SelfDecode™

Histamine Pathway

Sample Client

Report date: 18 September 2025

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Personal information

NAME

Sample Client

SEX AT BIRTH

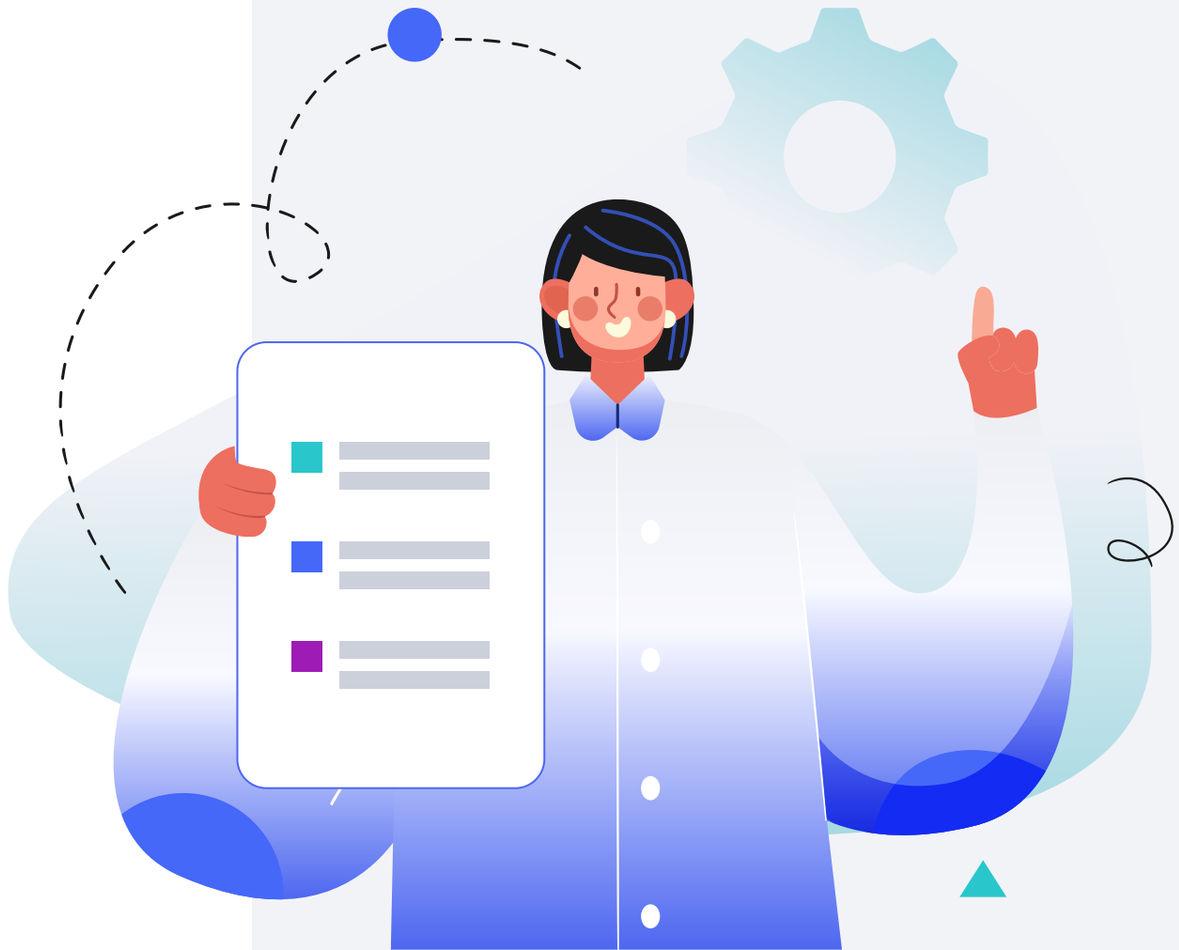
Female

HEIGHT

5ft 8" 173.0cm

WEIGHT

148lb 67.0kg



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.

How this works

Histamine is an important chemical. Among other roles, it helps your body [R, R]:

- Protect itself from foreign invaders, by activating parts of the immune system
- Stay awake, by signaling certain parts of the brain
- Digest food, by increasing stomach acid

Histamine can be released by immune cells, such as mast cells, and gut bacteria [R, R].

Histamine can also enter the body through the foods that you eat. Histamine-rich foods include [R, R]:

- Some fish (e.g., mackerel, tuna)
- Fermented foods and drinks (e.g., alcohol, yogurt, sauerkraut, cheese)
- Processed meats (e.g., sausages)
- Some fruits and vegetables (e.g., avocados, tomatoes, eggplant, spinach)

The way the food gets prepared may also play a role. Frying and grilling food may increase histamine levels. Boiling may decrease them [R].

Some people may be intolerant to histamine. In these people, high histamine levels can lead to symptoms similar to those experienced during an allergic reaction. These include [R, R, R]:

- Bloating and abdominal pain
- Diarrhea or constipation
- Dizziness or headaches
- Hives and itchiness
- Stuffy, runny nose
- Itchy, red eyes

Histamine is broken down by two main enzymes called **DAO** and **HNMT**. DAO is the main enzyme that breaks down histamine in the gut. HNMT deactivates histamine within cells [R, R].

Scientists currently think that DAO deficiency likely plays a more significant role in histamine intolerance related to dietary histamine. The gene that helps make DAO is called ***AOC1***. On the other hand, HNMT is more responsible for breaking down the histamine created by our body [R, R].

Other key players in histamine metabolism include:

- Histamine receptors, **H1-H4**
- Histamine production enzyme, **HDC**
- **NAT2, MAO-A, and MAO-B**, which help process tyramine and histamine
- Antioxidant enzymes like **GPx**
- Alcohol and aldehyde-metabolizing enzymes like **ALDH2**

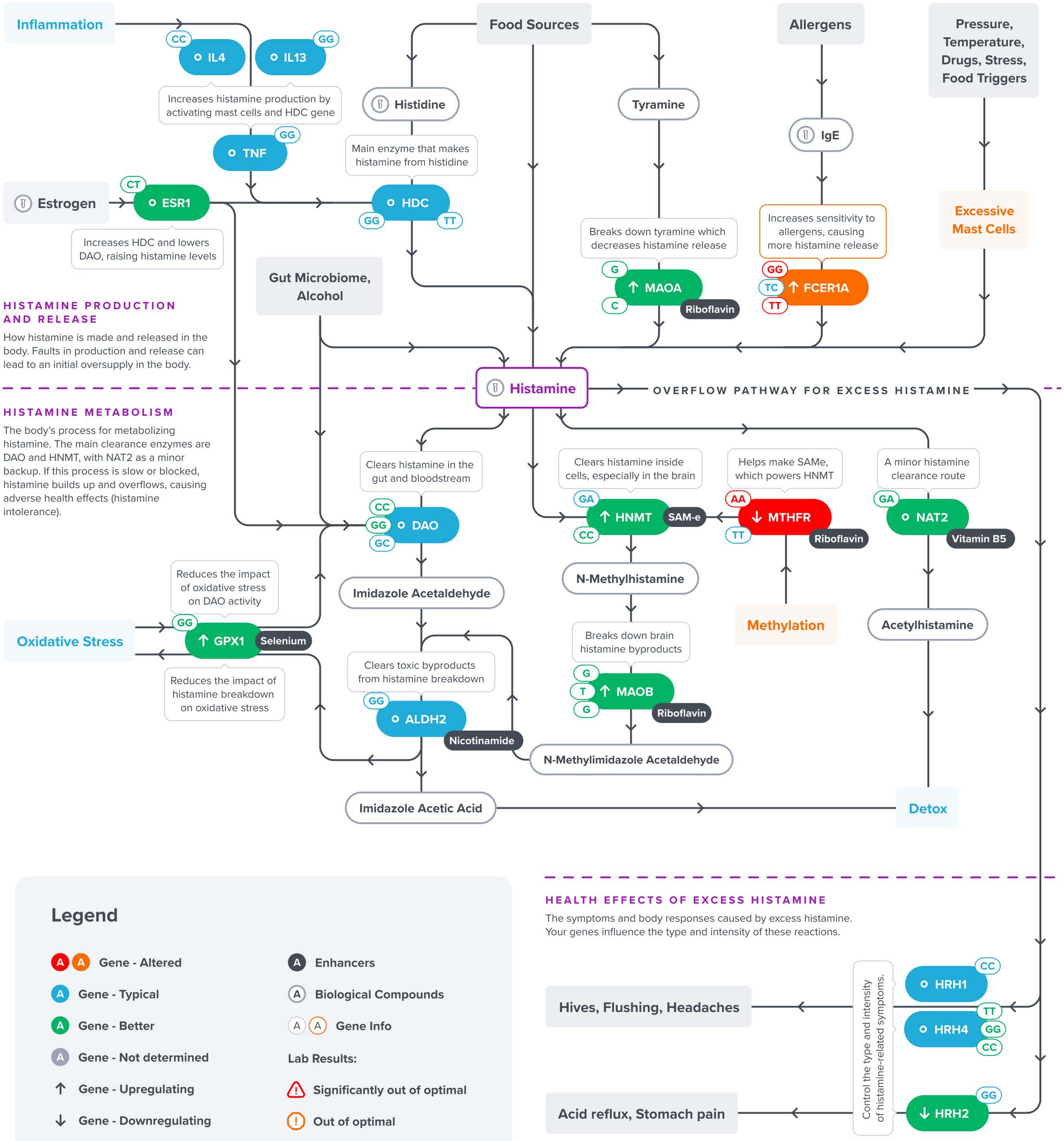
While genetic variants can influence histamine levels, research suggests that variants alone are probably **not sufficient** to cause full-blown histamine intolerance. Various environmental factors also play a key role [R].

Some of the factors that may contribute to histamine intolerance include [R, R, R, R, R, R, R, R]:

- Gut damage and inflammation (e.g., due to inflammatory bowel disease (IBD), gluten sensitivity, lactose intolerance, chemotherapy, etc.)
- Alcohol consumption
- Certain medications, such as some antibiotics and stomach acid blockers
- Underlying imbalances in the gut bacteria
- Consumption of foods containing high levels of biological *amines*, chemicals similar to histamine

Histamine Pathway

Histamine Pathway



Legend

- Gene - Altered
- Gene - Typical
- Gene - Better
- Gene - Not determined
- Gene - Upregulating
- Gene - Downregulating
- Gene - Neutral
- Genotype
- Genotype not determined
- Enhancers
- Biological Compounds
- Gene Info

Lab Results:

- Significantly out of optimal
- Out of optimal
- Normal
- Optimal
- Missing lab result

Results Overview

Gene - SNP Summary

MTHFR	rs1801133	↓ AA
	rs1801131	o TT
HDC	rs17740607	o GG
	rs2073440	o TT
	rs17187619	↓ TT
HRH4	rs527790	↓ CC
	rs487202	↓ GG
HRH2	rs2067474	o GG
MAOB	rs3027452	↑ G
	rs2283729	↑ G
	rs1799836	↑ T
FCER1A	rs2427837	↑ GG
	rs2251746	↑ TT
	rs2427827	o TC
HRH1	rs901865	o CC
IL13	rs20541	o GG
TNF	rs1800629	o GG
GPX1	rs1050450	↑ GG
MAOA	rs6323	↑ G
	rs909525	↑ C
ALDH2	rs671	o GG
AOC1	rs10156191	↑ CC
	rs1049793	o GC
	rs2052129	↑ GG
IL4	rs2243250	o CC
ESR1	rs2234693	o CT
HNMT	rs1050891	o GA
	rs11558538	↑ CC
NAT2	rs1495741	o GA

Labs Summary

Basophils (%) · Basophils (Absolute) · Betaine (TMG), Serum · Folate · Homocysteine · IgE · Vitamin B2 (Riboflavin), Plasma

Health Reports

Excessive Mast Cells · Methylation · Detox · Inflammation (CRP) · Oxidative Stress

Your recommendations

Your recommendations are prioritized according to the likelihood of it having an impact for you based on your lab results, 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
1	Betaine (TMG)	500 mg
2	Quercetin	250 mg
3	Riboflavin (Vitamin B2)	25 mg
4	Vitamin C	2000 mg

Betaine (TMG)

How to implement

To take Betaine (TMG) as a supplement, consume 500-2000 mg daily, preferably with a meal to enhance absorption. It is recommended to start at the lower end of the dosage range and adjust based on personal tolerance and effectiveness. This supplement can be taken indefinitely for ongoing support of heart health and liver function.

TYPICAL STARTING DOSE

500 mg

How it helps

Betaine may help histamine intolerance by serving as a methyl donor to support HNMT, the enzyme that methylates and breaks down histamine. By providing additional methyl groups, betaine can help ensure adequate histamine degradation when folate-dependent methylation pathways are insufficient.

Personalized to Your Genes

↓ MTHFR

Your variant (rs1801133-A) is linked to increased betaine needs. According to preliminary results, betaine may help people with MTHFR deficiency [R, R].

Quercetin

How to implement

Take 250-1000 mg of quercetin supplement daily with a glass of water, preferably with a meal to aid in its absorption.

TYPICAL STARTING DOSE

250 mg

How it helps

This natural plant compound found in onions and apples acts like a natural antihistamine. It helps calm down overactive immune cells (mast cells) that release histamine, reducing symptoms like headaches, skin reactions, and digestive upset.

Personalized to Your Genes

↑ FCER1A

Quercetin may inhibit FcεRI-mediated mast cell activation and histamine release [R].

Riboflavin (Vitamin B2)

How to implement

Take a riboflavin (vitamin B2) supplement daily, with a dose ranging from 5mg to 400mg, depending on the specific health concern or advice from a healthcare provider. Swallow the supplement with water, preferably with a meal to enhance absorption. This regimen can be continued long-term or as directed by a healthcare professional.

TYPICAL STARTING DOSE

25 mg

How it helps

This B vitamin supports the enzymes involved in histamine metabolism and helps maintain healthy cellular energy production. Adequate riboflavin levels are important for proper histamine breakdown.

Personalized to Your Genes

↓ MTHFR

Riboflavin supports MTHFR function. In people with your variant (rs1801133-A), riboflavin has stronger beneficial effects on homocysteine levels [R, R, R, R].

Vitamin C

How to implement

Take 500-2000 mg of vitamin C supplement daily. It can be taken at any time of the day, with or without food, according to personal preference or tolerance.

TYPICAL STARTING DOSE

2000 mg

How it helps

A powerful natural antihistamine that helps your body produce more DAO (the enzyme that breaks down histamine). Vitamin C also reduces inflammation and supports immune system balance.

Personalized to Your Genes

↑ FCER1A

Vitamin C acts as an antihistamine and may down-regulate FcεRI expression [R].

MTHFR

MTHFR Report

The MTHFR gene helps make an enzyme called methylenetetrahydrofolate reductase (MTHFR) [R].

MTHFR helps process folate (vitamin B9). Folate plays a role in [R, R, R, R]:

- DNA production
- Red blood cell production
- Normal fetus development
- Brain and heart health
- Clearing homocysteine, a protein breakdown product

Variants in the MTHFR gene can change how the enzyme functions. Two of the most widely studied variants reduce MTHFR enzyme activity [R, R, R, R].

MTHFR enables homocysteine recycling to methionine and production of **SAMe**. SAMe is required for histamine methylation by histamine-methyltransferase. **A deficit of SAMe may lead to high histamine levels**. Thus, MTHFR polymorphisms that reduce enzyme activity can indirectly impair histamine clearance [R].

Blockers:

Alcohol

Oxidative stress

Enhancers:

Riboflavin

Vitamin B12

Betaine (TMG)

SNP

rs1801133 C677T

Alleles

A: Reduced MTHFR activity

G: Typical MTHFR activity

Your Genotype

↓AA

Your genotype is linked to reduced MTHFR activity and methylation ability.

Intro and Health Effects

MTHFR **rs1801133 or C677T** variant at nucleotide 677 substitutes a valine for an alanine at amino acid 222. This variant is associated with reduced enzyme activity, elevated total homocysteine levels, and lower folate levels [R].

People heterozygous for this mutation present a 35% decrease in the normal enzyme activity and homozygous individuals a 70% decrease [R].

Impaired methylation caused by this variant may indirectly **affect histamine clearance through the HNMT enzyme**.

Studies found links between this variant, higher homocysteine, and [R, R, R, R, R, R]:

- Cognitive problems
- Heart disease and stroke
- Asthma and allergies
- Fertility and pregnancy issues
- Birth defects
- Mental health issues
- Migraines

SNP

rs1801131 A1298C

Alleles

G: Slightly reduced MTHFR activity

T: Typical MTHFR activity

Your Genotype

TT

Your genotype is linked to typical MTHFR activity and methylation ability

Intro and Health Effects

MTHFR **rs1801131** **or A1298C** variant causes Glu429-to-Ala substitution.

It also decreases MTHFR enzyme activity, but less so than rs1801133. The effects of this variant may only be meaningful in people who also have the “AA” genotype at rs1801133 [R, R, R, R, R].

However, according to some authors, the GG genotype results in 30-40% reduction in MTHFR enzyme activity, regardless of the other MTHFR variant [R].

Impaired methylation caused by this variant may indirectly **affect histamine clearance through the HNMT enzyme**.

Studies found links between these two variants, higher homocysteine, and [R, R, R, R, R, R]:

- Cognitive problems
- Heart disease and stroke
- Asthma and allergies
- Fertility and pregnancy issues
- Birth defects
- Mental health issues
- Migraines

FCER1A

FCER1A Report

The *FCER1A* gene encodes the IgE receptor, a protein that initiates the allergic response. It's essential for IgE binding on mast cells and basophils [R].

When two or more high-affinity IgE receptors are brought together by allergen-bound IgE molecules, mediators such as **histamine** that are responsible for allergy symptoms are released [R].

Several *FCER1A* variants have been associated with allergic conditions. They typically increase *FCER1A* expression, resulting in enhanced sensitivity to allergen-bound IgE antibodies. Carriers also tend to produce more IgE antibodies.

SNP	Your Genotype
rs2427837 344C>T Alleles **A:** Reduced FCER1A activity **G:** Increased FCER1A activity	↑GG **Your genotype is linked to higher FCER1A activity and higher odds of allergies.**

Intro and Health Effects

Several *FCER1A* variants have been associated with allergic conditions. They typically increase *FCER1A* expression, resulting in enhanced sensitivity to allergen-bound IgE antibodies. Carriers also tend to produce more IgE antibodies. These variants include:

- The 'G' allele of **rs2427837** (344C>T): associated with an increased risk of atopic dermatitis and aspirin-intolerant chronic urticaria [R, R].

SNP	Your Genotype
rs2251746 66T>C Alleles **C:** Reduced FCER1A activity **T:** Increased FCER1A activity	↑TT **Your genotype is linked to higher FCER1A activity and higher odds of allergies.**

Intro and Health Effects

Several *FCER1A* variants have been associated with allergic conditions. They typically increase *FCER1A* expression, resulting in enhanced sensitivity to allergen-bound IgE antibodies. Carriers also tend to produce more IgE antibodies. These variants include:

- The 'T' allele of **rs2251746** (66T>C): associated with an **increased risk of allergic disease** and better response to omalizumab in patients with severe uncontrolled asthma [R, R, R, R, R].

SNP	Your Genotype
rs2427827 315C>T	TC
Alleles	**Your genotype is linked to typical FCER1A activity and typical odds of allergies.**
C: Reduced FCER1A activity	
T: Increased FCER1A activity	

Intro and Health Effects

Several *FCER1A* variants have been associated with allergic conditions. They typically increase *FCER1A* expression, resulting in enhanced sensitivity to allergen-bound IgE antibodies. Carriers also tend to produce more IgE antibodies. These variants include:

- The 'T' allele of **rs2427827** (315C>T): associated with an **increased risk of allergic disease** [R, R, R].

ALDH2

ALDH2 Report

The ALDH2 gene encodes for part of an enzyme named aldehyde dehydrogenase (ALDH), which is involved in the breakdown of alcohol in the liver.

ALDH enzymes are responsible for the second step, breaking down acetaldehyde to acetic acid.

After histamine is oxidised by DAO or HNMT/MAO, the resulting aldehyde metabolites are further oxidised by aldehyde dehydrogenase (ALDH). Ethanol metabolite, acetaldehyde, competes with histamine metabolites for ALDH2, leading to **elevated histamine and alcohol-induced flushing**. Alcohol and acetaldehyde also liberate histamine from mast cells and inhibit DAO [R, R].

Blockers:

Alcohol | Cigarette smoke | Air pollution

Enhancers:

Vitamin B3 (Niacin) | N-acetylcysteine (NAC)

SNP

rs671

Alleles

A: Reduced ALDH2 activity

G: Typical ALDH2 activity

Your Genotype

GG

Your genotype is linked to typical ALDH2 activity and alcohol detox.

Intro and Health Effects

The “A” allele at rs671 produces fewer or less active ALDH enzymes, and may reduce the enzyme activity to zero, largely reducing the rate at which acetaldehyde is converted to acetic acid. This can lead to a **build-up of acetaldehyde** following alcohol consumption and result in negative effects such as [R, R, R]:

- Flushing
- Sweating
- Nausea
- Accelerated heart rate
- Vomiting

Carriers of the ‘A’ allele have been reported to get drunk faster and are more likely to experience a hangover, especially if they have a **vitamin B12 deficiency**. Vitamin B12 can assist in acetaldehyde breakdown [R, R].

This variant may also **impair histamine clearance** (its metabolite, imidazole acetaldehyde) and worsen the effects of alcohol on histamine release [R].

It is most prevalent in **Asian populations** and is almost non-existent in other populations. The so-called “Asian flush” happens due to **excessive histamine release** in people with this variant [R, R].

AOC1

AOC1 Report

The AOC1 gene encodes **diamine oxidase (DAO)**, the primary enzyme that breaks down histamine in the digestive system [R].

Two enzymes control histamine breakdown: histamine N-methyltransferase (HNMT) and DAO. These enzymes are extremely important. If either one starts malfunctioning, histamine can increase dramatically throughout the body [R, R].

Some people may be intolerant to histamine, often due to DAO enzyme dysfunction. In these people, high histamine levels can lead to symptoms similar to those experienced during an allergic reaction. These include [R, R, R]:

- Bloating and abdominal pain
- Diarrhea or constipation
- Dizziness or headaches
- Hives and itchiness
- Stuffy, runny nose
- Itchy, red eyes

Blockers:

Alcohol | Heavy metals

Enhancers:

Vitamin B6 (Pyridoxin) | Vitamin C | PLP (active vitamin B6)

SNP

rs10156191

Alleles

C: Increased DAO activity

T: Reduced DAO activity

Your Genotype

↑CC

Your genotype is linked to higher DAO activity and lower odds of histamine intolerance.

Intro and Health Effects

Different AOC1 variants have been associated with **lower levels of the DAO enzyme** and a higher incidence of migraine, due to histamine intolerance. One of the main variants is rs10156191-T [R, R, R].

Lower DAO enzyme activity reduces the body's capacity to break down and deactivate histamine, potentially leading to inflammation and pain [R, R, R].

SNP	Your Genotype
rs1049793 Alleles **G:** Reduced DAO activity **C:** Increased DAO activity	○ GC **Your genotype is linked to typical DAO activity and typical odds of histamine intolerance.**

Intro and Health Effects

Different AOC1 variants have been associated with **lower levels of the DAO enzyme** and higher incidence of migraine, due to histamine intolerance. One of the main variants is rs1049793-G [R, R, R].

Lower DAO enzyme activity reduces the body's capacity to break down and deactivate histamine, potentially leading to inflammation and pain [R, R, R].

SNP	Your Genotype
rs2052129 Alleles **G:** Increased DAO activity **T:** Reduced DAO activity	↑ GG **Your genotype is linked to higher DAO activity and lower odds of histamine intolerance.**

Intro and Health Effects

Different AOC1 variants have been associated with **lower levels of the DAO enzyme** and a higher incidence of migraine, due to histamine intolerance. One of the main variants is rs2052129-T [R, R, R].

Lower DAO enzyme activity reduces the body's capacity to break down and deactivate histamine, potentially leading to inflammation and pain [R, R, R].

HDC

HDC Report

The HDC gene encodes an enzyme called ‘histidine decarboxylase’ that catalyzes the decarboxylation of histidine to form histamine in a one-step process. **The HDC enzyme is the primary biological source of histamine** [R].

SNP

rs17740607 Thr31Met

Alleles

A: Reduced HDC activity

G: Typical HDC activity

Your Genotype

GG

Your genotype is linked to typical HDC activity.

Intro and Health Effects

Another important HDC polymorphism is rs17740607, also known as Thr31Met. Its minor ‘A’ allele may reduce HDC activity and has been associated with a decreased risk of chronic heart failure [R].

SNP

rs2073440 Asp644Glu

Alleles

G: Reduced HDC activity

T: Typical HDC activity

Your Genotype

TT

Your genotype is linked to typical HDC activity and typical odds of allergic rhinitis.

Intro and Health Effects

One of the main HDC polymorphisms is rs2073440, also known as Asp644Glu. Its minor ‘G’ allele may decrease histamine production and has been associated with a reduced risk of allergic rhinitis [R].

HRH1

HRH1 Report

The HRH1 gene encodes the H1 histamine receptor. Along with the H2, H3, and H4 receptors, H1 mediates the actions of histamine. Specifically, HRH1 is involved in the [R]:

- Contraction of smooth muscles
- Increase in capillary permeability
- Release of catecholamines from adrenals
- Neurotransmission in the central nervous system

HRH1 has been associated with multiple processes, including memory and learning, circadian rhythm, and thermoregulation. It also plays a role in allergic condiitons such as atopic dermatitis, asthma, anaphylaxis, and allergic rhinitis [R].

SNP	Your Genotype
rs901865 Alleles **C:** Typical HRH1 activity **T:** Altered HRH1 activity	CC **Your genotype is linked to typical HRH1 activity and typical odds of allergic reactions.**

Intro and Health Effects

The main HRH1 variant is rs901865 (17C>T). Its minor **'T' allele alters HRH1** activity. This variant has been associated with:

- Increased prevalence of allergic asthma [R]
- Increased prevalence of allergic rhinitis [R]

HRH4

HRH4 Report

The HRH4 gene encodes the **H4 histamine receptor**. Along with the H1, H2, and H3, H4 mediates the actions of histamine. Specifically, HRH4 is mainly found in hematopoietic cells and plays a role in **inflammation and allergy responses** [R].

H4R stimulation promotes mast-cell and basophil migration to sites of inflammation [R].

SNP

rs17187619

Alleles

C: Increased HRH4 activity

T: Reduced HRH4 activity

Your Genotype

↓TT

Your genotype is linked to lower HRH4 activity and lower odds of asthma.

Intro and Health Effects

Several HRH4 variants have been associated with allergic and inflammatory conditions. Although the effects of these variants on gene activity haven't been established, they may cause increased inflammation through **enhanced histamine signaling**. They include:

- The 'C' allele of rs17187619: associated with increased prevalence of asthma [R].

SNP

rs527790

Alleles

C: Reduced HRH4 activity

T: Increased HRH4 activity

Your Genotype

↓CC

Your genotype is linked to lower HRH4 activity and lower odds of asthma.

Intro and Health Effects

Several HRH4 variants have been associated with allergic and inflammatory conditions. Although the effects of these variants on gene activity haven't been established, they may cause increased inflammation through **enhanced histamine signaling**. They include:
The 'T' allele of rs527790: associated with increased prevalence of asthma [R].

SNP	Your Genotype
rs487202 Alleles **G:** Reduced HRH4 activity **C:** Increased HRH4 activity	↓GG **Your genotype is linked to lower HRH4 activity and lower odds of asthma.**

Intro and Health Effects

Several HRH4 variants have been associated with allergic and inflammatory conditions. Although the effects of these variants on gene activity haven't been established, they may cause increased inflammation through **enhanced histamine signaling**. They include:

- The 'C' allele of rs487202: associated with increased prevalence of asthma [R].

IL13

IL13 Report

The IL13 gene codes for interleukin 13 (IL-13), a cytokine that belongs to type 2 or “humoral” immunity. Along with IL-4, it fights pathogens and other outside threats that don’t enter our cells but stay in the fluids (humor=fluid) [R, R].

Elevated Th2 activity underlies a number of allergic diseases. Indeed, IL-13 is able to stimulate the release of a type of antibody called IgE from immune system cells. The release of IgE antibodies is an early step in the progression of allergic reactions. In the lungs, IL-13 can increase histamine production and the number of histamine receptors [R, R].

Elevated IL-13 may also decrease the production of filaggrin. Lack of filaggrin would compromise the structure of the outermost skin layer, allowing allergens to enter the skin and interact with components of the immune system [R].

Variants of this gene have been associated with allergic diseases, such as eczema, asthma, hay fever, and food allergies. These variants may increase the production or activity of IL-13, which can result in increased IgE antibody release [R, R, R].

SNP

rs20541

Alleles

A: Increased IL13 activity

G: Typical IL13 activity

Your Genotype

GG

Your genotype is linked to typical IL13 activity and typical odds of allergic conditions

Intro and Health Effects

The main IL13 variant is rs20541. Its minor ‘A’ allele has been linked to elevated IL-13 and IgE levels, along with an increased risk of:

- Allergic rhinitis [R, R, R, R]
- Asthma [R, R]
- COPD (only in Caucasians) [R]
- ARDS in critically ill patients [R]

IL4

IL4 Report

The IL4 gene codes for an immune messenger or cytokine called IL-4 (interleukin 4). IL-4 is mostly anti-inflammatory and is best known for stimulating the Th2 arm of the immune system [R].

However, IL-4 promotes IgE production and sensitises tissues to histamine. It increases the expression of the histamine H1 receptor (H1R) [R].

IL-4 also augments histamine-mediated allergic reactions and inflammation through the H2 receptors. Some researchers are developing anti-allergy therapies that block or decrease IL-4 signalling [R, R, R].

SNP	Your Genotype
rs2243250 589C>T Alleles **C:** Typical IL4 activity **T:** Increased IL4 activity	CC **Your genotype is linked to typical IL4 activity and typical odds of allergic conditions.**

Intro and Health Effects

The main IL4 variant is rs2243250 (589C>T). People with the minor 'T' allele may have increased Th2 immunity and IL-4 levels [R].

This variant has been associated with an increased risk of allergic conditions such as:

- Hay fever [R]
- Eczema [R]
- Asthma [R, R, R]

In contrast, the 'T' allele has been associated with a decreased risk of some autoimmune conditions, most likely due to enhanced Th2 immunity [R, R, R, R].

TNF

TNF Report

The TNF gene encodes a protein called tumor necrosis factor-alpha (TNF-alpha or cachexin). TNF-alpha plays a central role in the immune response and inflammation, and it has been implicated in a wide variety of inflammatory disorders [R].

TNF-α induces histamine release from human mast cells. Some of the effects of TNF-alpha include [R, R]:

- Inflammation and fever
- Appetite suppression
- Muscle soreness
- Stimulating phagocytosis, which helps remove harmful substances like bacteria

TNF-alpha accomplishes many of these effects by activating various inflammatory pathways (including NF-κB) [R].

SNP	Your Genotype
rs1800629 TNF -308 Alleles **A:** Increased TNF activity **G:** Typical TNF activity	GG **Your genotype is linked to typical TNF activity and inflammation levels**

Intro and Health Effects

The rs1800629 polymorphism (also known as TNF -308) is the main SNP in the TNF gene. The 'A' allele is associated with higher levels of TNF-alpha [R].

This variant is linked to:

- Asthma and COPD [R, R]
- ARDS and sepsis [R, R]
- IBD risk and severity[R, R, R]
- Chronic pain [R, R, R, R]
- Obesity [R, R, R, R]
- Hashimoto's disease [R]
- Acne [R]
- Insulin resistance and poor blood sugar control [R]
- Shorter lifespan [R, R, R] TNF-308

ESR1

ESR1 Report

The ESR1 gene encodes ERα, a nuclear hormone receptor that regulates the expression of genes involved in various physiological processes, including reproductive health, bone density, cardiovascular function, and cancer development [R, R].

Estrogen binding to ERα influences gene expression, impacting cell growth, differentiation, and metabolism [R, R].

ERα signalling enhances histamine responses by promoting mast-cell degranulation and histamine release. ESR1 variants may therefore increase histamine-related symptoms [R].

Variations in the ESR1 gene can affect receptor function and estrogen signalling, leading to differences in health outcomes, especially in females. [R].

SNP	Your Genotype
rs2234693 -397T>C or PvuII Alleles **C:** Increased ESR1 activity **T:** Reduced ESR1 activity	o CT **Your genotype is linked to balanced ESR1 activity.**

Intro and Health Effects

The main ESR1 variant is rs2234693 (-397T>C or PvuII). Its **“C” allele** increases ESR1 expression, leading to more pronounced effects of estrogen. It’s linked to [R]:

- Endometriosis [R]
- Breast cancer [R, R]
- Prostate cancer [R, R]
- Depression [R]

This variant could also be **negative in the context of histamine intolerance**, since estrogen increases mast-cell activity and histamine release. However, the evidence is preliminary [R].

On the bright side, it’s linked to the following positive health outcomes:

- Stronger bones (higher BMD) [R, R, R]
- Lower odds of endometrial cancer [R]
- Slower cognitive decline (only in European ancestry) [R]
- Lower odds of anxiety (phobia) [R]
- Better cardiovascular health [R]

- Increased fertility in men [R]

Expectedly, the effects of these variants are more **pronounced in women**. However, some studies have found **no links – or even opposite links** – of this variant with most of the above health outcomes [R, R, R, R, R, R].

GPX1

GPX1 Report

The GPX1 gene helps make glutathione peroxidase (GPx), one of the body's key antioxidant enzymes. This enzyme converts hydrogen peroxide and glutathione into glutathione disulfide and water. By doing so, GPx helps reduce oxidative stress [R].

Hydrogen peroxide can trigger histamine release. Thus, GPX1 deficiency may allow ROS accumulation, promoting histamine release and allergic symptoms [R].

Blockers:

Oxidative stress | Heavy metals

Enhancers:

Selenium | N-acetylcysteine (NAC) | Glycine

SNP

rs1050450

Alleles

A: Reduced GPX1 activity

G: Increased GPX1 activity

Your Genotype

↑GG

Your genotype is linked to higher GPX1 activity and lower oxidative stress.

Intro and Health Effects

One study found a direct link between a common GPX1 variant and human longevity. According to a cohort of elderly Danish people born in 1905, the heterozygous genotype 'AG' at rs1050450 was significantly more common in the very elderly than in the general population [R].

Other studies have strongly suggested that the **'G' allele** at rs1050450 confers **higher GPx activity**, which is linked to better health outcomes. It may also indirectly support histamine clearance and reduce oxidative stress due to histamine buildup [R, R].

HNMT

HNMT Report

The HNMT gene encodes histamine N-methyltransferase, the second major enzyme (after DAO) that breaks down histamine. HNMT is found throughout the body and (perhaps most importantly) in the brain. It deactivates histamine by adding a methyl group [R, R].

These enzymes are extremely important. If either one starts malfunctioning, histamine can increase dramatically throughout the body. While DAO deficiency likely plays a more significant role in histamine intolerance related to dietary histamine, HNMT is more responsible for breaking down the histamine created by our body [R, R].

Different HNMT gene variants have been linked to histamine-related conditions, such as [R, R, R, R, R]:

- Allergies
- Asthma
- Eczema
- Migraines
- ADHD

Blockers:

Oxidative stress | Heavy metals

Enhancers:

SAMe | Magnesium | Folate

SNP

rs1050891

Alleles

A: Reduced HNMT activity

G: Increased HNMT activity

Your Genotype

GA

Your genotype is linked to typical HNMT activity and typical odds of histamine intolerance.

Intro and Health Effects

In one interesting study, increased brain histamine **worsened behavioral symptoms in children with ADHD**. The children with the 'AA' genotype at rs1050891 were more likely to have worse symptoms when they were exposed to **artificial food colorings and additives** (sunset yellow, carmoisine, tartrazine, ponceau 4R, quinoline yellow, Allura red AC, and sodium benzoate) [R].

These additives seem to raise brain histamine, which may be more detrimental for people with underactive HNMT [R].

Another variant, the 'T' allele at rs11558538, is associated with decreased HNMT activity and increased risk of schizophrenia, ADHD, and migraine [R].

SNP	Your Genotype
rs11558538 Alleles **C:** Increased HNMT activity **T:** Reduced HNMT activity	↑CC **Your genotype is linked to higher HNMT activity and lower odds of histamine intolerance.**

Intro and Health Effects

One HNMT variant, the **'T' allele at rs11558538**, is associated with decreased HNMT activity and increased risk of schizophrenia, ADHD, and migraine [R].

HRH2

HRH2 Report

The HRH2 gene encodes the **H2 histamine receptor**. Along with the H1, H3, and H4 receptors, H2 mediates the actions of histamine. Specifically, HRH2 is involved in digestive function by stimulating **stomach acid secretion** and regulating gut motility. It may also play a role in cell growth and differentiation [R].

SNP

rs2067474 -1018 G>A

Alleles

A: Reduced HRH2 activity

G: Typical HRH2 activity

Your Genotype

GG

Your genotype is linked to typical HRH2 activity and typical stomach acid secretion.

Intro and Health Effects

The main HRH2 polymorphism is rs2067474 (-1018 G>A). Its minor 'A' allele may **reduce** gene expression, which may result in milder stomach acid secretion. This variant has been associated with:

- Decreased risk of stomach lining atrophy [R, R]
- Decreased risk of stomach cancer [R]

MAOA

MAOA Report

The MAOA gene makes an enzyme called MAO-A (monoamine oxidase A). It’s the primary enzyme responsible for breaking tyramine down. Tyramine is found in aged, fermented, and preserved foods like aged cheeses, wine, cured meats, and sauerkraut. **When MAOA activity is low, tyramine can accumulate** and cause blood vessels to first constrict and then rapidly dilate, often triggering intense headaches or migraines.

This is why some people get severe **headaches after eating certain cheeses or drinking red wine**—their MAOA isn't efficiently clearing the tyramine, leading to what's sometimes called the "cheese effect."

Histamine and tyramine are closely connected biogenic amines that share metabolic pathways, food sources, and symptoms. Both accumulate in aged/fermented foods, and MAOA serves as a backup enzyme for histamine breakdown.

When someone has low MAOA activity combined with other histamine-clearing issues, they may experience symptoms after eating histamine-rich foods. People with low MAOA activity often need to be more careful about their food choices, particularly avoiding aged and fermented foods that are high in tyramine and histamine. The same applies to individuals treated with **MAO-A inhibitors**.

Blockers:

Heavy metals Stress

Enhancers:

Riboflavin Flavonoids Exercise

SNP

rs6323

Alleles

G: Increased MAOA activity

T: Reduced MAOA activity

Your Genotype

↑G

Your genotype is linked to higher MAOA activity and lower tyramine buildup.

Intro and Health Effects

Low-activity MAOA variants lead to increased levels of the monoamine neurotransmitters (dopamine, serotonin, and norepinephrine) and other components like **tyramine**. The main one is rs6323, and its **“T” allele** encodes a MAO-A protein with **lower activity** [R].

When someone has low MAOA activity combined with other histamine-clearing issues, they may experience symptoms after eating histamine- and tyramine-rich foods.

SNP	Your Genotype
rs909525 Alleles **C:** Increased MAOA activity **T:** Reduced MAOA activity	↑C **Your genotype is linked to higher MAOA activity and lower tyramine buildup.**

Intro and Health Effects

Low-activity MAOA variants lead to increased levels of the monoamine neurotransmitters (dopamine, serotonin, and norepinephrine) and other components like tyramine. An important variant is rs909525, with the **“T” allele** linked to **lower activity** [R].

When someone has low MAOA activity combined with other histamine-clearing issues, they may experience symptoms after eating histamine- and tyramine-rich foods.

MAOB

MAOB Report

The MAOB gene makes an enzyme called MAO-B (monoamine oxidase B) that acts like a cleanup crew for histamine in your body. This enzyme breaks down histamine and prevents it from building up to problematic levels [R].

Some people have genetic variations in MAOB that make their MAO-B enzyme less effective at clearing histamine. This can lead to histamine intolerance - where normal amounts of histamine from foods (like aged cheese or wine) or your body's own production cause symptoms like headaches, digestive issues, or skin reactions.
Understanding your MAOB status helps explain why some people are more sensitive to histamine-rich foods or have unexplained symptoms related to poor histamine metabolism. It's one key factor in how efficiently your body processes histamine [R].

Blockers:

Oxidative stress

Enhancers:

Riboflavin Flavonoids

SNP

rs3027452

Alleles

A: Reduced MAOB activity

G: Increased MAOB activity

Your Genotype

↑G

Your genotype is linked to higher MAOB activity and lower histamine buildup.

Intro and Health Effects

Certain MAOB variants are linked to **increased activity**. In theory, people with those variants may **metabolize histamine more efficiently**. On the other hand, these variants have been associated with chronic fatigue syndrome, likely due to lower levels of key neurotransmitters [R, R].

The main variants associated with high MAO activity are [R]:

- **'G' at rs3027452**
- 'G' at rs2283729
- 'T' at rs1799836

SNP	Your Genotype
rs2283729 Alleles **A:** Reduced MAOB activity **G:** Increased MAOB activity	↑G **Your genotype is linked to higher MAOB activity and lower histamine buildup.**

Intro and Health Effects

Certain MAOB variants are linked to **increased activity**. In theory, people with those variants may **metabolize histamine more efficiently**. On the other hand, these variants have been associated with chronic fatigue syndrome, likely due to lower levels of key neurotransmitters [R, R].

The main variants associated with high MAO activity are [R]:

- 'G' at rs3027452
- **'G' at rs2283729**
- 'T' at rs1799836

SNP	Your Genotype
rs1799836 Alleles **C:** Reduced MAOB activity **T:** Increased MAOB activity	↑T **Your genotype is linked to higher MAOB activity and lower histamine buildup.**

Intro and Health Effects

Certain MAOB variants are linked to **increased activity**. In theory, people with those variants may **metabolize histamine more efficiently**. On the other hand, these variants have been associated with chronic fatigue syndrome, likely due to lower levels of key neurotransmitters [R, R].

The main variants associated with high MAO activity are [R]:

- 'G' at rs3027452
- 'G' at rs2283729
- **'T' at rs1799836**

NAT2

NAT2 Report

N-acetyltransferase 2 (NAT2) is an enzyme that plays a crucial role in the metabolism and detoxification of numerous drugs, environmental toxins, and endogenous substances. It is mostly active in the liver [R].

NAT2's role in detox is integral to the body's defense mechanism against potentially harmful substances. It enables the acetylation of certain compounds found in medications, carcinogens, and environmental toxins. This process makes these compounds more water-soluble, enhancing their removal from the body [R].

There are considerable differences in acetylator status among individuals, classifying them as slow or fast acetylators. Most resources also acknowledge an intermediate group [R].

Slow acetylators metabolize certain drugs and toxins more slowly, potentially leading to increased toxicity and a higher risk of adverse drug reactions. Rapid acetylators generally have better detox potential. However, they may be more vulnerable to toxins that get activated by NAT2 into more harmful metabolites [R, R].

NAT2 acetylates histamine to form N-acetylhistamine, an alternative minor pathway for histamine breakdown. Although less efficient than DAO or HNMT, NAT2 contributes to histamine clearance in the liver and gut. Slow-acetylator NAT2 variants may reduce histamine acetylation and predispose to symptoms [R].

Blockers:

Cigarette smoke

Air pollution

Enhancers:

Riboflavin

Flavonoids

SNP

rs1495741

Alleles

A: Reduced NAT2 activity

G: Increased NAT2 activity

Your Genotype

GA

Your genotype is linked to balanced NAT2 activity and detox ability

Intro and Health Effects

Most people with the ‘AA’ genotype at rs1495741 are **slow acetylators**. They might have higher odds of bladder cancer, especially when exposed to cigarette smoke and chemical dyes [R, R, R, R, R, R].

Slow acetylators may also have a harder time detoxing **histamine**, especially if DAO and HNMT are affected as well.

Lab markers to check

16-OH-E1 (DUTCH)

5-Hydroxyindoleacetic Acid (HIAA), Random Urine

ALT

AST

Basophils (%)

Personalized to Your Genes

↑ FCER1A — Higher levels may indicate FcεRI receptor hypersensitivity and histamine release.

Basophils (Absolute)

Personalized to Your Genes

↑ FCER1A — Higher levels may indicate FcεRI receptor hypersensitivity and histamine release.

Betaine (TMG), Serum

Personalized to Your Genes

↓ MTHFR People with your variant (rs1801133-A) may have increased betaine needs.

- C-Reactive Protein (CRP)
- Eosinophils (%)
- Eosinophils (Absolute)
- Estradiol
- Folate

Personalized to Your Genes

↓ MTHFR Your variant (rs1801133-A) is linked to lower folate levels.

- Glutathione Peroxidase (GPx)
- Histamine, Plasma
- Homocysteine

Personalized to Your Genes

↓ MTHFR

Due to impaired MTHFR activity, your variant (rs1801133-A) has a strong link with elevated homocysteine levels.

- hs-CRP
- IgE

Personalized to Your Genes

↑ FCER1A

IgE is central to FcεRI activation; higher IgE increases receptor cross-linking.

- IL-4
- SAM-e, Serum
- Selenium
- Serotonin, Serum
- TNF-alpha

Total Glutathione

Vitamin B2 (Riboflavin), Plasma

Personalized to Your Genes

↓ MTHFR This vitamin helps MTHFR work properly

Glossary

Acetylhistamine
A minor breakdown product of histamine cleared through the NAT2 enzyme.

Detox
The body’s natural process of clearing out harmful substances through the liver, kidneys, and other systems.

Estrogen
A hormone that, among other roles, can increase histamine and reduce the body's ability to break it down.

Excessive Mast Cells
Too many or overactive mast cells can release large amounts of histamine, leading to symptoms.

Gut Microbiome
The community of bacteria in your digestive tract that supports digestion, immune balance, and histamine regulation.

Histamine
A chemical involved in immune reactions, digestion, sleep, and brain function—too much can cause symptoms like rashes, headaches, or stomach issues.

Histidine
An amino acid found in protein-rich foods that your body can convert into histamine.

IgE
An antibody that reacts to allergens and signals mast cells to release histamine.

Imidazole Acetaldehyde
A byproduct created when histamine is broken down—can be toxic if it builds up.

Imidazole Acetic Acid
A final, less harmful breakdown product of histamine.

Inflammation
The body’s response to injury or infection, which can increase histamine production.

Mast Cells
Immune cells that store and release histamine in response to allergens, infections, and stress.

Methylation
A process that supports many body functions, including the breakdown of histamine in the brain.

N-Methylhistamine
A histamine breakdown product mostly found in the brain.

N-Methylimidazole Acetaldehyde
A further breakdown product formed after N-Methylhistamine is processed.

Oxidative Stress
An imbalance between harmful free radicals and the body’s ability to neutralize them, which can disrupt histamine breakdown.

Tyramine
A natural compound in aged or fermented foods that can trigger histamine release.

Vasodilatation
The widening of blood vessels—a common effect of histamine that can cause flushing or low blood pressure.