#### WHAT THE REPORT INCLUDES

- Detailed EXPLANATION of the test performed and recommendations to be followed;
- SUMMARY TABLE showing the metabolic areas investigated and the results obtained from the DNA analysis, in order to have a quick overview of one's general situation and to check for compromised situations;
- BIBLIOGRAPHY providing scientific references for the test.

# COLOURS USED

Green indicates that the variants identified in the analysis do not unfavourably alter enzymatic activity of the proteins they encode and/or the risk associated with certain diseases.

Orange indicates that the variants identified in the analysis slightly unfavourably alter enzyme activity and/or the risk associated with certain disorders or diseases.

Red indicates that the variants identified in the analysis alter enzyme activity in a particularly unfavourable way, resulting in an increased risk of developing certain disorders or associated diseases.

The results shown, as well as the considerations and explanations contained in the following pages of this booklet, should not be regarded as a medical diagnosis. It is important to bear in mind that the genetic information is only a part of the total information required to gain a complete picture of a person's state of health, and the data reported here is therefore a tool available to the treating physician to formulate a correct assessment of the patient's physiological state and suggest an appropriate personalised treatment.

#### Introduction

Alcohol, or ethanol, is a psychoactive substance found mainly in alcoholic beverages such as wine, beer and spirits. It is rapidly absorbed into the bloodstream through stomach and small intestine, reaching peak concentration approximately 30 to 90 minutes after intake. The metabolism of alcohol takes place mainly in the liver, where two key enzymesalcohol dehydrogenase (ADH) aldehyde dehydrogenase (ALDH), transform it into acetaldehyde (a toxic substance) and then into acetic acid, which is then disposed of as water and carbon dioxide. The ability to metabolise alcohol varies from person to person, influenced by genetic factors, gender, age and drinking habits. **Alcohol Use and effects:** 

People drink for various reasons, depending on the context, mood and habits. The most common reasons beyond the pleasure of taste, are to be able to relax and connect in social contexts, escape negative feelings, feel more extroverted.

The main effects of alcohol, which vary, depending on one's metabolism are the following:

• <u>Facial flushing (alcohol flush)</u> - Common in people with genetic variants that cause a faster accumulation of acetaldehyde.

- <u>Nausea and vomiting</u> Sign that the body is struggling to process alcohol.
- <u>Headache</u> This can also be caused by the accumulation of acetaldehyde or dehydration.
- <u>Rapid heartbeat (tachycardia)</u> Acetaldehyde can stimulate the nervous system, causing palpitations.

• <u>Dizziness and weakness</u> - Due to the toxic effect of alcohol on the central nervous system.

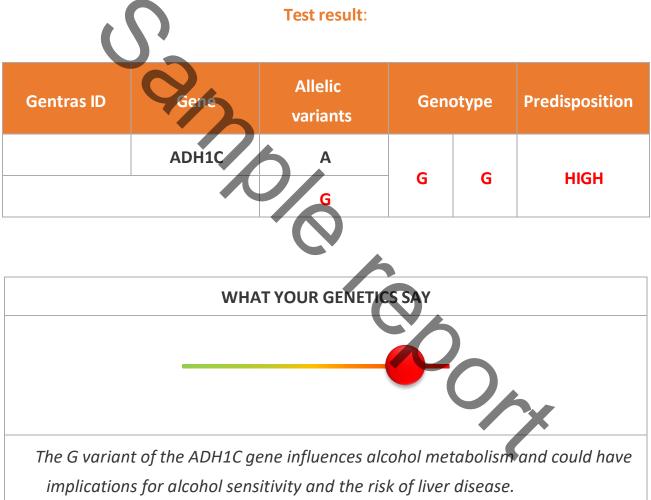
 <u>Sweating and feeling hot</u> – The buildup of acetaldehyde can dilate blood vessels, causing hot flashes.

#### ALCOHOL METABOLISM EFFICIENCY:

Genetic analysis involves interrogating the following gene:

#### a. ADH1C gene

The ADH1C gene encodes for one of the subunits of the enzyme alcohol dehydrogenase 1C (ADH1C), which plays a key role in alcohol metabolism. This enzyme is involved in the first step of ethanol degradation in the liver, turning it into acetaldehyde, a toxic substance that must be rapidly disposed of to avoid harmful effects.



## Role of the ADH1C gene in alcohol

The enzyme ADH1C oxidises ethanol into acetaldehyde, which is then metabolised into acetic acid by the enzyme ALDH2.

The speed of this conversion can affect alcohol tolerance and the risk of side effects. The ADH1C gene has variants that influence the activity of the enzyme:

- ADH1C\*1 (variant A) → Produces a more active enzyme, metabolizing alcohol more quickly into acetaldehyde.
- ADH1C\*2 (variant G) → Produces a less efficient enzyme, slowing down the conversion of ethanol.

What do the variants mean?

- Those with the AA variant (ADH1C\*1/\*1) tend to metabolize alcohol more quickly, which leads to obtaining positive effects, at low doses, such as euphoria, relaxation, disinhibition, and increased sociability but the negative effects will also be obtained more quickly: facial flushing, headache, nausea, tachycardia, sweating.
- Those with the GG variant (ADH1C\*2/\*2) metabolize alcohol more slowly, which can increase the risk of addiction and liver damage with prolonged consumption.
- Individuals with the AG variant have an intermediate metabolism.

Health implications:

In short, people with a more active ADH1C variant may be less likely to develop alcohol dependence, as the negative effects come on more quickly and they tend to manage accordingly. Those with a less active variant may tolerate alcohol better but may be more exposed to long-term risks such as liver and cardiovascular disease. Individuals with the AG variant have an intermediate metabolism.

#### **Recommendations:**

Countermeasures for the unfavourable variant in the ADH1C gene are:

### 1. Moderation of Alcohol Consumption

- People with the GG variant metabolize alcohol more slowly. Moderation in alcohol consumption is essential to avoid negative effects and prevent long-term damage.
- It is recommended not to exceed the health guidelines on alcohol consumption, which generally indicate no more than one drink per day women and two for men.

## 2. Avoiding Alcohol Abuse

- Since the GG variant leads to a slow metabolization of alcohol, there is a risk that people with this genotype may drink more frequently to achieve the same feelings of euphoria, relaxation, and disinhibition, compared to fast metabolizers, risking developing alcohol dependence.
- It is important to educate yourself about the risks of excessive consumption and try to limit the amount of alcohol to avoid problematic drinking behaviors.

## 3. Control and Monitoring of Liver Function

- Slow metabolism of alcohol may increase the risk of liver damage in the long term, even if the immediate effects are moderate. It is essential to monitor liver function by regular liver tests to detect early signs of hepatic steatosis (fatty liver), cirrhosis or other alcohol-related damage.
- Alcohol intake should be reduced if there is a family history of liver disease or other risk conditions.

# 4. Avoiding Additional Risk Factors

- If the GG variant is present, it is advisable to avoid combining alcohol with other health risk factors, such as smoking and taking hepatotoxic drugs, which can worsen liver damage and increase the risk of cardiovascular disease and other disorders.
- Moderate alcohol consumption is especially important for those exposed to genetic or environmental risk factors.

### 5. Supplementation with Protective Nutrients

• Antioxidants and liver nutrients can support liver health and reduce alcoholrelated damage. Some useful supplements include:

- N-acetylcysteine (NAC), which helps reduce oxidative stress and may support the liver.

- Milk thistle (Silybum marianum), which has been used historically as a liver protector and may aid in liver regeneration.

- Vitamin C and Vitamin E which have an antioxidant action, protecting the liver from damage.

### 6. Education to Alcohol Sensitivity

- People with the GG variant should be educated about their genetic risks for alcohol consumption. Awareness of one's genetic predisposition allows for a healthier and more controlled approach to alcohol.
- Education about the body's response to alcohol can help reduce the likelihood of irresponsibly drinking, improving long-term health.

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## 7. Consideration of Psychological Interventions or Addiction Support

• If the GG variant leads to a slow response to alcohol and increased consumption, psychological support, such as counseling or alcohol treatment programs, may be helpful to avoid the development of abuse or dependence.

### Sources of Alcohol

The main sources of alcohol are alcoholic beverages, but ethanol can also be found in other products. Here is a list by category:

### 1. Alcoholic drinks

- Distillates: whisky, vodka, gin, rum, tequila, brandy, grappa
- Wines: Red, white, rosé, sparkling wine, champagne
- Beers and related: beer, craft beer, cider, mead
- Liqueurs and bitters: Limoncello, amaro, sambuca, vermouth, alcoholic aperitifs (Campari, Aperol)

### 2. Food containing alcoho

- Alcoholic desserts (tiramisu with liqueur, baba with rum, panettone with liqueur)
- Sauces and condiments (wine sauce, beer in cooking)
- Chocolates filled with liqueur
- Food extracts (vanilla extract with alcohol)

### 3. Non-food products containing alcohol

- Cough syrups and medicines with ethanol
- Mouthwashes and oral disinfectants
- Cosmetic products (perfumes, deodorants)
- Hand sanitising gels
- Industrial solvents and fuels