive regulation of epithelial cell migration](https://www.ebi.ac.uk/QuickGO/term/GO:0010634) Source: CACAO
* [positive regulation of exosomal secretion](https://www.ebi.ac.uk/QuickGO/term/GO:1903543) Source: UniProtKB
* [positive regulation of fructose 1,6-bisphosphate 1-phosphatase activity](https://www.ebi.ac.uk/QuickGO/term/GO:0060550) Source: BHF-UCL
* [positive regulation of fructose 1,6-bisphosphate metabolic process](https://www.ebi.ac.uk/QuickGO/term/GO:0060552) Source: BHF-UCL
* [positive regulation of gene expression](https://www.ebi.ac.uk/QuickGO/term/GO:0010628) Source: UniProtKB
* [positive regulation of interleukin-12 production](https://www.ebi.ac.uk/QuickGO/term/GO:0032735) Source: UniProtKB
* [positive regulation of interleukin-23 production](https://www.ebi.ac.uk/QuickGO/term/GO:0032747) Source: BHF-UCL
* [positive regulation of killing of cells of other organism](https://www.ebi.ac.uk/QuickGO/term/GO:0051712) Source: BHF-UCL
* [positive regulation of membrane protein ectodomain proteolysis](https://www.ebi.ac.uk/QuickGO/term/GO:0051044) Source: BHF-UCL
* [positive regulation of nitric oxide biosynthetic process](https://www.ebi.ac.uk/QuickGO/term/GO:0045429) Source: BHF-UCL
* [positive regulation of osteoclast differentiation](https://www.ebi.ac.uk/QuickGO/term/GO:0045672) Source: BHF-UCL
* [positive regulation of peptidyl-serine phosphorylation of STAT protein](https://www.ebi.ac.uk/QuickGO/term/GO:0033141) Source: MGI
* [positive regulation of protein complex assembly](https://www.ebi.ac.uk/QuickGO/term/GO:0031334) Source: CAFA
* [positive regulation of protein deacetylation](https://www.ebi.ac.uk/QuickGO/term/GO:0090312) Source: CAFA
* [positive regulation of protein import into nucleus, translocation](https://www.ebi.ac.uk/QuickGO/term/GO:0033160) Source: CAFA
* [positive regulation of protein localization to plasma membrane](https://www.ebi.ac.uk/QuickGO/term/GO:1903078) Source: UniProtKB
* [positive regulation of protein phosphorylation](https://www.ebi.ac.uk/QuickGO/term/GO:0001934) Source: CAFA
* [positive regulation of protein serine/threonine kinase activity](https://www.ebi.ac.uk/QuickGO/term/GO:0071902) Source: CAFA
* [positive regulation of smooth muscle cell apoptotic process](https://www.ebi.ac.uk/QuickGO/term/GO:0034393) Source: BHF-UCL
* [positive regulation of tumor necrosis factor (ligand) superfamily member 11 production](https://www.ebi.ac.uk/QuickGO/term/GO:2000309) Source: BHF-UCL
* [positive regulation of tyrosine phosphorylation of STAT protein](https://www.ebi.ac.uk/QuickGO/term/GO:0042531) Source: BHF-UCL
* [positive regulation of vitamin D biosynthetic process](https://www.ebi.ac.uk/QuickGO/term/GO:0060557) Source: BHF-UCL
* [protein import into nucleus, translocation](https://www.ebi.ac.uk/QuickGO/term/GO:0000060) Source: UniProtKB
* [regulation of growth](https://www.ebi.ac.uk/QuickGO/term/GO:0040008) Source: UniProtKB-KW
* [regulation of insulin secretion](https://www.ebi.ac.uk/QuickGO/term/GO:0050796) Source: BHF-UCL
* [regulation of interferon-gamma-mediated signaling pathway](https://www.ebi.ac.uk/QuickGO/term/GO:0060334) Source: Reactome
* [regulation of protein ADP-ribosylation](https://www.ebi.ac.uk/QuickGO/term/GO:0010835) Source: CAFA
* [regulation of regulatory T cell differentiation](https://www.ebi.ac.uk/QuickGO/term/GO:0045589) Source: Reactome
* [response to virus](https://www.ebi.ac.uk/QuickGO/term/GO:0009615) Source: MGI

[View the complete GO annotation on QuickGO ...](http://www.ebi.ac.uk/QuickGO/annotations?geneProductId=P01579)

#### Keywordsi

|  |  |
| --- | --- |
| Molecular function | [Cytokine](http://www.uniprot.org/keywords/KW-0202) |
| Biological process | [Antiviral defense](http://www.uniprot.org/keywords/KW-0051), [Growth regulation](http://www.uniprot.org/keywords/KW-0341) |

#### Enzyme and pathway databases

|  |  |
| --- | --- |
| Reactomei | [R-HSA-877300](https://www.reactome.org/PathwayBrowser/#R-HSA-877300&FLG=P01579) Interferon gamma signaling [R-HSA-877312](https://www.reactome.org/PathwayBrowser/#R-HSA-877312&FLG=P01579) Regulation of IFNG signaling [R-HSA-8877330](https://www.reactome.org/PathwayBrowser/#R-HSA-8877330&FLG=P01579) RUNX1 and FOXP3 control the development of regulatory T lymphocytes (Tregs) [R-HSA-8950505](https://www.reactome.org/PathwayBrowser/#R-HSA-8950505&FLG=P01579) Gene and protein expression by JAK-STAT signaling after Interleukin-12 stimulation |
| SignaLinki | [P01579](http://signalink.org/protein/P01579) |
| SIGNORi | [P01579](http://signor.uniroma2.it/relation_result.php?id=P01579) |

###### [**Aplastic anemia (AA)**](http://www.uniprot.org/diseases/DI-02842)**1 Publication http://www.uniprot.org/citations/15327519**

Disease susceptibility may be associated with variations affecting the gene represented in this entry.

Disease descriptionA form of anemia in which the bone marrow fails to produce adequate numbers of peripheral blood elements. It is characterized by peripheral pancytopenia and marrow hypoplasia.

[See also OMIM:609135](http://www.omim.org/entry/609135)

|  |  |
| --- | --- |
| DrugBanki | [DB05676](https://www.drugbank.ca/drugs/DB05676) Apremilast [DB05111](https://www.drugbank.ca/drugs/DB05111) Fontolizumab [DB01296](https://www.drugbank.ca/drugs/DB01296) Glucosamine [DB01250](https://www.drugbank.ca/drugs/DB01250) Olsalazine [DB05110](https://www.drugbank.ca/drugs/DB05110) VIR201 |

<https://www.ncbi.nlm.nih.gov/gene/3458>

This gene encodes a soluble cytokine that is a member of the type II interferon class. The encoded protein is secreted by cells of both the innate and adaptive immune systems. The active protein is a homodimer that binds to the interferon gamma receptor which triggers a cellular response to viral and microbial infections. Mutations in this gene are associated with an increased susceptibility to viral, bacterial and parasitic infections and to several autoimmune diseases.

**Cytokines** are a broad and loose category of small proteins (~5–20 [kDa](https://en.wikipedia.org/wiki/KDa" \o "KDa)) that are important in [cell signaling](https://en.wikipedia.org/wiki/Cell_signaling). Their release has an effect on the behavior of cells around them. It can be said that cytokines are involved in [autocrine signaling](https://en.wikipedia.org/wiki/Autocrine_signaling), [paracrine signaling](https://en.wikipedia.org/wiki/Paracrine_signaling) and [endocrine signaling](https://en.wikipedia.org/wiki/Endocrine_signaling) as immunomodulating agents. Their definite distinction from hormones is still part of ongoing research. Cytokines may include [chemokines](https://en.wikipedia.org/wiki/Chemokine), [interferons](https://en.wikipedia.org/wiki/Interferon), [interleukins](https://en.wikipedia.org/wiki/Interleukin), [lymphokines](https://en.wikipedia.org/wiki/Lymphokine), and [tumour necrosis factors](https://en.wikipedia.org/wiki/Tumour_necrosis_factor" \o "Tumour necrosis factor) but generally not [hormones](https://en.wikipedia.org/wiki/Hormone) or [growth factors](https://en.wikipedia.org/wiki/Growth_factor) (despite some [overlap in the terminology](https://en.wikipedia.org/wiki/Growth_factor#Growth_factors_versus_cytokines)). Cytokines are produced by a broad range of cells, including immune cells like [macrophages](https://en.wikipedia.org/wiki/Macrophage), [B lymphocytes](https://en.wikipedia.org/wiki/B_cell), [T lymphocytes](https://en.wikipedia.org/wiki/T_cell) and [mast cells](https://en.wikipedia.org/wiki/Mast_cell), as well as [endothelial cells](https://en.wikipedia.org/wiki/Endothelium), [fibroblasts](https://en.wikipedia.org/wiki/Fibroblast), and various [stromal cells](https://en.wikipedia.org/wiki/Stromal_cell); a given cytokine may be produced by more than one type of cell.[[1]](https://en.wikipedia.org/wiki/Cytokine#cite_note-1)[[2]](https://en.wikipedia.org/wiki/Cytokine#cite_note-2)[[3]](https://en.wikipedia.org/wiki/Cytokine#cite_note-COPE-Cytokines-3)

They act through [receptors](https://en.wikipedia.org/wiki/Cell_surface_receptor), and are especially important in the [immune system](https://en.wikipedia.org/wiki/Immune_system); cytokines modulate the balance between [humoral](https://en.wikipedia.org/wiki/Humoral_immunity) and [cell-based](https://en.wikipedia.org/wiki/Cell-mediated_immunity) immune responses, and they regulate the maturation, growth, and responsiveness of particular cell populations. Some cytokines enhance or inhibit the action of other cytokines in complex ways.[[3]](https://en.wikipedia.org/wiki/Cytokine#cite_note-COPE-Cytokines-3)

They are different from [hormones](https://en.wikipedia.org/wiki/Hormones), which are also important cell signaling molecules, in that hormones circulate in less variable concentrations and hormones tend to be made by specific kinds of cells.

They are important in health and disease, specifically in host responses to infection, immune responses, [inflammation](https://en.wikipedia.org/wiki/Inflammation), trauma, [sepsis](https://en.wikipedia.org/wiki/Sepsis), cancer, and reproduction.

<https://www.ncbi.nlm.nih.gov/clinvar/variation/14724/>

## -179G-T

Acquired immunodeficiency syndrome, rapid progression to[[MedGen](https://www.ncbi.nlm.nih.gov/medgen/C4016227" \t "_blank)]

<https://www.ncbi.nlm.nih.gov/pubmed/12854077>

A polymorphism, -179G/T, in the promoter of the interferon (IFN)-gamma gene (IFNG) confers differential tumor necrosis factor-alpha (TNF-alpha) inducibility to the IFNG promoter. The rarer allele, -179T, but not -179G, is inducible by TNF-alpha. We investigated the effects of IFNG -179G/T on AIDS pathogenesis. In 298 African American human immunodeficiency virus (HIV)-1 seroconverters, the IFNG -179G/T genotype was associated with accelerated progression to CD4 <200 and AIDS-1993, a finding suggesting that IFNG -179T is a risk factor for AIDS progression, as measured by CD4 cell count. It is possible that increased IFN-gamma production induced by TNF-alpha when -179T is present causes CD4 cell depletion by apoptosis.

<https://www.ncbi.nlm.nih.gov/pubmed/16724074>

This study examines mucosa-specific regulatory pathways involved in modulation of interferon-gamma (IFN-gamma) in lamina propria T cells. Previous studies identified mucosa-specific CD2 cis-elements within the -204 to -108 bp IFNG promoter. Within this region, a single-site nucleotide polymorphism, -179G/T, imparts tumor necrosis factor-alpha stimulation of IFNG in peripheral blood lymphocytes, and is linked with accelerated AIDS progression. We discovered a putative estrogen response element (ERE) introduced by the -179T, which displays selective activation in peripheral blood mononuclear cells (PBMC) vs lamina propria mononuclear cells (LPMC). Transfection of PBMC with constructs containing the -179G or -179T site revealed CD2-mediated enhancement of the -179T compared to -179G allele, although, in LPMC, a similar level of expression was detected. Electrophoretic mobility shift assay (EMSA) analysis demonstrated CD2-mediated nucleoprotein binding to the -179T but not the -179G in PBMC. In LPMC, binding is constitutive to both -179G and -179T regions. Sequence and EMSA analysis suggests that the -179T allele creates an ERE-like binding site capable of binding recombinant estrogen receptor. Estrogen response element transactivation is enhanced by CD2 signaling, but inhibited by estrogen in PBMC but not in LPMC, although expression of estrogen receptor was similar. This is the first report to describe a potential molecular mechanism responsible for selectively controlling IFN-gamma production in LPMC.