

TRPM8 (Pain)

Gene Report

REPORT CATEGORIES —



PAIN



NERVE HEALTH

Sample Client

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DISCLAIMER

This report does not diagnose this or any other health conditions. Please talk to a healthcare professional if this condition runs in your family, you think you might have this condition, or you have any concerns about your results.

Personal information

NAME

Sample Client

SEX AT BIRTH

Male

HEIGHT

5ft 5" 165cm

WEIGHT

137lb 62kg



How this works

Our Wellness Reports analyze how your DNA influences your health.
We then use this analysis to give you personalized risk estimates and recommendations.



Similarly, our Trait Reports look at how your DNA influences your traits.



Your DNA is like an instruction manual — it contains a lot of information.
You can think of it as a blueprint for your body.

Genetic variants are parts of DNA that differ from person to person. Some can make you more vulnerable to certain health issues, while others may influence traits such as eye color.



We use artificial intelligence and machine learning to analyze all this information.
We then summarize your results as a risk score or display it on a gauge.

In total, we analyze up to 83 million genetic variants.

When we give a risk score, the risk icon tells you if you are at a higher or lower risk compared to other people:



Genotype color info:

AA

You don't have any risk alleles

AA

You have 1 risk allele

AA

You have 2 risk alleles

Your risk is also displayed as a percentile. This will tell you how your risks compare to our sample population. The lower your percentile number, the lower your risk. The "50th percentile" would be an average risk.

Similarly, the gauge tells you your relative risk score compared to our sample population, or it indicates a specific trait or haplotype you are more likely to have based on your genetic variants.

When applicable, we also list top evidence-based recommendations that may help lower your risk. The focus is on recommendations that may be of benefit to you, based on your genetics.

Our recommendations come in four categories: lifestyle, diet, supplements and drugs. The following icons tell you which category a recommendation falls into:



Our team of scientists also ranks each recommendation.
We rank based on impact and the strength of evidence in the medical literature.

Impact shows how strongly a recommendation will affect your health in a certain area.
Evidence is how much scientific support there is for the recommendation. Rankings are from 1 to 5 (low to high):



Impact

Impact scores range from 1-5. These scores reflect how much of an effect each recommendation can have. An impact score of 5 predicts the biggest effect.

When a recommendation affects something we can measure, we use those measurements to assign the impact score. For example, a recommendation that decreases cholesterol by 20% will have a higher impact score than one that decreases it by 5%.

Some recommendations affect things that we cannot directly measure, like stress or mood. For these, the impact score is based on how well they work relative to other recommendations and standard treatments. The best ones get the highest scores.

If there is a lot of research that shows a recommendation works especially well for your genotype, the impact score gets increased.

Recommendation Evidence

5 / 5

Recommendations that are considered effective and generally recommended by experts and medical bodies.

4 / 5

Recommendations that are considered likely effective and that have multiple independent meta-analyses and a great many studies supporting them.

3 / 5

Recommendations that are considered possibly effective and have many studies supporting them

2 / 5

Recommendations that have insufficient evidence, with two or several clinical trials supporting them, or many studies but with ambiguous results.

1 / 5

Recommendations that have insufficient evidence, with a single clinical trial, or with many studies most of which didn't find support for the recommendation.

0 / 5

No evidence in humans.

Genotype-specific Evidence

High-quality

Direct evidence that a recommendation helps more in people with your gene variant (many clinical trials, a few large clinical trials, or a meta-analysis).

Medium-quality

Direct evidence that a recommendation helps more in people with your gene variant (a few clinical trials or one large clinical trial).

Low-quality

Direct evidence that a recommendation helps more in people with your gene variant (a single clinical trial or more trials with inconsistent results).

Indirect

A recommendation may help more in people with your gene variant because it targets a specific gene or protein affected by your variant (e.g., MTHFR, dopamine).

In theory

A recommendation may help more in people with your gene variant because it targets a specific mechanism affected by your variant (e.g., inflammation, oxidative stress).

Some things to keep in mind:

- Genetics doesn’t play a considerable role in a condition or a trait.
- There is not enough research available to estimate a genetic predisposition.
- There are technical limitations to estimating or presenting a genetic predisposition.
- The topic is sensitive, and a genetic predisposition should only be estimated and presented by a healthcare professional.

Introduction

The [TRPM8](#) gene encodes the major sensory receptor of cold in our bodies. It is activated either by cold temperatures or by menthol (the active compound in peppermint), which is why mint makes our mouths feel cold [\[R\]](#).

TRPM8 becomes less sensitive in the presence of acidic pH and more sensitive in the presence of menthol [\[R\]](#), [\[R\]](#).

This cold receptor plays a complex role in [pain](#) perception. In “hot” or burning pain, the heat receptor [TRPV1](#) is activated and TRPM8 (which would produce a cooling sensation) is blocked. However, TRPM8 can also be sensitized to produce “cold” pain [\[R\]](#), [\[R\]](#).

While a lot of genes show variation between different populations of people, *TRPM8* is especially dramatic. A variant that increases *TRPM8* expression is much more common in Northern Europeans than in Africans: 88% in Finland compared with 5% in Nigeria [\[R\]](#)!

TRPM8 makes us more sensitive to cold sensations. One might think that reduced cold sensitivity would be an advantage for people living in cold climates, so it may seem strange that northern populations have increased *TRPM8* expression. However, increased sensitivity to cold may cause increased production of body heat, among other adaptations [\[R\]](#)

TRPM8 Genetics

People with higher TRPM8 might have had an advantage in colder climates, but they’re also more susceptible to certain types of pain disorders such as [migraines](#) and [IBS](#) [\[R\]](#).

The main TRPM8 variant associated with IBS is [rs10166942](#). At this SNP, the ‘T’ allele appears to increase expression of *TRPM8* and sensitivity to changes in cold temperature and to menthol. The ‘C’ allele, by contrast, is linked to relatively lower *TRPM8* expression and reduced sensitivity to changes in cold temperature [\[R\]](#).

The ‘T’ allele of this SNP is likewise associated with increased rates of IBS-C and IBS-M. Researchers don’t know for sure why TRPM8 is linked to IBS; however, most think it has something to do with this receptor’s role in pain perception. People with IBS often have something called visceral hypersensitivity; that is, their guts are more sensitive to internal pain triggers [\[R\]](#), [\[R\]](#).

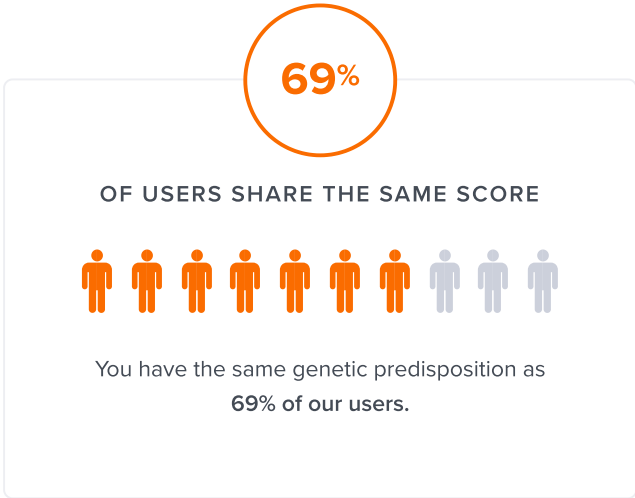
Each copy of the minor ‘T’ allele is also associated with a greater incidence of chronic migraines [\[R\]](#), [\[R\]](#), [\[R\]](#), [\[R\]](#), [\[R\]](#).

Finally, the minor variants at [rs7577262](#) and [rs17862920](#) have been found to be protective against migraines [\[R\]](#), [\[R\]](#), [\[R\]](#).



HIGHER ACTIVITY

Likely higher TRPM8 activity based on the genetic variants we looked at



Your top variants that most likely impact your genetic predisposition:

GENE	SNP	GENOTYPE
TRPM8	rs10166942	TT

The number of "risk" variants in this table doesn't necessarily reflect your overall result.

Your Recommendations

Your recommendations are prioritized according to the likelihood of it having an impact for you based on your genetics, along with the amount of scientific evidence supporting the recommendation.

You'll likely find common healthy recommendations at the top of the list because they are often the most impactful and most researched.

DOSAGE		DOSAGE	
1	Capsaicin	2	Hot Applications20 minutes
3	Peppermint Oil		180 mg

1



Capsaicin

IMPACT

3 / 5

EVIDENCE

3 / 5

How to implement

Apply a capsaicin cream or gel to the affected area up to 4 times daily. Make sure the skin is intact and not broken. Start with a lower concentration (0.025%) and gradually increase to 0.075% if needed for pain relief. Use continuously for at least 4 weeks to evaluate its effectiveness.

Description

Capsaicin, found in chili peppers, is known for its potential to boost metabolism and promote weight loss. It can also provide pain relief when used topically in certain creams and ointments.

How it helps

Capsaicin activates the heat receptor TRPV1 and blocks TRPM8; this activity leads to the hot feeling we get when we eat spicy foods [\[R\]](#).

Topical capsaicin (0.025-0.075% cream, applied 3-4 times/day for 4-8 weeks) may help relieve pain in some people [\[R\]](#).

High-concentration topical capsaicin (8% patch, applied for 30-90 minutes) may help with chronic nerve pain. This patch is only available by prescription and given to people under medical supervision. A doctor may recommend it for pain from conditions like herpes and diabetes [\[R\]](#).

Long-term use may reduce your pain sensitivity [\[R\]](#), [\[R\]](#).

The acute intranasal application of capsaicin (300 µg/100 µL) reduced headache severity in 4 placebo-controlled trials of 114 people suffering from cluster headaches [\[R\]](#), [\[R\]](#), [\[R\]](#), [\[R\]](#).

Please note: *Capsaicin may irritate the skin. Consult your doctor if the irritation is severe or lasts longer than 4 weeks. If capsaicin gets in your eyes, flush them with water right away, and consult your doctor* [\[R\]](#), [\[R\]](#), [\[R\]](#).

2



Hot Applications

IMPACT3 / 5

EVIDENCE3 / 5

How to implement

Apply a hot pack, heating pad, or a warm towel to the affected area for 15-20 minutes at a time. Do this several times a day, especially before activities that increase pain.

TYPICAL STARTING DOSE

20 minutes

Description

The use of hot applications, such as heating pads or warm compresses, can help relieve muscle tension, reduce pain, and improve blood flow to affected areas. It is a common approach for managing muscular discomfort and promoting relaxation.

People use hot applications to relieve pain, improve blood flow, and help muscles relax [R, R].

Types of hot applications include [R, R]:

- Heating pads
- Hot baths
- Saunas

How it helps

TRPM8 is activated by cold temperatures and suppressed by heat. Applying warmth to the skin using hot water bottles or heating pads may help block TRPM8 activation [R].

Experts suggest that **heat therapy may help with low back pain in combination with activating measures**. Both superficial and deep heating therapy may relieve pain but deep therapy may reduce disability more [R, R].

According to health experts, hot applications may help with osteoarthritis. They relieve joint pain by increasing blood flow to the affected area. This relaxes muscles and eases stiffness [R, R, R].

Hot pack application may reduce muscle pain and soreness after exercise [R].

Using a **hot sauna regularly for 8 weeks** may help make **tension headaches** less intense. However, it may not shorten them. **Heating pads** and **hot baths** may also help ease tension headaches [R, R].

Thermotherapy may help by increasing blood flow, relaxing muscles, and altering pain perception [R, R].

3



Peppermint Oil

IMPACT

2 / 5

EVIDENCE

2 / 5

How to implement

Take 180-400 mg of peppermint oil in capsule form daily before meals. It is recommended to continue this regimen for at least 4 weeks to evaluate its effects.

TYPICAL STARTING DOSE

180 mg

Description

Peppermint oil is an essential oil derived from the peppermint plant (*Mentha × piperita*). It has a long history of traditional use, dating back to ancient Egypt and Rome, where it was utilized for digestive and respiratory issues. Its main compounds, menthol and menthone are utilized for a variety of potential health benefits, including digestion, skin care, headaches, and respiratory congestion.

People use peppermint in foods, cosmetics, and supplements. [Peppermint oil](#) is an essential oil from peppermint leaves. It may ease muscle pain, relieve headaches, and improve digestion [\[R\]](#), [\[R\]](#).

Please note: *Peppermint oil may interact with certain medications. If you are taking any medications, consult your doctor before using peppermint oil* [\[R\]](#), [\[R\]](#).

How it helps

High expression of the *TRPM8* gene and high activation of the TRPM8 receptor may be associated with pain in some people. The most obvious genetic “solution” would then be to either decrease or block TRPM8 and to avoid any compounds, such as menthol, that activate it. However, researchers have suggested that menthol can also desensitize TRPM8 over time [\[R\]](#).

A study investigated 10% menthol solution's efficacy in migraine treatment. Menthol showed superiority over placebo in pain relief, sustained relief, and symptom alleviation, suggesting it as a safe and effective option [\[R\]](#).

Peppermint oil may improve stomach pain and bloating by **relaxing gut muscles** [\[R\]](#), [\[R\]](#), [\[R\]](#).

In a study of 127 women, taking peppermint oil (1 capsule/day for 3 days) reduced pain severity, nausea, and diarrhea. However, it did not offer greater benefits compared to standard painkiller therapy [\[R\]](#).

In a placebo-controlled trial of 41 people with tension headaches, topical peppermint oil (10%) reduced headache intensity after 15 minutes as effectively as Tylenol (1,000 mg) [\[R\]](#).

However, the combination of peppermint oil and eucalyptus oil had a muscle and mentally relaxing effect, but little influence on pain sensitivity in another placebo-controlled trial of 32 healthy subjects [\[R\]](#).

Next Steps

Remember, your genes only tell one important part of your health story!

Now that you've seen your DNA-based results for this health topic, let's take a look at other contributing factors.

Your lab results

Your lab results are impacted by the combined effect of your genes, environment and lifestyle.

Lab tests will give you the best picture of your current health status, while your genes provide insight into your health predispositions and which recommendations are best for you.