

# HMGB1 (Inflammation)

## Gene Report

### REPORT CATEGORIES —



HEART & BLOOD  
VESSELS



INFLAMMATION &  
AUTOIMMUNITY



CANCER

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 [HMGB1](#) gene encodes a protein called ‘*high mobility group box 1*’ that, together with other proteins such as *histones*, binds to nuclear DNA to form a complex called *chromatin*. HMGB1 organizes nuclear DNA and regulates gene expression. By doing so, it participates in several processes such as inflammation, cell differentiation, and cancer cell migration [\[R\]](#).

In response to injuries or infections, HMGB1 is released outside cells into the blood. There, it acts as a danger signal to trigger the inflammatory response. While this can help fight off infections when kept in balance, high levels of this protein may cause organ failure and sepsis [\[R\]](#), [\[R\]](#), [\[R\]](#), [\[R\]](#).

# HMGB1 Genetics

The best-researched *HMGB1* variant is [rs2249825](#). Its minor ‘C’ allele may increase *HMGB1* expression and has been associated with a decreased risk of [\[R\]](#):

- Colorectal cancer [\[R\]](#)
- Cervical cancer [\[R\]](#)
- Sepsis [\[R\]](#)
- Pneumonia [\[R\]](#)
- Hypertension [\[R\]](#)
- Delayed cerebral ischemia after subarachnoid hemorrhage [\[R\]](#)
- Atrial fibrillation after coronary artery bypass surgery [\[R\]](#)
- Delayed cerebral ischemia [\[R\]](#)
- Breast cancer progression [\[R\]](#)

However, this variant has also been associated with a decreased risk of rheumatoid arthritis and ischemic stroke [\[R\]](#), [\[R\]](#).

Another variant linked to higher *HMGB1* levels is the ‘T’ allele of [rs1045411](#). This variant has been associated with an increased risk of:

- Cancer (particularly, breast and liver cancer) [\[R\]](#), [\[R\]](#)
- Atrial fibrillation [\[R\]](#)
- Sepsis [\[R\]](#), [\[R\]](#)
- Ischemic stroke [\[R\]](#)
- Lupus nephritis [\[R\]](#)
- Death in patients with advanced lung cancer [\[R\]](#)
- Prostate cancer progression [\[R\]](#)

However, this variant has also been associated with a decreased risk of COVID-19 infection, a better prognosis in patients with aggressive stomach cancer, and a reduced risk and invasiveness of urothelial cell carcinoma [\[R\]](#), [\[R\]](#), [\[R\]](#).

Another well-researched variant is [rs1412125](#). Its minor ‘T’ allele reduces *HMGB1* expression and has been associated with a decreased risk of [\[R\]](#):

- Cancer (overall and cervical) [\[R\]](#), [\[R\]](#)
- Kawasaki disease and complications in people with this condition [\[R\]](#), [\[R\]](#)
- Pneumonia [\[R\]](#)
- Ischemic stroke [\[R\]](#)
- Prostate cancer progression [\[R\]](#)



TYPICAL ACTIVITY

Predisposed to typical HMGB1 activity based on 4 genetic variants we looked at

Your top variants that most likely impact your genetic predisposition:

| GENE  | SNP       | GENOTYPE |
|-------|-----------|----------|
| HMGB1 | rs1412125 | CC       |
| HMGB1 | rs1360485 | TT       |
| HMGB1 | rs2249825 | GG       |
| HMGB1 | rs1045411 | CC       |

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

- Breast cancer progression [\[R\]](#)

However, this allele has been associated with an increased risk of lung cancer and distant metastasis in patients with liver cancer [\[R\]](#), [\[R\]](#).

Finally, the minor ‘T’ allele of [rs1360485](#) may increase *HMGB1* expression and has been associated with a decreased risk of:

- Pneumoconiosis in coal workers [\[R\]](#)
- Breast cancer progression [\[R\]](#)
- Poorly differentiated, fast-spreading lung carcinoma [\[R\]](#)

However, this variant has been associated with an increased risk of:

- Lung cancer [\[R\]](#)
- Prostate cancer progression [\[R\]](#)
- Rheumatoid arthritis [\[R\]](#)