**# Gene symbol**

TRPM8

**# Full name of gene**

Transient receptor potential cation channel subfamily M member 8

**# What does the <gene\_symbol> gene do?**

The TRPM8 gene encodes a cation channel that allows the movement of sodium, potassium, calcium, and cesium across plasma barriers activated by [low temperatures](https://www.ncbi.nlm.nih.gov/pubmed/14757700?dopt=Abstract). It allows the body to detect [temperature changes](https://www.ncbi.nlm.nih.gov/pubmed/17217067), respond to cold, balance calcium in the body, and feel the cooling effects of menthol. Variants in TRPM8 are associated with [breast](https://www.ncbi.nlm.nih.gov/pubmed/20482834), [pancreatic](https://www.ncbi.nlm.nih.gov/pubmed/27038374), [lung](https://www.ncbi.nlm.nih.gov/pubmed/24037916), and [prostate](https://www.ncbi.nlm.nih.gov/pubmed/25065497) cancer. Additional issues include increased susceptibility to [metabolic syndrome](https://www.ncbi.nlm.nih.gov/pubmed/25967713), [migraines](https://www.ncbi.nlm.nih.gov/pubmed/23294458?dopt=Abstract), [alcohol dependence](https://www.ncbi.nlm.nih.gov/pubmed/23942779?dopt=Abstract), [COPD](https://www.ncbi.nlm.nih.gov/pubmed/27789940), [pain](https://www.ncbi.nlm.nih.gov/pubmed/22072275?dopt=Abstract) and [cold sensitivity](https://www.ncbi.nlm.nih.gov/pubmed/21542321?dopt=Abstract), [asthma](https://www.ncbi.nlm.nih.gov/pubmed/26272603), and [inflammation](https://www.ncbi.nlm.nih.gov/pubmed/26660531). Other variants reduce natural killer cell function in the immune system and are associated with [CFS](https://www.ncbi.nlm.nih.gov/pubmed/27099524).

This gene is located on chromosome 2. The cation channel it creates acts in your nervous, immune, and sensory systems.

<body part brain, immune, circularity, muscles>

<gene\_expression\_location location="D001921; D007107;>

**# What are some common mutations of <gene\_symbol>?**

**trpm8\_G3264+630A**

**trpm8\_G3264+2567A**

**trpm8\_G750C**

**trpm8\_C-990T**

There are 4 well known variants in this gene: <variant list?>

< G3264+630A variant view with G to A transformation>

This variant is a change at a specific point in the <gene\_symbol> gene from guanine (G) to adenine (A), resulting in reduced protein function. This substitution of a single nucleotide is known as a missense variant.

< G3264+2567A variant view with G to A transformation>

This variant is a change at a specific point in the <gene\_symbol> gene from guanine (G) to adenine (A), resulting in reduced protein function. This substitution of a single nucleotide is known as a missense variant.

< G750C variant view with G to C transformation>

This mutation is a change at a specific point in the <gene\_symbol> gene from guanine (G) to cytosine (C), resulting in reduced natural killer cell function. This substitution of a single nucleotide is known as a mis-sense mutation.

< C-990T variant view with C to T transformation>

This mutation is a change at a specific point in the <gene\_symbol> gene from cytosine (C) to thymine (T), resulting in reduced natural killer cell function. This substitution of a single nucleotide is known as a mis-sense mutation.

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<user variant viewer>

<user what does this mean>

<user gene list>

<UserGenotypeBox gene="comt">

<Genotype name=" G3264+630A (A;A)">

# What does this mean?

People with this variant have two copies of the G3264+630A variant. This substitution of a single nucleotide is known as a mis-sense mutation.

# What is the effect of this variant?

Your variant is not associated with any loss of function.

# How common is this gene in the general population?

<pie\_chart level=" G3264+630A (A;A)", frequency>

<frequency> of the population has a moderate loss of function

</Genotype>

<Genotype name=" G3264+630A (G;A)">

<line\_graph level="severe">

# What does this mean?

People with this variant have one copy of the G3264+630A variant. This substitution of a single nucleotide is known as a mis-sense mutation.

# What is the effect of this variant?

You are in the Severe Risk category. See below for more information

# How common is this gene in the general population?

<pie\_chart level=" G3264+630A (G;A)", frequency>

<frequency> of the population has a severe loss of function

<pie\_chart level=" G3264+630A (G;A)", frequency>

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

</Genotype>

<Genotype name=" G3264+2567A (G;G)”>

# How common is this gene in the general population?

<pie\_chart level=" G3264+2567A (G;G), frequency>

Your <gene\_name> is found to have no variants. A normal gene is referred to as a "wildtype" gene.

</Genotype>

<Genotype name=" G3264+2567A (G;A)">

# What does this mean?

People with this variant have one copy of the G3264+2567A variant. This substitution of a single nucleotide is known as a mis-sense mutation.

# What is the effect of this variant?

You are in the Severe Risk category. See below for more information

# How common is this gene in the general population?

<pie\_chart level=" G3264+2567A (A;G)", frequency>

<frequency> of the population has a high risk

</Genotype>

<Genotype name=" G3264+2567A (A;A)">

<line\_graph level="wildtype">

# What does this mean?

People with this variant have two copies of the G3264+2567A variant. This substitution of a single nucleotide is known as a mis-sense mutation.

# What is the effect of this variant?

Your variant is not associated with any loss of function.

# How common is this gene in the general population?

<pie\_chart level=" G3264+2567A (A;A)", frequency>

<frequency> of the population has no loss of function

<pie\_chart level=" G3264+2567A (A;A)", frequency>

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

</Genotype>

<Genotype name=" G3264+2567A (G;G)”>

# How common is this gene in the general population?

<pie\_chart level=" G3264+2567A (G;G), frequency>

Your <gene\_name> is found to have no variants. A normal gene is referred to as a "wildtype" gene.

</Genotype>

<Genotype name=" C-990T (C;T)">

<line\_graph level="moderate">

# What does this mean?

People with this variant have one copy of the C-990T variant. This substitution of a single nucleotide is known as a mis-sense mutation.

# What is the effect of this variant?

This variant is not associated with increased risk.

# How common is this gene in the general population?

<pie\_chart level=" C-990T (C:T)", frequency>

<frequency> of the population has a moderate loss of function

</Genotype>

<Genotype name=" C-990T (T;T)">

<line\_graph level="severe">

# What does this mean?

People with this variant have two copies of the C-990T variant. This substitution of a single nucleotide is known as a mis-sense mutation.

# What is the effect of this variant?

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

# How common is this gene in the general population?

<pie\_chart level=" C-990T (T;T)", frequency>

<frequency> of the population has a severe loss of function

<pie\_chart level=" C-990T (T;T)", frequency>

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

</Genotype>

<Genotype name=" C-990T (C;C)”>

# How common is this gene in the general population?

<pie\_chart level=" C-990T (C;C), frequency>

Your <gene\_name> is found to have no variants. A normal gene is referred to as a "wildtype" gene.

</Genotype>

<Genotype name=" G750C(G;C)">

<line\_graph level="moderate">

# What does this mean?

People with this variant have one copy of the G750C variant. This substitution of a single nucleotide is known as a mis-sense mutation.

# What is the effect of this variant?

This variant is not associated with increased risk.

# How common is this gene in the general population?

<pie\_chart level=" G750C(G;C)", frequency>

<frequency> of the population has a moderate loss of function

</Genotype>

<Genotype name=" G750C(C;C)">

<line\_graph level="severe">

# What does this mean?

People with this variant have two copies of the G750C variant. This substitution of a single nucleotide is known as a mis-sense mutation.

# What is the effect of this variant?

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

# How common is this gene in the general population?

<pie\_chart level=" G750C(C;C)", frequency>

<frequency> of the population has a severe loss of function

<pie\_chart level=" G750C(C;C)", frequency>

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

</Genotype>

<Genotype name=" G750C(G;G)”>

# How common is this gene in the general population?

<pie\_chart level=" G750C(G;G), frequency>

Your <gene\_name> is found to have no variants. A normal gene is referred to as a "wildtype" gene.

</Genotype>

# How sure are you?

<user gene chip graph level="user gene surity">

We have <user gene surity> confidence in the read of the gene due to the coverage of our chipset process.

</UserGenotypeBox>

# How sure are you?

<if chipset to low graph>

<level graph>

We have low confidence of this gene due to the data our chipset provides.

<else if chipset to medium graph>

<level graph>

We have medium confidence of this gene due to the data our chipset provides.

<else check chipset to high graph>

<level graph>

We have high confidence of this gene due to the data our chipset provides.

```

**# What are the effects of variants in <gene\_symbol>?**

For the vast majority of people, the overall risk associated with the common <gene\_symbol> variants is small, and do 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 in the gene panel.

**<call variants with the multiple categories>**

G3264+630A (G;G)

**<function meter level="wildtype">**

**<efficiency level = "100%" >**

**<variant and population data>**

**# Normal Function**

The fully functional TRPM8 channels allow normal natural killer cells (NKC) function with no increased risk of CFS.

**# What should I do about this?**

No medical therapies are indicated at the moment.

G3264+630A (A;A)

**<function meter level="wildtype">**

**<variant and population data>**

**# Homozygous**

The fully functional TRPM8 channels allow normal natural killer cells (NKC) function with no increased risk of CFS.

**# What should I do about this?**

No medical therapies are indicated at the moment.

G3264+630A (G;A)

**<function meter level="severe">**

**<variant and population data>**

**# Severe Risk**

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 G3264+630A variant decreases gene expression in both the DNA and RNA, causing significant reduction in NKC activity. This variant was 2X as common in [CFS patients at 82.1% with an odds ratio of 7.19.](https://www.ncbi.nlm.nih.gov/pubmed/27099524)

**# What should I do about this?**

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 valproic acid](https://www.ncbi.nlm.nih.gov/pubmed/17349632/) impair NKC function and should be avoided.

G3264+2567A (G;G)

**<function meter level="wildtype">**

**<efficiency level = "100%" >**

**<variant and population data>**

**# Normal Function**

The fully functional TRPM8 channels allow normal natural killer cells (NKC) function with no increased risk of CFS.

**# What should I do about this?**

No medical therapies are indicated at the moment.

G3264+2567A (A;A)

**<function meter level="wildtype">**

**<variant and population data>**

**# Homozygous**

The fully functional TRPM8 channels allow normal natural killer cells (NKC) function with no increased risk of CFS.

**# What should I do about this?**

No medical therapies are indicated at the moment.

G3264+2567A (G;A)

**<function meter level="severe">**

**<variant and population data>**

**# Severe Risk**

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 G3264+2567A variant decreases gene expression in both the DNA and RNA, causing significant reduction in NKC activity. This variant was 2X as common in [CFS patients at 73.3% with an odds ratio of 3.56.](https://www.ncbi.nlm.nih.gov/pubmed/27099524)

**# What should I do about this?**

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 valproic acid](https://www.ncbi.nlm.nih.gov/pubmed/17349632/) impair NKC function and should be avoided.

G750C (G;G)

**<function meter level="wildtype">**

**<variant and population data>**

**# Normal Function**

The TRPM8 channels function normally.

**# What should I do about this?**

No therapies are medically indicated at the moment.

G750C (G;C)

**<function meter level="wildtype">**

**<variant and population data>**

**# Heterozygous**

The heterozygous GC variant has multiple effects. Firstly, it causes [increased sensitivity to cold](https://www.ncbi.nlm.nih.gov/pubmed/21542321?dopt=Abstract) as well as increased [inflammation](https://www.ncbi.nlm.nih.gov/pubmed/26660531) due to improper temperature regulation. It may also cause increased cold-induced airway hyperresponsiveness (CAH) in bronchial asthma (BA) patients. As the TRPM8 gene regulates cold perception, improper function may lead to hyperstimulation and increased CAH events. The GC genotype has an [odds ratio of 3.73](https://www.ncbi.nlm.nih.gov/pubmed/26272603), a decrease in forced expiratory volume.

**# What should I do about this?**

If possible, avoid cold air [below 25˚ C](http://www.uniprot.org/uniprot/Q7Z2W7). The carboxamide [WS-12](https://www.ncbi.nlm.nih.gov/pubmed/18930858) (a menthol derivative with much higher efficacy and potency) or [icilin](https://www.ncbi.nlm.nih.gov/pubmed/17517434) may protect against increased cold perception by upregulating the TRPM8 gene, reducing bronchial shock. Other medications include [menthol and eucalyptol](https://www.ncbi.nlm.nih.gov/pubmed/14757700), but this variant causes [lower menthol efficacy](https://www.ncbi.nlm.nih.gov/pubmed/21542321?dopt=Abstract). Users should avoid alcohol and smoking.

G750C (C;C)

**<function meter level="high risk">**

**<variant and population data>**

**# High Risk**

The homozygous GG variant has greatly decreased gene function, causing greatly increased sensitivity to cold and greatly increased [inflammation](https://www.ncbi.nlm.nih.gov/pubmed/26660531). This may cause increased asthmatic attacks<https://www.ncbi.nlm.nih.gov/pubmed/26272603> in cold weather and decreased lung function.

**# What should I do about this?**

Avoid cold air [below 25˚ C](http://www.uniprot.org/uniprot/Q7Z2W7). The carboxamide [WS-12](https://www.ncbi.nlm.nih.gov/pubmed/18930858) (a menthol derivative with much higher efficacy and potency) or [icilin](https://www.ncbi.nlm.nih.gov/pubmed/17517434) may protect against increased cold perception by upregulating the TRPM8 gene, reducing bronchial shock. Other medications include [menthol and eucalyptol](https://www.ncbi.nlm.nih.gov/pubmed/14757700). Users should avoid alcohol and smoking.

C-990T (C;C)

**<function meter level="low\_risk">**

**<variant and population data>**

**# Normal Function**

TRPM8 a cold and cold-burning pain receptor linked to [migraines](https://www.ncbi.nlm.nih.gov/pubmed/23294458?dopt=Abstract), [neuropathic chronic pain](https://www.ncbi.nlm.nih.gov/pubmed/22072275?dopt=Abstract), and [inflammation](https://www.ncbi.nlm.nih.gov/pubmed/26660531). It processes [cold-mediated pain relievers](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5541777/#R30) and may modulate pain sensation and set [vascular tone](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5541777/#R31), which may influence migraines. This variant is protective, with a [0.7X lower risk](https://www.nature.com/articles/ng.856) for migraines.

**# What should I do about this?**

No therapies are medically indicated at the moment.

C-990T (C;T)

**<function meter level="low\_risk">**

**<variant and population data>**

**# Heterozygous**

TRPM8 a cold and cold-burning pain receptor linked to [migraines](https://www.ncbi.nlm.nih.gov/pubmed/23294458?dopt=Abstract), [neuropathic chronic pain](https://www.ncbi.nlm.nih.gov/pubmed/22072275?dopt=Abstract), and [inflammation](https://www.ncbi.nlm.nih.gov/pubmed/26660531). It processes [cold-mediated pain relievers](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5541777/#R30) and may modulate pain sensation and set [vascular tone](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5541777/#R31), which may influence migraines. This variant is protective, with a [0.85X lower risk](https://www.nature.com/articles/ng.856) for migraines.

**# What should I do about this?**

No therapies are medically indicated at the moment.

C-990T (T;T)

**<function meter level="high risk">**

**<variant and population data>**

**# High Risk**

TRPM8 a cold and cold-burning pain receptor linked to [migraines](https://www.ncbi.nlm.nih.gov/pubmed/23294458?dopt=Abstract), [neuropathic chronic pain](https://www.ncbi.nlm.nih.gov/pubmed/22072275?dopt=Abstract), and [inflammation](https://www.ncbi.nlm.nih.gov/pubmed/26660531). It processes [cold-mediated pain relievers](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5541777/#R30) and may modulate pain sensation and set [vascular tone](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5541777/#R31), which may influence migraines. This variant increases the risk for migraines as compared to CC or CT.

**# What should I do about this?**

Many compounds may decrease pain due to TRMP8 variants.

* [WS-12](https://www.ncbi.nlm.nih.gov/pubmed/18930858) (a menthol derivative) has much higher potency and is twice as efficient as menthol as therapy for chronic neuropathic pain
* Cannabinoid receptors [CB1 and CB2](https://www.ncbi.nlm.nih.gov/pubmed/18511441) are associated with pain modulation, but smoking should be avoided to reduce COPD and lunch cancer risk.
* [Nerve growth factor](https://www.ncbi.nlm.nih.gov/pubmed/18511441) administered topically decreases thermal and mechanical pain

Other therapies may include [antibodies, siRNA, gene therapy](https://www.ncbi.nlm.nih.gov/pubmed/18511441), and avoiding air [below 25˚ C](http://www.uniprot.org/uniprot/Q7Z2W7).

**<symptoms>**

**<references>**

**<creator comment section>**

**What should I do about this?**

<symptoms pain, inflamation>

D005221,