DNA LIFESTYLE OPTIMIZER TEST FOR LYMPHEDEMA REPORT

Dear John,

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

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 lymphedema 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

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 introductive session, you will find your results in tabular form. Here, the color code uses the same rational 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.

Lymphatic System Function

The lymphatic system plays a pivotal role in maintaining our overall health. It comprises a complex network of lymphatic vessels, lymph nodes, and various lymphoid organs. It primarily serves three critical functions: fluid balance, immune response, and detoxification.

The first function is realized by collecting the fluids that are continuously leaking while the blood circulates in the body. This important function avoids tissue swelling, maintaining the correct balance for cells nourishment.

For the second function, a crucial role is played by lymph nodes, which act as hubs for leukocytes (white blood cells), the cells defending our organism from pathogens.

Finally, the last function is realized by gathering waste products, toxins, and cellular debris and safely remove them from the body.

Analyzed Genes and Polymorphisms:

Gene	Gene Function	SNP
FOXC2	**Forkhead Box C2.** Transcription factor regulating the expression of genes involved in various processes, including lymphatic vessels development and function.	Locus1
VEGFC	**Vascular Endothelial Growth Factor C.** Signaling protein with a crucial role in angiogenesis, the process of formation of new blood vessels. VEGFC is specifically involved in lymphangiogenesis, which is the formation of new lymphatic vessels.	Locus1
FLT4	**Fms-Related Tyrosine Kinase 4.** Receptor protein playing a crucial role in regulating the development and formation (lymphangiogenesis) of lymphatic vessels.	Locus1
		Locus2

Your Results:

SNP	Alleles	Outcome
Locus1	G/G	Typical.
Locus1	C/T	Imbalance in the lymphangiogenesis process.[1]
Locus1	T/T	Typical.
Locus2	T/T	Typical.

Recommendations:

[1] Miaskowski C et al., Lymphatic and angiogenic candidate genes predict the development of secondary lymphedema following breast cancer surgery. PloS one (2013).

The VEGFC gene encodes the protein Vascular Endothelial Growth Factor C, a signaling protein which is part of a family of protein regulating the angiogenesis, the process of formation of new blood vessels. VEGFC, in particular, regulates lymphangiogenesis, the formation of new lymphatic vessels. The presence of the Locus1 polymorphism in one copy (heterozygosity) has been associated with an imbalance in this process. These may potentially lead to an exacerbation of the symptoms of lymphedema.

Based on these results, your healthcare provider may recommend you have a physically active lifestyle, use compression garments to help improve circulation in the areas affected and use specific dietary supplements for lymphatic and vein system function, such as bioflavonoids, olive polyphenols, and vitamin A.

Cardiovascular Function and Angiogenesis

The cardiovascular system consists of the heart, blood vessels, and blood. It plays a crucial role for the organism's survival, not only ensuring cells oxygenation, but carrying nutrients to cells and collecting waste products from them. Given that, a functioning cardiovascular system is crucial for your health.

The process called angiogenesis is the growth of new blood vessels from existing ones. It occurs in response to stimuli such as tissue repair, wound healing, and exercise. Angiogenesis ensures that tissues receive adequate blood supply and oxygen, promoting their health and function.

In the context of lymphedema, cardiovascular function and angiogenesis play a significant role, since adequate blood supply to the affected areas is crucial for tissue health and repair. Angiogenesis can facilitate the development of collateral circulation, providing alternative pathways for fluid and nutrient exchange, potentially alleviating some symptoms of lymphedema.

Analyzed Genes and Polymorphisms:

Gene	Gene Function	SNP
MMP2	**Matrix Metallopeptidase 2.** Enzyme involved in the degradation and remodeling of the extracellular matrix, which provides support to the tissues.	Locus1
VEGFA	**Vascular Endothelial Growth Factor A.** Signaling protein with a crucial role in angiogenesis, the process of formation of new blood vessels.	Locus1
NRP2	**Neuropilin 2.** Receptor involved in various processes, particularly during development and in the context of nervous and cardiovascular systems.	Locus1
VCAM1	**Vascular Cell Adhesion Molecule 1.** Protein found in the surface of endothelial cells (part of blood vessels), involved in cell adhesion and inflammation.	Locus1
ANGPT2	**Angiopoietin 2.** Signaling protein involved in angiogenesis (formation of new blood vessels) and vascular remodeling.	Locus1

Your Results:

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

Locus1	T/T	Better cardiovascular function and decrease in inflammation.[2]
Locus1	C/C	Typical.

Recommendations:

The VCAM1 gene encodes the protein Vascular Cell Adhesion Molecule 1, a protein localized on the surface of endothelial cells, which is the interior surface of blood vessels, and it is constituted by a single layer of cells. This protein is involved in cell adhesion (process by which neighboring cells interact each other) and inflammation. The presence of the Locus1 polymorphism in two copies (homozygosity) has been associated with a better cardiovascular function and a decrease in inflammation.

These results suggest that you may have a good predisposition towards a good cardiovascular function and low inflammation. These aspects may be beneficial for your general health and in relation to lymphedema. Anyway, remember that other genetic, environmental, and lifestyle factors may negatively impact them.

[2] Miaskowski C et al., Lymphatic and angiogenic candidate genes predict the development of secondary lymphedema following breast cancer surgery. PloS one (2013).

Inflammation and Immune Response

Inflammation and the immune response are two critical defense mechanisms, tightly interwoven, and play a crucial role in protect against infections, injuries, and other threats to our health.

Inflammation is the body's natural response to harmful stimuli, and it is realized through the release of various chemicals and immune cells. Then, acute inflammation is crucial for healing and defense, but chronic inflammation can lead to various health problems.

The immune response is performed by the immune system, which comprises various types of white blood cells, antibodies, and other molecules that work together to identify and neutralize bacteria, viruses, and toxins.

In the context of lymphedema, inflammation and the immune response can have both positive and negative effects: on one hand, they can contribute to tissue damage and worsen symptoms, on the other hand they play a role in combating infections that may lead to or exacerbate lymphedema.

Analyzed Genes and Polymorphisms:

Gene	Gene Function	SNP
LTB4R	**Leukotriene B4 Receptor.** Receptor binding leukotriene B4, a lipid mediator involved in inflammation and immune response.	Locus1
LTA4H	**Leukotriene A4 Hydrolase.** Enzyme catalyzing the conversion of leukotriene A4 to leukotriene B4, a lipid mediator involved in inflammation and immune response.	Locus1
TNF	**Tumor Necrosis Factor-alpha.** Signaling protein (cytokine) involved in immune response, inflammation, and cell death (apoptosis).	Locus1
TLR2	**Toll-Like Receptor 2.** Receptor involved in the recognition of microbial pathogens, thus playing a crucial role in the immune system.	Locus1
TLR4	**Toll-Like Receptor 4.** Receptor involved in the recognition of microbial pathogens, thus playing a crucial role in the immune system.	Locus1
HGF	**Hepatocyte Growth Factor.** Signaling protein promoting cell growth, tissue repair, and regeneration in various body parts, particularly in the liver.	Locus1
EPHB4	**Eph Receptor B4.** Receptor protein playing a crucial role in a wide range of functions, such as cell-to-cell communication, the development of various tissues	Locus1

	(including lymphatic vessels), and the regulation of cell movement.	
IL1R1	**Interleukin 1 Receptor Type 1.** Receptor binding interleukin 1 cytokines. It is involved in the response of the immune system to inflammation, infection, and injury.	Locus1
IL4	**Interleukin 4.** Signaling protein involved in immune response, inflammation, and various physiological process.	Locus1
IL6	**Interleukin 6.** Signaling protein involved in immune response, inflammation, and various physiological process.	Locus1
IL10	**Interleukin 10.** Signaling protein involved in immune response, inflammation, and various physiological process.	Locus1
NFKB2	**Nuclear Factor Kappa B Subunit 2.** Transcription factor regulating the expression of genes involved in inflammation, immune response, cell survival.	Locus1
SYK	**Spleen Tyrosine Kinase.** Enzyme found in immune cells and involved in immune receptor signaling, cell activation, and inflammation.	Locus1

Your Results:

SNP	Alleles	Outcome
Locus1	A/A	Typical.
Locus1	A/A	Typical.
Locus1	G/G	Typical.
Locus1	C/C	Typical.
Locus1	C/C	Typical.
Locus1	A/A	Typical.
Locus1	T/T	Typical.
Locus1	A/A	Increase in inflammation.[3]
Locus1	C/C	Typical.
Locus1	G/G	Typical.
Locus1	A/A	Typical.
Locus1	C/C	Typical.
Locus1	T/T	Typical.

Recommendations:

[3] Leung G et al., Cytokine candidate genes predict the development of secondary lymphedema following breast cancer surgery. *Lymphatic research and biology* (2014).

The IL1R1 gene encodes the protein Interleukin 1 Receptor Type 1, a receptor protein which binds to interleukin 1 cytokines mediating their effects. These molecules are released in response to infections and injuries and have an inflammatory effect. The presence of the Locus1 polymorphism in two copies (homozygosity) has been associated with an increase in inflammation.

Based on these results, your healthcare provider may recommend you a healthy lifestyle, which can contribute to contrast inflammation. This includes, physical activity, a healthy diet and dietary supplementation, such as curcumin, resveratrol, and olive polyphenols.

Conclusions

Main results:

Gene	SNP	Alleles	Outcome
VEGFC	Locus1	C/T	Imbalance in the lymphangiogenesis process.
VCAM1	Locus1	T/T	Better cardiovascular function and decrease in inflammation.
IL1R1	Locus1	A/A	Increase in inflammation.

Your genetic makeup has been correlated to:

- An imbalance in the lymphangiogenesis process, which means that your organism produces less new lymphatic vessels than normal. This may negatively impact lymphedema. Based on these results, your healthcare provider may recommend you have a physically active lifestyle, use compression garments to help improve circulation in the areas affected and use specific dietary supplements for lymphatic and vein system function, such as bioflavonoids, olive polyphenols, and vitamin A.
- A better cardiovascular function and decrease in inflammation, which can have a good impact on general well-being and in lymphedema conditions. Anyway, remember that other genetic, environmental, and lifestyle factors may negatively impact them.
- An increase in inflammation, which may worsen lymphedema symptoms. Based on these results, your healthcare provider may recommend you a healthy lifestyle, which can contribute to contrast inflammation. This includes, physical activity, a healthy diet and dietary supplementation, such as curcumin, resveratrol, and olive polyphenols.

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 Lymphedema* and can be repeated periodically to monitor your health and well-being. Some examples are our metabolomic and proteomic 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.