

**DNA LIFESTYLE OPTIMIZER TEST FOR CFS
REPORT**

Dear John,

Thank you for choosing to take the MAGISNAT DNA Lifestyle Optimizer Test for CFS.

Below, you will find the report that we have prepared for you. We trust that the insights on your genetic makeup provided in there will be a powerful tool to better live with CFS and improve your overall well-being, making the most out of your individuality.

We encourage you to take the time to review this report thoroughly and discuss the findings with your healthcare provider.

Thank you for entrusting us with your genetic information, and we hope that this report will be valuable in guiding your journey towards a healthier and happier life.

Sincerely,

Personal Information

SUBJECT INFORMATION	
First name	Last name
Date of Birth	Place of birth
ZIP Code	City
Mailing address	State
Telephone	E-mail

Summary

1. Scientific Glossary
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 - b. Inflammation, Detoxification, and Immune Response
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SCIENTIFIC GLOSSARY

When discussing genetics, it's often necessary to use many technical terms, and there's no way to avoid it if we want to maintain accuracy in explanations. That's why we have compiled a scientific glossary - to enable everyone to understand without getting overwhelmed.

Anyway, it is important to emphasize that our scientific glossary does not aim to be exhaustive and is not intended to replace the advice provided by your healthcare provider. Professional medical support is essential for a proper interpretation of genetic data and for developing a personalized health and wellness plan.

- **Allele:** An allele is one of the different forms of a specific gene. The differences among alleles arise from small changes in the DNA sequence and can lead to changes in the characteristic controlled by the gene itself.
- **Chromosome:** The chromosome is the structure in which the DNA is organized in the nucleus of the cells. Humans have 23 pairs of chromosomes, with one copy coming from the mother and one copy from the father.
- **Dietary supplement:** A dietary supplement is a product that contains one or more dietary ingredients, such as vitamins, minerals, herbs, amino acids, enzymes, or other substances, intended to supplement the diet. These supplements are available in various forms, including pills, capsules, tablets, powders, or liquids.
- **DNA:** DNA stands for Deoxyribonucleic Acid. It is the macromolecule containing the information to build the organism. It is made up of 4 different nucleotides (Adenine, Cytosine, Guanine and Thymine). The human DNA have 3 billion nucleotide base pairs.
- **Gene:** A gene is a segment of a chromosome that occupies a given locus on it and codes for a protein, each one with a specific function: some build the structure of our cells, some respond to signaling molecules, some catalyze reactions (these are called enzymes), and so on.
- **Genomics:** Genomics is a field of biology that focuses on the study of an organism's entire genome, which is the complete set of its genetic material. It involves the comprehensive analysis of genes, their functions, interactions, and variations within and between populations.
- **Genotype:** The genotype is the genetic makeup of an organism, then the combination of alleles present in an individual's DNA at a particular locus on a chromosome. The genotype represents the specific genetic information that an organism inherits from its parents.
- **Heterozygosity:** Heterozygosity refers to having two different alleles at a specific genetic locus. If an individual has one copy of the "A" allele and one copy of the "B" allele for a certain gene (AB genotype), they are said to be heterozygous for that gene.

- **Homozygosity:** Homozygosity refers to having two identical alleles at a specific genetic locus. If an individual has two copies of the "A" allele for a certain gene (AA genotype), they are said to be homozygous for that gene.
- **Macronutrient:** Macronutrients are essential nutrients that are required by the body in large quantities to maintain proper functioning, growth, and overall health. These nutrients provide the necessary energy and building blocks needed for various physiological processes. The three primary macronutrients are: carbohydrates, lipids (fat), and proteins.
- **Micronutrient:** Micronutrients are essential nutrients required by the body in smaller quantities but are equally important for maintaining overall health and supporting various physiological functions. Micronutrients include two main groups: vitamins and minerals.
- **Mutation:** A mutation is a change or alteration in the DNA sequence of a gene. The main mutation types include base substitutions, deletions, or insertions.
- **Nutritional deficiency:** Nutritional deficiency, also known as malnutrition, refers to a condition in which the body does not receive enough macronutrients or micronutrients, which are needed to support proper growth, development, and overall health.
- **Phenotype:** The phenotype is any observable trait arising from a complex interplay between a given genotype and environmental factors. Examples of phenotypes are height, eye color and blood type.
- **rsID number:** rsID numbers are identifiers used by researchers to name different SNPs.
- **SNPs (Single Nucleotide Polymorphism):** A SNP, or single nucleotide polymorphism, is a mutation in one of the nucleotide bases composing DNA and found in more than 1% of the population.

How to read this report

In this report, you will find insights about the characteristic under analysis, followed by a table listing the genes and polymorphisms considered for that characteristic. After this introductory session, you will find your results in tabular form. Here, the color code uses the same rationale as above: in **green** we report polymorphism with a beneficial outcome (*e.g.*, increased enzyme function), in **orange** when the outcome is a slight increase in the risk (*e.g.*, reduced enzyme function), in **red** when the outcome is a higher increase in the risk (*e.g.*, enzyme loss of function). Finally, you will find the section recommendations, in which the outcome of the polymorphism is treated in more details. In any case, remember that this information is intended to be discussed with your healthcare provider.

Please note: in this sample report genomic coordinates are not reported. These will be available in the actual report.

Infection and Pain

Individuals with CFS often report the onset of the condition following an acute infection, mostly viral infections, such as the flu or the Epstein-Barr virus (EBV). This has led to speculation about the association between infections and the triggering or exacerbation of CFS.

However, the relationship between infections and CFS is complex. Not everyone who contracts an infection develops CFS, and many people with CFS do not report a prior infection. It is believed that in some cases, infections may trigger an abnormal immune response or alter the nervous system, contributing to the symptoms of CFS.

Moreover, a higher sensibility to pain, which may have also genetic bases, may exacerbate the symptoms of CFS.

Analyzed Genes and Polymorphisms:

Gene	Gene Function	SNP
SCN9A	Sodium Voltage-Gated Channel Alpha Subunit 9. Channel protein responsible of the creation and propagation of the action potential in neurons and muscle cells.	Locus1
CLTRN	Clathrin. Protein crucial for the immune system response to pathogens, by recognizing carbohydrate in the membrane of microbes.	Locus1
RAVER1	Ribonucleoprotein. Protein involved in RNA processing and splicing, which are processes crucial for protein synthesis.	Locus1
TLR7	Toll-Like Receptor 7. Receptor involved in the recognition of microbial pathogens, thus playing a crucial role in the immune system.	Locus1
TMPRSS2	Transmembrane Serine Protease 2. Enzyme playing a role in various cellular functions, primarily by proteolytic cleavage of other proteins. It has gained great attention due to its role as host cell factor for viral infections (including covid-19).	Locus1
		Locus2
		Locus3
		Locus4

Your Results:

SNP	Alleles	Outcome
Locus1	G/G	Typical.

Locus1	G/G	Sensibility to infections. ¹
Locus1	T/A	Sensibility to some infections. ²
Locus1	A/A	Typical.
Locus1	G/G	Typical.
Locus2	G/A	Typical.
Locus3	A/A	Typical.
Locus4	G/A	Typical.

Recommendations:

The CLTRN gene encodes the enzyme Chlatriin, which recognizes microbes by binding to specific carbohydrates found in their membranes. Thus, it plays a crucial role for the functioning of the immune system. The presence of the Locus1 polymorphism in two copies (homozygosity) has been associated with a reduced efficiency in the activity of this protein. This means that individuals with this genetic variant may show sensibility to infections.

The RAVR1 gene encodes the enzyme ribonucleoprotein, which is involved in RNA processing and splicing. These processes are part of the protein synthesis and allow to have more than one protein out of one gene. The presence of the Locus1 polymorphism in one copy (heterozygosity) has been associated with a reduced activity of this enzyme and sensibility to some infections.

Based on these results, your healthcare provider may recommend you embrace a healthy lifestyle that supports your immune system to avoid or reduce the impact of infections, which are known to trigger or exacerbate CFS. This includes also dietary supplements, such as olive polyphenols, vitamins (C, D, B1, B6, B9, B12), and/or minerals (Zinc).

¹ Hossain Md S et al., Prediction of the Effects of Variants and Differential Expression of Key Host Genes *ACE2*, *TMPRSS2*, and *FURIN* in SARS-CoV-2 Pathogenesis: An *in Silico* Approach. *Bioinformatics* (2021).

² Fink-Baldauf I M et al., CRISPRi links COVID-19 GWAS loci to LZTFL1 and RAVR1. *EBioMedicine* (2022).

Inflammation, Detoxification, and Immune Response

Alterations in the processes of inflammation, detoxification, and immune system response (closely linked to viral infections, another trigger of CFS) are of great relevance in this syndrome. In fact, immune dysregulation and inflammatory markers are often found in patients with CFS, and the symptoms of the syndrome partially overlap with those observed in individuals with immune activation and inflammation.

It's important to emphasize that the relationship between the immune system, inflammation, and CFS is not fully understood, and not all individuals with CFS exhibit the same immune-related abnormalities. CFS is a heterogeneous condition, and its underlying mechanisms may vary among patients.

Analyzed Genes and Polymorphisms:

Gene	Gene Function	SNP
CYP2D6	Cytochrome P450 2D6. Enzyme involved in many detoxification processes and the metabolism of many drugs.	Locus1
IRF5	Interferon Regulatory Factor 5. Transcription factor regulating the expression of genes involved in inflammation and immune system.	Locus1
IRF5	Interferon Regulatory Factor 5. Transcription factor regulating the expression of genes involved in inflammation and immune system.	Locus1
TERT	Telomerase Reverse Transcriptase. Protein crucial for telomeres (found at the ends of the chromosome and protecting the DNA) maintenance.	Locus1
PON1	Paraoxonase 1. Enzyme with a crucial role in the breakdown of some molecules, detoxification and antioxidant activity. It is primarily associated to High-Density Lipoproteins (HDL), which is often referred as good cholesterol.	Locus1
		Locus2
		Locus3
LTA	Lymphotoxin Alpha. Signaling protein also known as Tumor Necrosis Factor-beta. It is crucial for immune and inflammatory processes.	Locus1
TNFRSF1B	Tumor Necrosis Factor Receptor Superfamily Member 1B. Receptor binding to the Tumor Necrosis Factor (TNF), thus playing a crucial role in immune and inflammatory responses.	Locus1
IL17A	Interleukin 17A. Signaling protein crucial for immune responses, inflammation, and autoimmune conditions.	Locus1

IL6	Interleukin 6. Signaling protein involved in immune response, inflammation, and various physiological process.	Locus1
C5orf52	Chromosome 5 Open Reading Frame 52. Protein with function still not completely understood, but probably involved in neurodevelopment.	Locus1
ARMH4	Armadillo-like helical domain-containing protein 4. Protein with function still not completely understood, but associated with inflammation and immune response, particularly in the nervous system.	Locus1

Your Results:

SNP	Alleles	Outcome
Locus1	A/A	Typical.
Locus1	G/G	Typical.
Locus1	C/C	Typical.
Locus1	G/G	Typical.
Locus1	G/G	Typical.
Locus2	G/G	Better response to antioxidant and polyphenols in diet. ³
Locus3	C/C	Typical.
Locus1	C/C	Typical.
Locus1	A/A	Typical.
Locus1	G/G	Typical.
Locus1	G/G	Typical.
Locus1	G/G	Typical.
Locus1	G/G	Typical.

Recommendations:

The PON1 gene encodes the enzyme Paraoxonase 1, which is an enzyme produced by the liver and found in the bloodstream, where it is associated with high-density lipoproteins (HDL), often referred to as “good cholesterol”. It has a crucial role in detoxification and has antioxidant and anti-inflammatory properties. The presence of the Locus2 polymorphism in two copies (homozygosity) has been associated with a better response to antioxidant and polyphenols in diet, with a benefic effect on cardiovascular system and overall inflammation.

³ Rizzi F et al., Interaction between polyphenols intake and PON1 gene variants on markers of cardiovascular disease: a nutrigenetic observational study. Journal of translational medicine (2016).

Based on these results, your healthcare provider may recommend you ensure the right amount of antioxidant (resveratrol, vitamin C and E, beta-carotene, selenium, curcumin) and polyphenols in your diet (also through dietary supplementation) to have the greatest possible benefits.

Cardiovascular Function and Energy Metabolism

Cardiovascular function and energy metabolism are essential for overall well-being, and disruptions in these processes can contribute to fatigue. In CFS, there is evidence of abnormalities in cellular energy production, such as impaired mitochondrial function. Also, it is often observed an imbalance in cardiovascular function, probably due to autonomic nervous system dysfunctions.

Inflammation and oxidative stress are processes often associated with cardiovascular dysfunction and can impact energy metabolism. Some studies have found elevated markers of inflammation and oxidative stress in individuals with CFS, which may contribute to cardiovascular and metabolic abnormalities.

Moreover, prolonged inactivity and deconditioning due to CFS can also affect cardiovascular function and energy metabolism. A sedentary lifestyle can lead to reduced cardiovascular fitness and exacerbate symptoms of fatigue.

Analyzed Genes and Polymorphisms:

Gene	Gene Function	SNP
ACE2	Angiotensin-Converting Enzyme 2. Protein involved in the regulation of blood pressure, fluid balance, and electrolyte homeostasis in the body.	Locus1
BDKRB2	Bradykinin B2 Receptor. Receptor involved in inflammation, pain perception, and blood vessel dilation.	Locus1
TH	Tyrosine Hydroxylase. Enzyme involved in the synthesis of neurotransmitters (dopamine, norepinephrine, and epinephrine).	Locus1
PPARGC1B	Peroxisome Proliferator-Activated Receptor Gamma Coactivator 1 Beta. Protein involved in the regulation of cellular metabolism, energy homeostasis, and mitochondrial function.	Locus1
NOS3	Nitric Oxide Synthase 3. Enzyme involved in the production of nitric oxide, a signaling molecule crucial for the regulation of blood vessel dilation, blood pressure, and vascular health.	Locus1

Your Results:

SNP	Alleles	Outcome
Locus1	C/C	Typical.
Locus1	C/C	Typical.
Locus1	A/A	Typical.

Locus1	C/C	Lower protein activity, deficit in energy metabolism. ⁴
Locus1	T/T	Typical.

Recommendations:

The PPARGC1B gene encodes the enzyme Peroxisome Proliferator-Activated Receptor Gamma Coactivator 1 Beta 1, which is a coactivator involved in the regulation of energy metabolism mitochondrial biogenesis, the process by which new mitochondria (the organelles producing energy within cells) are generated. The presence of the Locus1 polymorphism in two copies (homozygosity) has been associated with a lower protein activity and a deficit in energy metabolism, probably linked to a lower number of mitochondria in cells.

Based on these results, your healthcare provider may recommend you ensure an as much as possible active lifestyle (which stimulates mitochondrial biogenesis) and that you control your diet and dietary supplementation to support mitochondrial function, such as B-vitamins, creatine, carnitine, and magnesium.

⁴ Maciejewska-Skrendo A et al., Genetic Markers Associated with Power Athlete Status. Journal of human kinetics (2019).

Conclusions

Main results:

Gene	SNP	Alleles	Outcome
CLTRN	Locus1	G/G	Sensibility to infections.
RAVER1	Locus1	T/A	Sensibility to some infections.
PON1	Locus2	G/G	Better response to antioxidant and polyphenols in diet.
PPARGC1B	Locus1	C/C	Lower protein activity, deficit in energy metabolism.

Your genetic makeup has been correlated to:

- Sensibility to infections, which are of crucial importance in CFS since they are thought to trigger it or exacerbate its symptoms. Based on these results, your healthcare provider may recommend you embrace a healthy lifestyle that supports your immune system to avoid or reduce the impact of infections, which are known to trigger or exacerbate CFS. This includes also dietary supplements, such as olive polyphenols, vitamins (C, D, B1, B6, B9, B12), and/or minerals (zinc).
- A better response to antioxidant and polyphenols in diet, which are important allies for a healthy cardiovascular function and overall well-being. Based on these results, your healthcare provider may recommend you ensure the right amount of antioxidant (resveratrol, vitamin C and E, beta-carotene, selenium, curcumin) and polyphenols in your diet (also through dietary supplementation) to have the greatest possible benefits.
- A deficit in energy metabolism linked to mitochondrial biogenesis and activity. Based on these results, your healthcare provider may recommend you ensure an as much as possible active lifestyle (which stimulates mitochondrial biogenesis) and that you control your diet and dietary supplementation to support mitochondrial function, such as B-vitamins, creatine, carnitine, and magnesium.

With this, our journey of discovering your genetic makeup comes to an end. It's essential to note that the genetic test does not need to be repeated since it remains constant over time. However, your healthcare provider may suggest other tests that can complement the information obtained from the *DNA Wellness Test* and the *DNA Lifestyle Optimizer Test for CFS* and can be repeated periodically to monitor your health and well-being. Some examples are our metabolomics and proteomics tests. For more details, please refer to our website (www.magisnat.com).

DISCLAIMERS

The final results obtained by the Low-Risk General Wellness Tests have not been evaluated by the Food and Drug Administration, and they are not intended to diagnose, treat, cure, or prevent any disease.

All information regarding the DNA Wellness Test and the DNA Lifestyle Optimizer Tests is provided in good faith. While we have made every attempt to ensure that the information contained in these tests is accurate to the best of our knowledge, we are not responsible for any errors or omissions or for the results obtained from the use of this information.

Before taking any action based on the information provided by the DNA Wellness Test or the DNA Lifestyle Optimizer Tests, we urge you to consult with appropriate professionals as it is not a substitute for professional medical advice. In any case, we are not liable if you receive inadequate or even dangerous advice or recommendations for your health from third parties.

Genetic test results can have psychological implications, so it's important to be prepared for potential emotional distress or anxiety related to learning about health risks.

The use, any losses and/or damages incurred because of the use of the DNA Lifestyle Optimizer Tests, and the reliance of any information contained in these DNA Lifestyle Optimizer Test are solely the responsibility of the user.

Any testimonials regarding the DNA Wellness Test or the DNA Lifestyle Optimizer Tests are personal and are not representative of all users. We do not claim, and you should not assume that all users have the same experiences.

We make every effort to ensure the highest standards, the analysis for the DNA Wellness Test and the DNA Lifestyle Optimizer Tests is performed in a CLIA (Clinical Laboratory Improvement Amendments)-certified laboratory and have validated the process to the best of our abilities. The sensitivity and specificity of the DNA Wellness Test and the DNA Lifestyle Optimizer Tests are computed and may be consulted at this [link](#). As a result, different tests may yield partially different results, also due to technical details. We do not assume any responsibility if such events were to occur.

Polymorphisms, due to a phenomenon known as pleiotropy, can be associated with multiple characteristics. For the purposes of the DNA Wellness Test and the DNA Lifestyle Optimizer Tests, the considered polymorphisms are analyzed from the perspective of general well-being, even in the context of diseases or clinical conditions. Similarly, the interpreted significance of these analyzed polymorphisms may vary in other contexts, potentially leading to unsought results and/or genetic discrimination. This could affect aspects like determining family relationships, potential health conditions, ethnic associations, and more. We are not responsible for any improper use of the information provided by the DNA Wellness Test and the DNA Lifestyle Optimizer Tests.

The data collection and processing system is secure, and the DNA sample is discarded 180 days after the analysis. We are not liable for any data breaches resulting from cyber-attacks or rare events beyond the control of our standard security measures. If consent has been provided, the collected data, both genetic and non-genetic, may be used solely for the purpose of improving our tests and conducting scientific research approved by the ethics committee. The information may be shared, in an anonymous and aggregated form, exclusively through publications in scientific journals or books, communications in medical courses/congresses, and theses as part of university and post-graduate training courses.

We make no warranty of any kind, expressed or implied, as to the accuracy, adequacy, validity, reliability, or completeness of the information regarding the DNA Wellness Test and the DNA Lifestyle Optimizer Test.

If you have any questions, concerns, or need support in understanding the test, please call our support team on +1 470-482-1800 or email info@magisnat.com or visit our website www.magisnat.com.