ADVANCED Nutrigenomics
Nutrition for You

Genetis precision medicine

Advanced NGx

Your Nutrigenetic Report

Optimize your nutrition according to your genetic background

Clinical Laboratory Improvement Amendments

This test was performed in a CLIA and CAP accredited laboratory

CAP ACCREDITED
COLLEGE of AMERICAN PATHOLOGISTS

Introduction

Advanced Nutrigenomics and **Smart EpiGenetX** generated your personalized nutrigenetic report based on your genetic background. This report includes those packages you have selected. This report was compiled based on the currently available scientific knowledge in the field of nutrigenetics.

Advanced NGx brings to you a new approach in nutrigenetics, and it is the result of expertize in academic nutrigenetic research accumulated over two decades.

This report allows you to:

- Evaluate your personal nutrient requirements based on your genetic background;
- Talk to your nutritionist and customize your meal plans according to your requirements;
- Informs you about the structure of several other genes, with educational purposes.

The genetic analyses used in this report have been performed in a US laboratory that is CLIA and CAP accredited.

Advanced Nutrigenomics and **Smart EpiGenetX** are ready to answer any questions you may have.

You can contact us at:

Smart EpiGenetX
https://www.genetx.eu/

Email: simona.ivanov@genetx.eu
Tel: +40 722 516 200

Advanced Nutrigenomics
www.advancednutrigenomics.com

Email: contact@advancednutrigenomics.com

Thank you for using our product.

Mihai Niculescu, MD, PhD
Founder & CEO Advanced Nutrigenomics

Advanced Nutrigenomics LLC is a registered company in the State of North Carolina, U.S.A.
Smart EpiGenetX SRL is a registered company in Romania.

ADVANCED Nutrigenomics	Protected Information		Method
	Personal Details		
	NAME:		Next Generation Sequencing – NGS
	Barcode:		
Advanced NGx test Test version: 1.1 Report version: 1-4	**Date of birth:**		**Sample collected on:**
	Gender:		
	Ethnicity:		**Sample received on:**
Report approved by: Mihai Niculescu, MD, PhD			**Report generated on:** August 14, 2018

Packages ordered:	
Package 1. Nutrition in pregnancy and lactation	No
Package 2. Adult nutrition	Yes
Package 3. Metabolic imbalances	Yes
Package 4. Physical activity	Yes
Free bonus: Package 5. Other genetic variations	

This document reflects the legal provisions regarding the use of your personal data (including genetic data and data provided online to Advanced Nutrigenomics LLC) as set out in (EU) REGULATION 2016/679 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL from April 27th 2016.

You can access this document here:

- Regulation 2016/679: http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32016R0679

Advanced Nutrigenomics LLC and its partners agree that:

- You are the only owner of your genetic data that was generated by us using your biological sample provided to us;
- You have the right, at any time, to request that your personal information, as well as your genetic information, be deleted from any database owned by us or our partners;
- Advanced Nutrigenomics LLC and its partners have the obligation to respond to such a request as soon as technically possible, and letting you know about this procedure either by email or in written form;
- Advanced Nutrigenomics LLC and Smart EpiGenetX will never share any information included in this report with any third parties. This information includes your personal identifiable information as well as your genetic information;
- As long as your genetic information is still present in our databases, you have the right to recover such information (such as obtaining a new copy of this report), without additional costs, except for costs involved in the printing or mailing the report to you. However, this right will be forfeited from the moment you requested the deletion of your data from our databases.

Table of Contents

Objectives, context and limitations

This report contains a maximum of five packages. Depending on the combination of packages chosen by you, this report contains at least three packages. Regardless your selection, package 5 is offered to you as a free bonus.

The results provided in this report must be carefully interpreted by your medical health care provider or by a certified nutritionist/dietician. Only a doctor can interpret the results provided in Package 5.

Risks
The Advanced NGx test is performed in a CLIA and CAP certified laboratory, and using FDA approved sequencing technology and reagents. In rare instances, laboratory error can occur, which might lead to incorrect results. Examples include, but are not limited to, sample or DNA mislabeling or contamination, failure to obtain an interpretable report, and other operational laboratory errors. In such situation, you may be required to provide a new biological sample, and a new test will be performed at no additional cost to you.

Limitations
This report provides information about how specific genetic variations found in your DNA affect your nutritional needs, metabolism, weight, exercise, and energy use. However, you should not change your diet, physical activity, or any medical treatments you are currently using based on these results without consulting your personal health care provider or nutritionist.

As the science of nutrigenetics is continuously developing, and as many other personal health factors affect diet and health, you should use this report in conjunction with such other factors, and do not make decisions regarding your health based solely on this report.

Another limitation of this nutrigenetic report is that it used studies performed mostly on Caucasian population. Therefore, some results may or may not be relevant to individuals of different ethnicities.

The association between genetic variations and your nutritional needs is an active area of scientific research, and future scientific studies might change the way we understand the relationship between the reported genetic variations and your nutritional needs.

Based on these results and other medical knowledge that you might have, your nutritionist or health care provider might consider additional testing.

How to interpret this report

This personalized report is meant to provide you with the latest information on how the existence of genetic variations (changes in your DNA sequence) can influence the amount of nutrients you need in order to optimize your health, or to mitigate the consequences that certain metabolic dysfunctions have on your metabolism.

The entire report includes up to 5 packages, structured on the basis of nutritional particularities needed in certain physiological or metabolic conditions, or for a physically active lifestyle. The report also includes a series of genetic variations than are not related to nutrition (package 5). The results of this report are for you and you alone.

Depending on your choice, this report may include 3, 4 or 5 packages. To the extent that you have opted for 3 or 4 packages, remember that you can order the rest of the packages at any time without having to provide biological samples again.

The 5 packages are:

1) **Nutrition in pregnancy and lactation** includes the analysis of genetic variations present in women and that influence the amounts of nutrients necessary for a healthy development of the fetus during pregnancy, and of the newborn during breastfeeding. This package is especially aimed at women who want to become pregnant. The package is also useful for pregnant women (in the early pregnancy) or for those who are breastfeeding.

2) **Adult nutrition** includes the analysis of genetic variations that influence the optimal nutrient requirements for healthy adults (non-pregnant women and men). This package is intended to provide you with the information you need to optimize your nutrition and, therefore, reduce the risk of metabolic diseases that might occur due to unbalanced nutrition.

3) **Metabolic imbalances** provides the analysis of genetic variations which, in the presence of certain metabolic problems, may lead to complications, in the absence of adequate nutrition. This can help optimizing the nutritional management required in such conditions.

4) **Physical activity** includes an estimate, on a genetic basis, of the potential you have to practice certain types of exercise, and the impact that physical effort can have on your metabolism. Therefore, this package can help you or your coach (fitness specialist, trainer, etc.) to decide whether certain nutritional changes are necessary to improve your physical performance.

5) **Other genetic variations** are provided in a bonus package that includes certain genetic variantions in genes that might be of interest to you. It also includes several pharmacogenetic assessments. The results of this package should be interpreted by a doctor.

SCIENTIFIC AND TECHNICAL TERMS

To understand the results in this report, it Is useful to define some terms and abbreviations that you will encounter. The terms below are listed in the order in which they appear in this report.

UNITS	Generic term used in the summary tables (packages 1 and 2) to denote the recommended daily nutrient quantities.
Standard recommendations	Daily nutritient intakes recommended for all individuals (of a certain age and gender), regardless of the existence of genetic variations.
Personal recommendations	Daily nutritient intakes recommended for you based on this test. These recommendations (values or comments marked in blue in the summary table) take precedence over standard recommendations where these values differ.
LOCUS	Term used to designate a standardized unique number (preceded by the letters "rs") identifying a certain genetic variation in the human genome.
GENOTYPE	Association of genetic variations defined by the presence of nucleic acids (nucleotides) in both copies of a gene. The two letters (examples C/T) denote the two nucleotides in the two copies of the gene, for a given genomic position. Each gene within the human genome is present in two copies, each copy being inherited from one parent. Exceptions make the genes located in chromosomes X and Y in men, for which there is only one copy.
Gene-gene interactions	Interactions arising from the concomitant presence (in the same individual) of multiple genetic variations in several genes, and defining a specific nutrition recommendation.
HAPLOTYPE	A combination of genetic variations in the same genomic region (usually in the same gene or adjacent genes) that are found in a large segment of a population. Haplotypes are inherited from one generation to another.
Genetic score	A numeric value or a positive/negative assessment, established using a specific algorithm, and associated with a specific recommendation.
Risk	A term used in the context in which the existence of one or more genetic variations or haplotype(s) is associated in the scientific literature with an increase in the chances of occurrence of a particular disease or metabolic disorder. An increased risk denotes greater chances for a disorder to occur, compared to the average chances in a population surveyed. An increased risk does not mean that the person will definitely have a certain illness, but only that he or she has a higher chance of having this condition than the average chance in the studied population. For example, the risk for women to get breast cancer is 10% in the general population (10 out of 100 women). A woman who has a specific mutation in the BRCA1 gene has a 65% chance of breast cancer (65 out of 100 women who have this mutation). The risk is increased 6,5 times.
In/Del	Indicates the presence (In, insertion) or the absence (Del, deletion) of a nucleotide sequence. Terms used to define a genotype.

Tolerable upper limits (UL)

The table at the end of this report indicates the tolerable upper limits for each nutrient, according to age and sex. These limits are the maximum daily amounts in which nutrients can be consumed without unpleasant or adverse health effects. In certain situations, and always following a medical advice, these tolerable limits can be exceeded for a short period (days or weeks), but only for the purpose of treating a specific disorder. In rare cases, these limits can be exceeded continuously, but only at the doctor's advice, as treatment against a chronic condition.

ND (not determined)

In rare situations (1-2% of genetic variations), sequencing can not identify a DNA sequence, probably due to neighborhood mutations that interfere with the sequencing process used by this test. In such instance a genotype is declared ND (not determined). In other instances, although sequencing is successful, certain genotypic combinations (haplotypes) can not be determined either due to the ambiguity of the sequences or because a possible haplotipic combination has not yet been described in the scientific literature.

OTHER CONSIDERATIONS

Because packages 1-4 refer to different physiological contexts, some of the recommendations from packckages 1, 3, and 4 could differ from those in package 2. In this case, priority should be given to packages 1, 3 or 4, because these take into consideration specific physiological or metabolic states. That is the reason why this report needs to be interpreted by a specialist who applies the existing recommendations in the context of your specific health and lifestyle.

It is important to know that all of the genetic sequences in this test are declared on the basis of the "forward" DNA strand. Therefore, certain DNA sequences, well known in the literature as genotypes declared on the reverse strand, will be annotated differently in this report. One example is the well-known C677T mutation in the *MTHFR* gene (rs1801133), thus declared on the reverse strand, but which in this report appears as G677A on the forward strand. The annotation of all the sequences in this report, according to the "forward" strand, is provided in order to streamline further search in genomic databases.

Package 2. Adult nutrition

This package identifies the nutrient targets you need as adult. Because your DNA structure contributes to defining these tagets, these results define the personalized nutritional needs just for you, and can not be considered appropriate for another person. These personalized recommendations are for you only.

What are the benefits?

Some of the health issues occuring during your lifetime could be due to inadequte nutrition. Personalized nutrition, when correlated with your genetic structure, is the main way to prevent such disorders and metabolic diseases, including type-2 diabetes, obesity, hepatosteatosis, osteoporosis, and premature decrease in cognitive and memory abilities.

This package provides your specific recommendations, consistent with the scientific information presently available. In this way, by optimizing your nutrition, you can considerably reduce the risk of health problems that may occur in your life.

What should I do with these results?

It is important to realize that nutrition is a complex science and that is why you need the advice of a specialist. These results are very useful not only to you, but also to a nutritionist who, based this report, can design a meal plan that is appropriate to your specific needs.

That is why we recommend that you talk about these results to your doctor or your nutritionist.

SUMMARY

Your recommendations are the following:

Alcohol

Limit alcohol consumption to a maximum of 5 g/day (total alcohol 100%).

Coffee

Limit coffee consumption to a maximum of 250 mL/day (equivalent coffee filter) or equivalent caffeine contained in other beverages (Cola type, energy drinks, etc.). Alternatively, decaffeinated coffee (up to 1000 mL/day equivalent coffee filter) can be consumed. A cup of coffee (European type) is equivalent to 250 ml coffee filter (or "American cup").

Omega-6 and omega-3 fatty acids

Polyunsaturated OMEGA-6 (N6)		Polyunsaturated OMEGA-3 (N3)		RATIO N6/N3
Linoleic acid (LA)	<8 g/d	Alpha-linolenic acid (ALA)	>1,1 g/d	<10
		Eicosapentaenoic acid (EPA)	>0,4 g/d	
		Docosahexaenoic acid (DHA)	>0,88 g/d	

Vitamin A

Intake of Vitamin A and its precursors of at least 875 micrograms/day (retinol equivalent).

Vitamin B_2 (riboflavin)

Intake of Vitamin B2 of at least 2,2 milligrams/day.

Vitamin B_3 (niacin)

Intake of Vitamin B3 of at least 21 milligrams/day.

Vitamin B_{12} (cobalamin)

Intake of Vitamin B12 of at least 4,8 micrograms/day.

Vitamin C

Intake of Vitamin C of at least 75 milligrams/day.

Vitamin D

Intake of Vitamin D of at least 20 micrograms/day (equivalent cholecalciferol). 1 microgram cholecalciferol = 40 IU Vitamin D.

Vitamin E

Intake of Vitamin E of at least 30 milligrams/day (equivalent alpha-Tocopherol).

Vitamin K

Intake of Vitamin K of approximately 120 micrograms/day.

Continue on next page...

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Betaine	Intake of Betaine of at least 200 milligrams/day.
Choline	Intake of Choline of at least 425 milligrams/day.
Folates	Intake of Folates of at least 400 DFE/day as 5-methyltetrahydrofolate (5-MTHF) or natural folates from foods. Avoid supplements containing folic acid.
Calcium	Intake of Calcium of at least 1500 milligrams/day.
Iron	Intake of Iron of at least 8 milligrams/day.
Magnesiu	Intake of Magnesium of at least 390 milligrams/day.
Selenium	Intake of Selenium of at least 85 micrograms/day.
Zinc	Intake of Zinc of at least 10 milligrams/day.

YOUR RECOMMENDED NUTRIENT INTAKES

As a result of the genetic analysis of your DNA, the table on next page suggests your recommended nutrient intakes. These intakes are recommended only for healthy adults. These values are for you and only you. In some instances, it is possible that other metabolic conditions might require further modifications of these nutrient intakes, as indicated in packages 1, 3, 4, and 5, but such a decision should be made under medical supervision or by a certified nutritionist/dietician.

We do not recommend these intakes to exceed the upper tolerable limits indicated at the end of this report.

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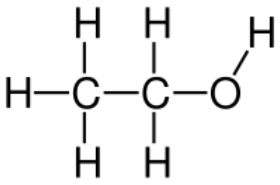
The custom recommendations are for nutrients **marked in blue**, which are the subject of this genetic testing. For the rest of the nutrients (**marked in black**) there are still insufficient scientific data to justify changes from standard recommendations, or the existing scientific data have not yet been sufficiently confirmed*.

* The algorithms used in this package take into account the latest scientific findings published in specialized, peer reviewed, scientific journals. These algorithms are the intellectual property of Advanced Nutrigenomics. The genetic variations included in this package, as well as the nutrients for which personalized values are offered, are the result of continuous evaluation of existing published studies.

NUTRIENT	UNITS	STANDARD RECOMMENDATIONS	YOUR RECOMMENDATIONS
Water	L/d	2,7	**2,7**
Carbohydrates	g/d	130	**130**
Fiber	g/d	21	**21**
Linoleic acid	g/d	11	**<8**
α-linolenic acid	g/d	1,1	**>1,1**
Proteins	g/d	46	**46**
Vitamin A	µg/d	700	**875**
Vitamin C	mg/d	75	**75**
Vitamin D	µg/d	15	**20**
Vitamin E	mg/d	15	**30**
Vitamin K	µg/d	90	**120**
Thiamine	mg/d	1,1	**1,1**
Riboflavin	mg/d	1,1	**2,2**
Niacin	mg/d	14	**21**
Vitamin B_6	mg/d	1,5	**1,5**
Folates	µg DFE/d	400	****400**
Vitamin B_{12}	µg/d	2,4	**4,8**
Pantothenic acid	mg/d	5	**5**
Betaine[1]	mg/d	-	**200**
Biotin	µg/d	30	**30**
Choline	mg/d	425	**425**
Calcium	mg/d	1200	**1500**
Chromium	µg/d	20	**20**
Copper	µg/d	900	**900**
Iron	mg/d	8	**8**
Fluoride	mg/d	3	**3**
Phosphorus	mg/d	700	**700**
Iodine	µg/d	150	**150**
Magnesium	mg/d	320	**390**
Manganese	mg/d	1,8	**1,8**
Molybdenum	µg/d	45	**45**
Selenium	µg/d	55	**85**
Zinc	mg/d	8	**10**
Potassium	g/d	4,7	**4,7**
Sodium	g/d	1,3	**1,3**
Chloride	g/d	2	**2**

L (liter), g (grams), mg (milligrams), µg (micrograms, mcg), DFE (dietary folate equivalents)
* = as 5-methyltetrahydrofolate (5-MTHF).
** = as 5-methyltetrahydrofolate (5-MTHF). Avoid using supplementation with folic acid.
[1]There are no standard recommendations for Betaine.

ALCOHOL



Test 19 (gene-gene interaction)		
Locus	**Gene**	**Genotype**
rs1230025	ADH1	A/A
rs16941667	ALDH2	C/C
ADH1 x ALDH2:		Favorable

Comment

The result of this interaction does not recommend an exact limit of daily consumption of acohol. Alcohol should be consumed with moderation in any situation.

The *ADH1* gene controls the metabolism of alcohol to acetic aldehyde. The *ALDH2* gene controls the metabolism of acetic aldehyde to acetic acid. The concomitant presence of the A genetic variant (*ADH1*) and T genetic variant (*ALDH2*) increases the risk of gastric cancer at an alcohol intake of more than 5 g/day.

Test 20 (haplotype ADH1)		
Locus	**Gene**	**Genotype**
rs1230025	ADH1	A/A
rs13123099	ADH1	G/G
rs17033	ADH1	T/T
rs13133908	ADH1	T/G
Haplotype AGTT:		Present

Comment

This haplotype recommends limiting alcohol consumption to a maximum of 5 g alcohol/day.

The AGTT haplotype is associated with an increased risk of gastric cancer at an alcohol intake of more than 5 g/day.

Test 21 (haplotype ALDH2)		
Locus	**Gene**	**Genotype**
rs16941667	ALDH2	C/C
rs886205	ALDH2	A/A
rs968529	ALDH2	C/C
Haplotype CGT:		Absent

Comment

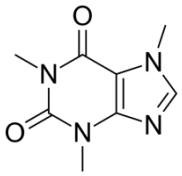
This haplotype does not recommend defining an exact limit of daily consumption of alcohol. Alcohol should be consumed with moderation in any situation.

The CGT haplotype is associated with an increased risk of gastric cancer at an alcohol intake of more than 5 g/day.

Recommendation:

Limit alcohol consumption to a maximum of 5 g/day (total alcohol 100%).

COFFEE



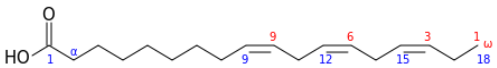
Test 22		
Locus	**Gene**	**Genotype**
rs762551	CYP1A2	C/C

Comment
This genotype requires limiting coffee consumption (caffeine).

The *CYP1A2* gene controls the metabolism of caffeine. Carriers of the genetic variation C have an increased risk of myocardial infarction if they consume more than one cup of coffee per day (or caffeine equivalent).

Recommendation:
Limit coffee consumption to a maximum of 250 mL/day (equivalent coffee filter) or equivalent caffeine contained in other beverages (Cola type, energy drinks, etc.). Alternatively, decaffeinated coffee (up to 1000 mL/day equivalent coffee filter) can be consumed. A cup of coffee (European type) is equivalent to 250 ml coffee filter (or "American cup").

OMEGA-6 AND OMEGA-3 FATTY ACIDS



Test 23 (haplotype FADS1/FADS2)

Locus	Gene	Genotype	Locus	Gene	Genotype	
rs174544	FADS1	C/C	rs174562	FADS1/2	A/A	
rs174545	FADS1	C/C	rs174564	FADS2	A/A	
rs174546	FADS1	C/C	rs28456	FADS2	A/A	
rs174547	FADS1	T/T	rs174566	FADS2	ND	
rs174548	FADS1	C/C	rs174567	FADS2	A/A	
rs174549	FADS1	G/G	rs174568	FADS2	C/C	
rs174550	FADS1	T/T	rs99780	FADS2	C/C	
rs174551	FADS1	T/T	rs1535	FADS2	A/A	
rs174553	FADS1	A/A	rs174574	FADS2	C/C	
rs174554	FADS1	A/A	rs174576	FADS2	C/C	
rs174555	FADS1	T/T	rs174577	FADS2	C/C	
rs174556	FADS1	C/C	rs174578	FADS2	T/T	
rs174560	FADS1/2	T/T	rs174580	FADS2	A/A	Haplotype D:
rs174561	FADS1/2	T/T	rs174581	FADS2	G/G	Present

COMMENT

The presence of haplotype D modifies the nutritional needs of omega-3 and omega-6 unsaturated fatty acids.

The *FADS1* and *FADS2* genes control the fatty acid desaturation rate and the synthesis of omega-3 and omega-6 fatty acids. Haplotype D carriers have an increased risk of developing coronary artery disease without an increased intake of omega-3 fatty acids.

Test 24 (haplotype SIRT1)

Locus	Gene	Genotype
rs7069102	SIRT1	G/G
rs2273773	SIRT1	T/T
rs3818292	SIRT1	A/A
Haplotype CCG/GTA:		GTA

Comment

The result of this test does not indicate a change of the recommended ratio of omega-6 / omega-3 fatty acids.

The *SIRT1* gene controls the activation of cellular receptors to which unsaturated fatty acids bind. The presence of CCG or GTA haplotypes in men, or CCG haplotype in women, associates with an increased risk of high levels of LDL cholesterol, depending on the nutritional intake of omega-6 and omega-3 fatty acids.

Continue on next page...

...continue from previous page (fatty acids).

Test 25 (haplotype SREBF1)		
Locus	**Gene**	**Genotype**
rs2297508	SREBF1	G/G
rs11656665	SREBF1	A/A
Haplotype GG:		Absent

Comment
This result does not require strict monitoring of omega-6 fatty acid intake.

The *SREBF1* gene (*SREBP1*) controls the transcription of the LDL receptor. The presence of GG haplotype in menopausal women over 55 years of age contraindicates the consumption of linoleic acid (a precursor of omega-6 fatty acids), which is associated with an increased risk of coronary artery disease.

Recommendation:

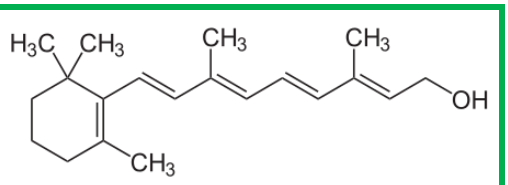
The table below shows the recommended nutrient intake (including dietary supplements) of omega-6 and omega-3 unsaturated fatty acids, as well as the maximum ratio between omega-6 and omega-3. These values are specific to you only.

OMEGA-6 (N6)		OMEGA-3 (N3)		RATIO N6/N3
Linoleic acid (LA)	<8 g/d	Alpha-linolenic acid (ALA)	>1,1 g/d	**<10**
		Eicosapentaenoic acid (EPA)	>0,4 g/d	
		Docosahexaenoic acid (DHA)	>0,88 g/d	

Foods rich in **omega-3** unsaturated fatty acids include **fish (especially mackerel, salmon, cod, herring, sardines, anchovies), shells, flax seeds/flaxseed oil, nuts, peanuts and almonds**.

Foods rich in **omega-6** unsaturated fatty acids include **corn oil, sunflower oil, avocado oil, soybean oil**.

VITAMIN A



Test 26 (haplotype SCARB1)		
Locus	**Gene**	**Genotype**
rs5888	SCARB1	A/G
rs4238001	SCARB1	C/C
rs61932577	SCARB1	G/G
Haplotip GCA:		Absent

Comment

This result does not change the standard recommendations for daily intake of Vitamin A.

The *SCARB1* gene controls the intestinal uptake of some vitamin A precursors. The presence of the GCA haplotype requires an increased nutritional intake of these precursors.

Test 27 (haplotype CD36)		
Locus	**Gene**	**Genotype**
rs1984112	CD36	A/G
rs1761667	CD36	G/A
rs1527479	CD36	T/C
rs1527483	CD36	G/G
rs13230419	CD36	C/T
Haplotip GGTGC:		Prezent

Comment

The presence of this haplotype requires an increased daily intake of Vitamin A precursors.

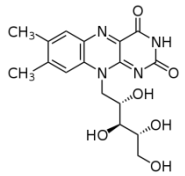
The *CD36* gene controls the intracellular transport of some vitamin A precursors. The presence of the GGTGC haplotype requires an increased nutritional intake of these precursors.

Recommendation:

Intake of Vitamin A and its precursors of at least 875 micrograms/day (retinol equivalent).

Foods rich in Vitamin A or Vitamin A precursors include **sweet potatoes, carrots, lettuce, dried apricots, cantaloupe, fish, liver**.

VITAMIN B_2 (RIBOFLAVIN)



Test 28		
Locus	**Gene**	**Genotype**
rs1801133	MTHFR	G/A
rs1801394	MTRR	G/G
rs1532268	MTRR	C/T

Comment

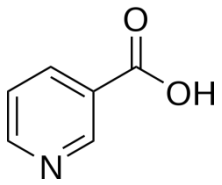
This result requires an increased daily intake of Vitamin B2.

The *MTHFR* gene controls the endogenous synthesis of 5-methyltetrahydrofolate (5-MTHF, the active form of folate). The presence of genetic variation A requires increased intake of Vitamin B2 in order to control homocysteine levels. The *MTRR* gene is also involved in maintaining normal levels of homocysteine in conjunction with Vitamin B2. The presence of genetic variations G (rs1801394) or T (rs1532268) correlates with an increased risk of increased homocysteine in the absence of adequate intake of Vitamin B2.

Recommendation:
Intake of Vitamin B2 of at least 2,2 milligrams/day.

Foods rich in Vitamin B2 include **eggs, lean meats, milk, broccoli, bananas, plum juice, asparagus**.

VITAMIN B_3 (NIACIN)



Test 29 (haplotype SIRT1)		
Locus	**Gene**	**Genotype**
rs7895833	SIRT1	A/A
rs1467568	SIRT1	G/G
rs497849	SIRT1	C/T
Haplotip AGC:		Present

Comment

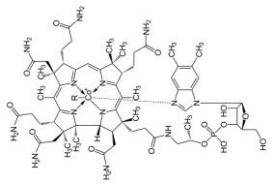
The presence of this haplotype requires an increased daily intake of Vitamin B3.

The *SIRT1* gene is involved in the control of insulin resistance. Niacin acts as a cofactor in the catalytic activity of the SIRT1 protein. AGC haplotype carriers with type 2 diabetes are at increased risk of death with insufficient vitamin B3 intake.

Recommendation:
Intake of Vitamin B3 of at least 21 milligrams/day.

Foods rich in Vitamin B3 include **turkey meat, chicken breast, peanuts, mushrooms, liver, tuna, green peas, beef (grazed)**.

VITAMIN B_{12} (COBALAMIN)



Test 30 (haplotype FUT2)		
Locus	**Gene**	**Genotype**
rs492602	FUT2	A/A
rs602662	FUT2	G/A
Haplotip AG:		Present

Comment

The presence of this haplotype requires an increased daily intake of Vitamin B12.

The FUT2 gene is associated with the absorption capacity of Vitamin B_{12} in the intestine. The presence of AG haplotype is associated with lower blood levels of vitamin B_{12}.

Test 31 (haplotype MTHFR)		
Locus	**Gene**	**Genotype**
rs1537514	MTHFR	G/G
rs2274976	MTHFR	C/C
Haplotip (bloc H1) GC:		Present

Comment

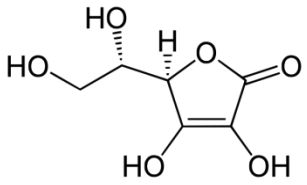
The presence of this haplotype requires an increased daily intake of Vitamin B12.

The *MTHFR* gene controls the endogenous synthesis of 5-methyltetrahydrofolate (5-MTHF, the active form of folate). Vitamin B_{12} is used as a co-factor in the use of 5-MTHF for methionine synthesis. The GC haplotype is associated with elevated homocysteine levels in the absence of an increased intake of Vitamin B_{12}.

Recommendation:
Intake of Vitamin B12 of at least 4,8 micrograms/day.

Foods rich in Vitamin B_{12} include **clams, beef and cow liver, turkey meat, chicken, crustaceans, salmon, eggs, trout**.

VITAMIN C (ASCORBIC ACID)



Test 32		
Locus	**Gene**	**Genotype**
rs11950646	SLC23A1	G/A
rs33972313	SLC23A1	C/C

Comment

This result does not change the standard recommendations for daily intake of Vitamin C.

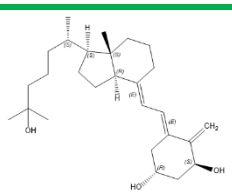
The *SLC23A1* gene (also known as *SLC23A2*) controls the intestinal absorption and intracellular transport of Vitamin C (ascorbic acid). Persons carrying the genotypes G/G (rs11950646), or C/T or T/T (rs33972313) have an increased risk of vitamin C.

Recommendation:

Intake of Vitamin C of at least 75 milligrams/day.

Foods rich in Vitamin C include **strawberries, citrus fruits (lemons, oranges, grapefruit, lime), papaya, kiwi, guava, kale, brussel sprouts, melon, cantalupe, broccoli, cauliflower, tomatoes.**

VITAMIN D



Test 33 (haplotype CYP2R1)		
Locus	**Gene**	**Genotype**
rs10741657	CYP2R1	A/G
rs10766197	CYP2R1	G/A
Diplotype:		12

Comment
This combination of haplotypes does not change the standard recommendations for daily intake of Vitamin D.

The *CYP2R1* gene controls the synthesis of the active form of Vitamin D from its precursor. The individuals carrying the "11" or "33" diplotypes are at increased risk of having low levels of active vitamin D in the absence of adequate nutritional intake.

Test 34 (haplotype GC)		
Locus	**Gene**	**Genotype**
rs12512631	GC	T/C
rs842999	GC	C/C
rs4588	GC	G/T
Diplotype:		Nedeterminat

Comment
This result does not change the standard recommendations for daily intake of Vitamin D.

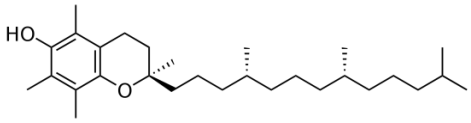
The *GC* gene controls the transport of Vitamin D to other organs and tissues. Carriers of "22", "45" or "25" diplotypes are at increased risk of having low levels of active vitamin D in the absence of adequate nutritional intake.

Recommendation:

Intake of Vitamin D of at least 20 micrograms/day (equivalent cholecalciferol). 1 microgram cholecalciferol = 40 IU Vitamin D.

Foods rich in Vitamin D and Vitamin D precursors include **fatty fish species (tuna, mackerel, salmon, etc.), vitamin D fortified products, cheeses, beef, liver, eggs**.

VITAMIN E



Test 35 (haplotype CD36)		
Locus	**Gene**	**Genotype**
rs1984112	CD36	A/G
rs1527479	CD36	T/C
rs7755	CD36	G/A
rs1527483	CD36	G/G
Diplotype:		12

Comment

This combination of haplotypes requires an increased daily intake of Vitamin E.

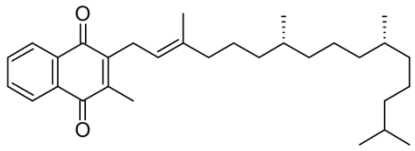
The *CD36* gene controls the intracellular transport of Vitamin E (alpha-tocopherol). Persons carrying haplotype combinations which DO NOT CONTAIN haplotypes "5" or "7" (eg. "24", "46", "89", etc.) exhibit, on average, lower plasma tocopherol and need an increased nutritional intake of Vitamin E.

Recommendation:

Intake of Vitamin E of at least 30 milligrams/day (equivalent alpha-Tocopherol).

Foods rich in Vitamin E include **sunflower oil and seeds, nuts, peanuts, avocado, shrimp, fish (trout, herring, salmon), olive oil, broccoli, pumpkin, kiwi, mango, peaches, nectarines, apricots, guava**.

VITAMIN K



Test 36		
Locus	**Gene**	**Genotype**
rs2359612	VKORC1	G/G

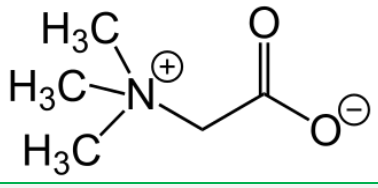
Comment
This result requires an increased daily intake of Vitamin K.

The VKORC1 gene controls blood clotting due to Vitamin K activation. G/G genotype carriers require increased intake of Vitamin K. IMPORTANT: If this test results in the G/G genotype identification, it is necessary to inform your doctor as this genotype may require a reduction of the usual doses of some anticoagulant drugs.

Recommendation:
Intake of Vitamin K of approximately 120 micrograms/day.

Foods rich in Vitamin K include **brussel sprouts, cabbage, broccoli, fermented dairy products, plums, cucumbers**.

BETAINE



Test 37		
Locus	**Gene**	**Genotype**
rs6445606	CHDH	T/T

Comment
This genotype requires increased daily intake of Betaine.

The *CHDH* gene controls the synthesis of betaine from choline. People carrying two copies of genetic variation T (genotype T/T) have increased nutritional requirement of betaine.

Test 38		
Locus	**Gene**	**Genotype**
rs526264	BHMT2	A/T

Comment
This genotype does not require the monitoring of Betaine daily intake.

Test 39		
Locus	**Gene**	**Genotype**
rs625879	BHMT2	A/C

Comment
This genotype does not require the monitoring of Betaine daily intake.

The *BHMT2* gene is one of the two genes (together with the *BHMT* gene) that control the transfer of a methyl group from betaine to homocysteine, resulting in methionine. T/T genotype (rs526264) or C/C genotype (rs625879) require higher daily intakes of betaine.

Test 40		
Locus	**Gene**	**Genotype**
rs7356530	BHMT	G/A

Comment
This genotype does not require the monitoring of Betaine daily intake.

Test 41		
Locus	**Gene**	**Genotype**
rs600473	BHMT	G/T

Comment
This genotype does not require the monitoring of Betaine daily intake.

Test 42		
Locus	**Gene**	**Genotype**
rs3733890	BHMT	G/A

Comment
This genotype does not require the monitoring of Betaine daily intake.

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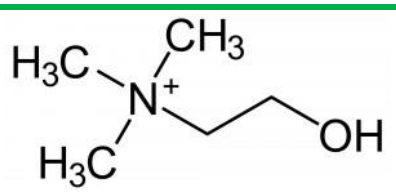
The *BHMT2* gene is one of the two genes (together with the *BHMT* gene) that control the transfer of a methyl group from betaine to homocysteine, resulting in methionine. T/T genotype (rs526264) or C/C genotype (rs625879) require higher daily intakes of betaine.

Recommendation:
Intake of Betaine of at least 200 milligrams/day.

Foods rich in betaine include **wheat bran, quinoa, beets, spinach.**

CHOLINE



Test 43		
Locus	**Gene**	**Genotype**
rs4646343	PEMT	G/T

Comment
This genotype requires a standard daily intake of Choline.

Test 44		
Locus	**Gene**	**Genotype**
rs3760188	PEMT	C/T

Comment
This genotype requires a standard daily intake of Choline.

Test 45		
Locus	**Gene**	**Genotype**
rs1531100	PEMT	G/A

Comment
This genotype requires a standard daily intake of Choline.

Test 46		
Locus	**Gene**	**Genotype**
rs4646365	PEMT	C/T

Comment
This genotype requires a standard daily intake of Choline.

The PEMT gene controls the endogenous synthesis of choline. People carrying at least one of several genetic variations in both copies of the gene have a different nutritional requirement for choline. IMPORTANT: these recommendations should not be followed by pregnant or lactating women because choline requirements during pregnancy and lactation are increased. See Package 1 for such recommendations.

Test 47		
Locus	**Gene**	**Genotype**
rs6591331	CHKA	A/A

Comment
This genotype requires a minimum daily intake of Choline.

The *CHKA* gene controls the first reaction required for phosphatidylcholine synthesis. Those who carry the genetic variation T have an increased nutritional requirement for choline.

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Test 48			Comment
Locus	**Gene**	**Genotype**	
rs1557502	CHKB	C/C	This genotype requires a minimum daily intake of Choline.

The *CHKB* gene controls the synthesis of phosphocoline. Those who carry the genetic variation T have an increased nutritional requirement for choline.

Test 49			Comment
Locus	**Gene**	**Genotype**	
rs7873937	SLC44A1	G/C	This genotype requires a standard daily intake of Choline.

Test 50			Comment
Locus	**Gene**	**Genotype**	
rs2771040	SLC44A1	G/A	This genotype requires a standard daily intake of Choline.

Test 51			Comment
Locus	**Gene**	**Genotype**	
rs6479313	SLC44A1	C/G	This genotype requires a standard daily intake of Choline.

Test 52			Comment
Locus	**Gene**	**Genotype**	
rs16924529	SLC44A1	G/A	This genotype requires a standard daily intake of Choline.

Test 53			
Locus	**Gene**	**Genotype**	
rs3199966	SLC44A1	T/G	This genotype requires a standard daily intake of Choline.

Test 54			Comment
Locus	**Gene**	**Genotype**	
rs440290	LOC 101928609	T/T	This genotype requires a minimum daily intake of Choline.

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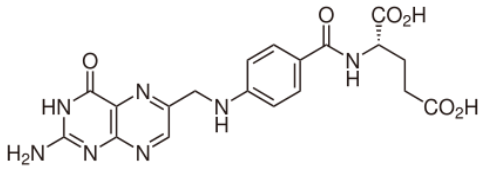
The *SLC44A1* gene controls intracellular choline transport. LOC101928609 is included in the promoter of this gene. People carrying at least one of some genetic variations have a different nutritive requirement of choline when compared to most of the population. IMPORTANT: these recommendations should not be followed by pregnant or lactating women as the choline needs during pregnancy and lactation are increased. See Package 1 for such recommendations.

Recommendation:
Intake of Choline of at least 425 milligrams/day.

Foods rich in choline include **meat (chicken, beef, pork), beef liver, fish, dairy, rice, eggs**.

FOLATES



Test 55		
Locus	**Gene**	**Genotype**
rs1801133	MTHFR	G/A

Comment
This genotype requires 5-methyltetrahydrofolate (5-MTHF) as daily intake of Folates.

The *MTHFR* gene controls the endogenous synthesis of 5-methyltetrahydrofolate (5-MTHF, the active form of folate). Individuals carrying the genetic variation A (also known as the C677T variation) have an increased nutritional requirement of folate in its active form (5-methyltetrahydrofolate, 5-MTHF).

Test 56		
Locus	**Gene**	**Genotype**
rs70991108	DHFR	Del/In

Comment
This genotype suggests avoidance of folic acid supplementation.

The *DHFR* gene controls the synthesis of tetrahydrofolic acid from dihydrofolic acid. Individuals carrying the Del genetic variation (deletion of 19 nucleotides) have an increased risk of cancer if they consume supplements containing folic acid.

Recommendation:
Intake of Folates of at least 400 DFE/day as 5-methyltetrahydrofolate (5-MTHF) or natural folates from foods. Avoid supplements containing folic acid.

Foods rich in folates include **lentil, beans and peas, leafy green vegetables**.

CALCIUM	Ca

Test 57		
Locus	**Gene**	**Genotype**
rs1544410	VDR	C/C

Comment
This genotype does not change the standard recommended daily intake of Calcium.

Test 58		
Locus	**Gene**	**Genotype**
rs731236	VDR	A/A

Comment
This genotype does not change the standard recommended daily intake of Calcium.

The *VDR* gene indirectly controls calcium metabolism in the body due to its role in vitamin D-induced gene activation. Menopausal or over 50-year-old women having the genetic variation T (rs1544410) or G (rs731236) have an increased nutritional requirement of calcium.

Test 59		
Locus	**Gene**	**Genotype**
rs17251221	CASR	A/G

Comment
This genotype requires increased daily Calcium intake.

The *CASR* gene controls calcium concentration in the blood. Individuals carrying the genetic variation A have an increased risk for lower blood calcium concentrations in the absence of adequate calcium intake.

Recommendation:
Intake of Calcium of at least 1500 milligrams/day.

Foods rich in calcium include **milk, sardines, yogurt, kefir, broccoli, cheese**.

IRON	Fe

Test 60

Locus	Gene	Genotype
rs855791	TMPRSS6	A/A

Comment

This genotype does not change the standard recommended daily intake of Iron.

Test 61

Locus	Gene	Genotype
rs4820268	TMPRSS6	A/A

Comment

This genotype does not change the standard recommended daily intake of Iron.

The *TMPRSS6* gene indirectly controls intestinal absorption and iron stores in the body as well as the distribution of iron to organs and tissues. Individuals (males) carrying the genetic variation A (rs855791) or genetic variation G (both sexes, rs4820268) are at increased risk for low levels of iron in the body without a higher daily intake of iron.

Recommendation:
Intake of Iron of at least 8 milligrams/day.

Foods rich in iron include **red meat, pork, poultry, marine food, beans, green leafy vegetables, dried fruits (raisins, apricots), fortified foods with iron (iron fortified cereals, fortified bread with iron, etc.)**.

MAGNESIUM	Mg

Test 62		
Locus	**Gene**	**Genotype**
rs4072037	MUC1	T/T

Comment
This genotype requires increased daily Magnesium intake.

The *MUC1* gene controls the synthesis of mucin, a glycoprotein involved in the protection of the intestines, lungs, stomach, eyes and other organs against pathogens. Carriers of genetic variation T have lower magnesium levels than non-carriers, in the absence of increased magnesium intake.

Test 63		
Locus	**Gene**	**Genotype**
rs13146355	SHROOM3	G/A

Comment
This genotype requires increased daily Magnesium intake.

The *SHROOM3* gene controls the permeability of intercellular junctions. Carriers of genetic variation A have lower magnesium levels than non-carriers, in the absence of increased magnesium intake.

Test 64		
Locus	**Gene**	**Genotype**
rs11144134	TRPM6	T/C

Comment
This genotype requires increased daily Magnesium intake.

The *TRPM6* gene controls the intestinal absorption of magnesium as well as its reabsorption in the kidneys. Carriers of genetic variation C have lower magnesium levels than non-carriers, in the absence of increased magnesium intake.

Test 65		
Locus	**Gene**	**Genotype**
rs3925584	DCDC5	C/C

Comment
This genotype does not change the standard recommended daily intake of Magnesium.

The *DCDC5* gene controls the microtubule polymerization inside the cell, which helps stabilize the three-dimensional shape of a cell. The rs3925584 locus is located in the vicinity of this gene. Carriers of genetic variation T have lower magnesium levels than non-carriers, in the absence of increased magnesium intake.

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Test 66		
Locus	**Gene**	**Genotype**
rs7965584	ATP2B1	A/A

Comment
This genotype requires increased daily Magnesium intake.

The *ATP2B1* gene controls extracellular calcium transport, and the product of this gene (a calcium pump) requires the presence of magnesium. The rs7965584 locus is located in the vicinity of this gene. Carriers of genetic variation A have lower magnesium levels non-carriers, in the absence of increased magnesium intake.

Test 67		
Locus	**Gene**	**Genotype**
rs7197653	PRMT7	G/G

Comment
This genotype requires increased daily Magnesium intake.

The *PRMT7* gene controls the methylation of specific amino acids within the histone H4 structure, contributing to the epigenetic control of gene expression. Carriers of genetic variation G have lower magnesium levels than non-carriers, in the absence of increased magnesium intake.

Recommendation:
Intake of Magnesium of at least 390 milligrams/day.

Magnesium rich foods include **green leafy vegetables (spinach, kale), walnuts and peanuts, pumpkin seeds, fish (mackerel, tuna), beans, soybeans, whole wheat, chinoa, brown rice, avocados, yoghurt, bananas, dried fruits (plums, apricots, raisins), black chocolate**.

SELENIUM	Se

Test 68		
Locus	**Gene**	**Genotype**
rs3877899	SEPP1	C/T

Comment
This genotype requires increased daily Selenium intake.

Test 69		
Locus	**Gene**	**Genotype**
rs7579	SEPP1	C/C

Comment
This genotype does not change the standard recommended daily intake of Selenium.

The *SEPP1* gene encodes an antioxidant selenoprotein for the extracellular space. Carriers of genetic variation T (rs3877899) or T (rs7579) have selenium levels lower than noncarriers, in the absence of increased selenium intake.

Test 70		
Locus	**Gene**	**Genotype**
rs561104	SEP15	T/T

Comment
This genotype requires increased daily Selenium intake.

The *SEP15* gene encodes a selenoprotein with potential antioxidant role. Carriers of genetic variation T have selenium levels lower than non-carriers, in the absence of increased selenium intake.

Recommendation:
Intake of Selenium of at least 85 micrograms/day.

Foods rich in Selenium include **nuts and hazelnuts (different varieties), shellfish, shrimp, lobster, fish (tuna, tilapia, mackerel, etc.), whole flour bread, sunflower seeds, chia seeds, sesame, lean pork, lamb, beef, chicken, turkey, mushrooms**.

ZINC	Zn

Test 71		
Locus	**Gene**	**Genotype**
rs11126936	SLC30A3	G/G

Comment
This genotype requires increased daily Zinc intake.

The *SLC30A3* gene controls the transport and absorption of zinc. People carrying the genetic variation G in both copies of the gene (G/G genotype) have zinc levels lower than non-carriers, in the absence of increased zinc intake.

Recommendation:
Intake of Zinc of at least 10 milligrams/day.

Zinc-rich foods include **shellfish, lamb, beef, wheat germ, spinach, whole grains, pumpkin seeds, peanuts, cocoa, pork, chicken, beans, and mushrooms**.

Package 3. Risks of metabolic imbalances

This package aims to identify metabolic risks associated with your genetic structure, for which nutritional management is available. Because your genetic structure may contribute to such risks, these tests identify personalized solutions just for you, that can not be considered appropriate for another person. These personalized recommendations are for you only.

What are the benefits?

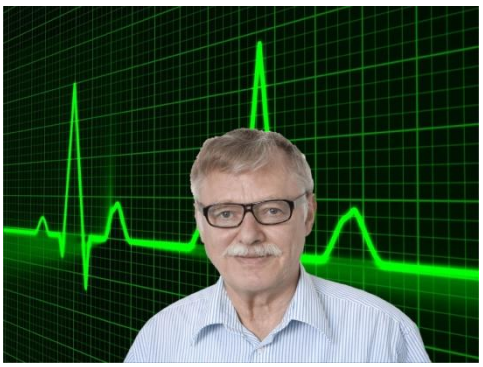
Some risks for metabolic disturbances are increased by inadequate nutrition. These risks may vary from person to person due to genetic differences. Often there are nutritional solutions to reduce these risks or to diminish unwanted metabolic outcomes, according to the structure of your genes. Such solutions can be applied for a wide range of disorders such as type 2 diabetes, hypercholesterolemia or hepatosteatosis.

This package provides you with specific recommendations, consistent with the scientific information obtained from many published studies. As such, you may reduce the risk of metabolic diseases, or even reduce their amplitude.

What should I do with these results?

The identification of metabolic risks should be performed by your doctor. A doctor is the only one that can correctly integrate the information provided by this package with an effective dietary meal plan or medication. If certain metabolic disorders are already present and this package indicates possible solutions, the doctor is the only one who can apply these solutions correctly.

That is why we recommend that you present these results to your doctor.



SUMMARY

The recommendations below should only be followed if you suffer from the aforementioned metabolic conditions or to reduce the risk of their occurrence.

Non-alcoholic hepatosteatosis (NASH)	Supplementation with Choline, Betaine, 5-methyltetrahydrofolate (5-MTHF), Vitamin B12, Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA) in doses recommended by your specialist. It is recommended to start at high doses (3-4 times higher than the recommended standard nutritional values). Subsequently, if the degree of hepatosteatosis is reduced, the successive decreases in these doses will determine the effective minimal dose with which it will continue in the long term, depending on the specialist's advice. It is mandatory to also use adequate nutritional recommendations to reduce body weight.
Obesity	You have a relatively high risk of weight gain. Consult a specialist for proper nutrition recommendations.
Hyperhomocysteinemia	If your doctor has rejected the diagnosis of hyperhomocysteinemia, it is not necessary to make changes for the purpose of decreasing your homocysteine. If hyperhomocysteinemia is present, follow the treatment recommended by your doctor.
Cholesterol	Continuous monitoring of cholesterol levels is recommended. It is advisable to consult with a specialist (nutritionist or your doctor) to implement an appropriate lifestyle that minimizes the risk of high LDL cholesterol. If LDL cholesterol is higher than normal, your doctor may use this information to personalize and enhance the efficacy of antihypercholesterolemic treatments and for proper nutritional management.

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Type 2 Diabetes / Insulin resistance	If you have not been diagnosed with type 2 diabetes, an aggressive approach to preventing type 2 diabetes is required, according to your doctor's advice. This approach includes both a healthy diet and an active lifestyle. Continuous monitoring of biochemical parameters that may indicate insulin resistance or type 2 diabetes may be required. If you have already been diagnosed with diabetes, your doctor may use this information to personalize and make more effective your antidiabetic treatment, and for adequate nutritional management.
Cardiovascular disease in the aging adult	Daily zinc intake of minimum 16 milligrams.
Postprandial hyperlipidemia	Reduce significantly the intake of foods rich in animal fats, according to your nutritionist's advice.
Alcohol intake	Limit alcohol consumption to a maximum of 5 g/day (total alcohol 100%).

The algorithms used in this package take into account the latest scientific findings published in specialized, peer reviewed, scientific journals. These algorithms are the intellectual property of Advanced Nutrigenomics. The genetic variations included in this package, as well as the nutrients for which personalized values are offered, are the result of continuous evaluation of existing published studies.

NON-ALCOHOLIC HEPATOSTEATOSIS (NASH)

Test 72 (genetic score)

Locus	Gene	Genotype	Locus	Gene	Genotype
rs1109859	PEMT	A/A	rs7238	CHKB	A/A
rs12103822	PEMT	C/C	rs2526678	FADS2	G/G
rs16961845	PEMT	C/C	rs526126	FADS2	C/C
rs13342397	PEMT	T/T	rs10135928	MTHFD1	T/T
rs4479310	PEMT	C/T	rs1801133	MTHFR	G/A
rs936108	PEMT	C/T	rs2066471	MTHFR	C/C
rs8068641	PEMT	A/G	rs4846048	MTHFR	A/A
rs7946	PEMT	C/T	rs4846052	MTHFR	C/C
rs7214988	PEMT	C/C	rs7525338	MTHFR	C/C
rs4244593	PEMT	T/G	rs868014	MTHFR	G/G
rs6502603	PEMT	G/T	rs1580820	PCYT1A	A/A
rs1149222	ABCB4	T/T	rs4898190	PCYT1B	C/C
rs1202283	ABCB4	G/G	rs2281135	PNPLA3	G/G
rs2071645	ABCB4	G/C	rs738409	PNPLA3	C/C
rs31672	ABCB4	T/T	rs11557927	SCD	T/T
rs4148811	ABCB4	T/G	rs11599710	SCD	G/G
rs9655950	ABCB4	T/T	rs12247426	SCD	C/C
rs2854117	APOC3	T/C	rs2167444	SCD	T/T
rs12676	CHDH	C/C	rs7849	SCD	T/T
rs2289209	CHDH	C/C	rs10120572	SLC44A1	T/T
rs4563403	CHDH	C/T	rs10820799	SLC44A1	A/A
rs4687591	CHDH	A/A	rs193008	SLC44A1	T/T
rs6807783	CHDH	G/C	rs328006	SLC44A1	G/G
rs7634578	CHDH	C/C	rs440290	SLC44A1	T/T
rs881883	CHDH	A/G	rs443094	SLC44A1	G/G
rs1557502	CHKB	C/C	rs7018875	SLC44A1	C/C
rs1557503	CHKB	G/G	rs9891119	STAT3	A/A
rs470117	CHKB	C/T	Genetic score:		Positive

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This test uses 55 genetic variations to generate a genetic score. Its development is based on existing clinical studies. **The test is for overweight or obese people** rather than those with normal body weight. This test only refers to metabolic (non-alcoholic) hepatosteatosis in the context of an increased body weight.

A positive genetic score indicates:

1. The fact that an **overweight or obese person** has developed or will likely develop hepatosteatosis as long as they do not alter their obesogenic lifestyle that has contributed to this pathological condition;

2. The fact that such a person could benefit from specific nutritional management for the reduction of hepatosteatosis.

A negative genetic score indicates:

1. The fact that an **overweight or obese person** will probably not develop hepatosteatosis associated with increased body weight (approximately 10% of obese cases);

2. The fact that, if an obese or overweight person develops hepatosteatosis, there is no scientific information that would allow specific nutritional management, except for what is generally recommended for losing body weight.

Recommendation applicable only if you are overweight or obese:
Supplementation with Choline, Betaine, 5-methyltetrahydrofolate (5-MTHF), Vitamin B12, Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA) in doses recommended by your specialist. It is recommended to start at high doses (3-4 times higher than the recommended standard nutritional values). Subsequently, if the degree of hepatosteatosis is reduced, the successive decreases in these doses will determine the effective minimal dose with which it will continue in the long term, depending on the specialist's advice. It is mandatory to also use adequate nutritional recommendations to reduce body weight.

OBESITY

Test 73 (Haplotype UCP2/UCP3)		
Locus	**Gene**	**Genotype**
rs659366	UCP2	C/C
rs653529	UCP2	T/T
rs15763	UCP3	G/G
rs1726745	UCP3	T/T
Identified haplotype:		CTGT

Comment

This haplotype associates with the same risk of obesity as in the general population.

The *UCP2* and *UCP3* genes are involved in mitochondrial energy generation. Carriers of TCAC haplotype have a low risk of weight gain, when compared to carriers of other haplotypes UCP2/UCP3 (Block 2).

Test 74 (haplotype FABP2)		
Locus	**Gene**	**Genotype**
rs6857641	FABP2	T/C
Indicates haplotype:		AB

Comment

This haplotype is not associated with changes in body weight.

The *FABP2* gene is involved in the metabolism of fatty acids. Individuals carrying the haplotype BB and who are normoponderal (with body weight within normal range) tend to have a weight below the average of the general population and relative protection against obesity.

Test 75 (haplotype PLIN1)		
Locus	**Gene**	**Genotype**
rs2304795	PLIN1	A/A
rs1052700	PLIN1	A/T
Haplotype AT or GT:		Present

Comment

This haplotype is associated with an increased risk of obesity.

The *PLIN1* gene controls the storage and release of fat in the adipocytes. Female individuals carrying the AT or GT haplotype have an increased risk of obesity.

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Test 76		
Locus	**Gene**	**Genotype**
rs17817449	FTO	T/T

Comment
This genotype does not change the standard food recommendations.

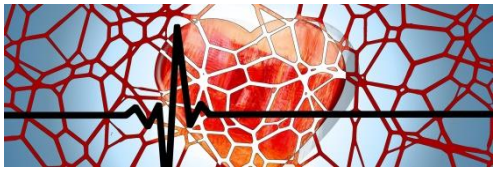
Test 77		
Locus	**Gene**	**Genotype**
rs1421085	FTO	T/T

Comment
This genotype is generally not associated with increased hunger.

The *FTO* gene helps control hunger sensation within the hypothalamus, as well as food preferences.

Recommendation:
You have a relatively high risk of weight gain. Consult a specialist for proper nutrition recommendations.

HYPERHOMOCYSTEINEMIA



Test 78 (haplotype BHMT2)		
Locus	**Gene**	**Genotype**
rs506500	BHMT2	C/C
rs3733890	BHMT2	G/A
rs585800	BHMT2	A/A
Haplotype ACT:		Absent

Comment

This result is not associated with an increased risk of hyperhomocysteinemia.

The *BHMT2* gene (together with *BHMT*) controls the conversion of homocysteine to methionine, using betaine as methyl donor. Carriers of the ACT haplotype have an increased risk of hyperhomocysteinemia when compared to general population.

Test 79 (gene-gene interaction)		
Locus	**Gene**	**Genotype**
rs1801133	MTHFR	G/A
rs2274976	MTHFR	C/C
Interaction rs x rs:		Favorable

Comment

The result of this interaction is not associated with an increased risk of hyperhomocysteinemia, taking into account your gender.

Test 80 (gene-gene interaction)		
Locus	**Gene**	**Genotype**
rs1801133	MTHFR	G/A
rs1801131	MTHFR	T/T
Interaction rs x rs:		Favorable

Comment

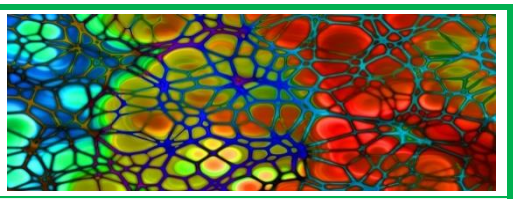
The result of this interaction is not associated with an increased risk of hyperhomocysteinemia.

The *MTHFR* gene controls the endogenous synthesis of 5-methyltetrahydrofolate (5-MTHF, the active form of folate). Carriers of specific combinations of genetic variations have an increased risk of hyperhomocysteinemia, depending on gender, age, lifestyle and diet.

Recommendation:

If your doctor has rejected the diagnosis of hyperhomocysteinemia, it is not necessary to make changes for the purpose of decreasing your homocysteine. If hyperhomocysteinemia is present, follow the treatment recommended by your doctor.

CHOLESTEROL



Test 81 (haplotype UCP3)		
Locus	**Gene**	**Genotype**
rs3781907	UCP3	A/A
rs11235972	UCP3	G/G
rs1800849	UCP2	G/G
Haplotip GAA:		Absent

Comment

This result is not associated with cholesterol changes.

The *UCP2* and *UCP3* genes are involved in mitochondrial energy generation. Carriers of the GAA haplotype have, on average, elevated total cholesterol and LDL cholesterol versus mean values in the general population. Higher than average values may be within or above normal limits.

Test 82 (haplotype PON1)		
Locus	**Gene**	**Genotype**
rs662	PON1	G/G
rs854560	PON1	A/T
Haplotip GA:		Present

Comment

This haplotype is associated with higher risk for increased total cholesterol and LDL cholesterol when compared to the mean values in the general population.

The *PON1* gene contributes to the anti-atherosclerotic function of HDL cholesterol, and indirectly to the control of LDL cholesterol levels. GA haplotype carriers have, on average, elevated levels of LDL cholesterol, when compared to the average values in general population. Higher than average values may be within or above normal limits.

Recommendation:

Continuous monitoring of cholesterol levels is recommended. It is advisable to consult with a specialist (nutritionist or your doctor) to implement an appropriate lifestyle that minimizes the risk of high LDL cholesterol. If LDL cholesterol is higher than normal, your doctor may use this information to personalize and enhance the efficacy of antihypercholesterolemic treatments and for proper nutritional management.

TYPE 2 DIABETS / INSULIN RESISTANCE

Test 83 (haplotype IRS1)		
Locus	**Gene**	**Genotype**
rs7578326	IRS1	A/A
rs2943641	IRS1	C/C
Haplotip AC:		Present

Comment

The presence of this haplotype increases the risk of insulin resistance, then of type 2 diabetes, compared to the general population.

The *IRS1* gene is involved in molecular processes that allow insulin to enter cells. Carriers of the AC haplotype have an increased risk of developing insulin resistance, followed by type 2 diabetes. These metabolic disorders may occur more frequently in overweight or obese individuals but may also be present in normal-weight individuals.

Test 84 (haplotype TRPM6)		
Locus	**Gene**	**Genotype**
rs3750425	TRPM6	C/C
rs2274924	TRPM6	T/T
Haplotip TC:		Absent

Comment

This result does not associate with increased risk for type 2 diabetes.

The *TRPM6* gene controls the intestinal absorption of magnesium as well as its reabsorption in the kidneys. Women carrying the TC haplotype have an increased risk of type 2 diabetes if the daily intake of magnesium is less than 250 milligrams.

To analyze the interaction between other genetic variations and physical activity, with roles in modifying the risk of type 2 diabetes, see **Package 4 - Genotypes associated with physical exercise or sports performance**.

Recommendation:

If you have not been diagnosed with type 2 diabetes, an aggressive approach to preventing type 2 diabetes is required, according to your doctor's advice. This approach includes both a healthy diet and an active lifestyle. Continuous monitoring of biochemical parameters that may indicate insulin resistance or type 2 diabetes may be required. If you have already been diagnosed with diabetes, your doctor may use this information to personalize and make more effective your antidiabetic treatment, and for adequate nutritional management.

CARDIOVASCULAR RISK

Test 85 (haplotype MT1A)		
Locus	**Gene**	**Genotype**
rs8052394	MT1A	A/G
rs11640851	MT1A	C/A
Haplotip GC:		Present

Comment

This haplotype is associated with an increased risk of cardiovascular disease in people over 60 years old, in the absence of sufficient zinc intake.

The *MT1A* gene is involved in the synthesis of zinc-containing metalloproteins. These proteins have antioxidant and protective roles against cardiovascular pathological changes. Carriers of the GC haplotype, over 60 years of age, who have insufficient zinc intake, are at increased risk for cardiovascular disease compared to those of the same age and carriers of other MT1A haplotypes.

Recommendation:
Daily zinc intake of minimum 16 milligrams.

POSTPRANDIAL HYPERLIPIDEMIA

Test 86 (haplotype APOA5)		
Locus	**Gene**	**Genotype**
rs662799	APOA5	A/A
rs3135506	APOA5	G/G
Haplotip APOA5*1:		Absent

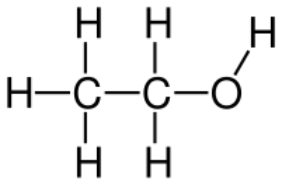
Comment

The absence of this haplotype is associated with an increased risk of postprandial hyperlipidemia, which may favor the development of cardiovascular disease.

The *APOA5* gene controls plasma levels of triglycerides, having an important role in preventing cardiovascular disease due to excessive fat intake. Carriers of the APOA5*1 haplotype have a degree of protection against high plasma triglyceride increases immediately after a high fat meal and are therefore relatively protected against this risk factor.

Recommendation:
Reduce significantly the intake of foods rich in animal fats, according to your nutritionist's advice.

ALCOHOL CONSUMPTION AND GASTRIC CANCER RISK



Test 87 (interacție gene)		
Locus	**Gene**	**Genotip**
rs1230025	ADH1	A/A
rs16941667	ALDH2	C/C
ADH1 x ALDH2:		Favorable

Comment

The result of this interaction does not recommend an exact limit of daily consumption of acohol. Alcohol should be consumed with moderation in any situation.

The *ADH1* gene controls the metabolism of alcohol to acetic aldehyde. The *ALDH2* gene controls the metabolism of acetic aldehyde to acetic acid. The concomitant presence of the A genetic variant (*ADH1*) and T genetic variant (*ALDH2*) increases the risk of gastric cancer at an alcohol intake of more than 5 g/day.

Test 88 (haplotip ADH1)		
Locus	**Gene**	**Genotip**
rs1230025	ADH1	A/A
rs13123099	ADH1	G/G
rs17033	ADH1	T/T
rs13133908	ADH1	T/G
Haplotip AGTT:		Present

Comment

This haplotype recommends limiting alcohol consumption to a maximum of 5 g alcohol/day.

The AGTT haplotype is associated with an increased risk of gastric cancer at an alcohol intake of more than 5 g/day.

Test 89 (haplotip ALDH2)		
Locus	**Gene**	**Genotip**
rs16941667	ALDH2	C/C
rs886205	ALDH2	A/A
rs968529	ALDH2	C/C
Haplotip CGT:		Absent

Comment

This haplotype does not recommend defining an exact limit of daily consumption of alcohol. Alcohol should be consumed with moderation in any situation.

The CGT haplotype is associated with an increased risk of gastric cancer at an alcohol intake of more than 5 g/day.

Recommendation:

Limit alcohol consumption to a maximum of 5 g/day (total alcohol 100%).

Package 4. Physical activity and sports performance

This package aims to identify the link between your genetic structure and the impact that physical activity can have on your health. These genetic tests identify personalized solutions for you that can not be considered appropriate for another person. These personalized recommendations are for you only.

What are the benefits?

Many of the risks for metabolic alterations are due not only to inadequate nutrition but also to the way the genetic structure may limit the ability to perform physical activity. These risks may vary from person to person due to genetic differences between different people. Nutrition and adequate physical activity can reduce these risks or solve these metabolic problems, depending on the structure of your genes.

This package provides you with specific recommendations, consistent with the scientific information obtained from many published studies. In this way, by optimizing your physical activity, you can reduce the risk of developing metabolic disorders.

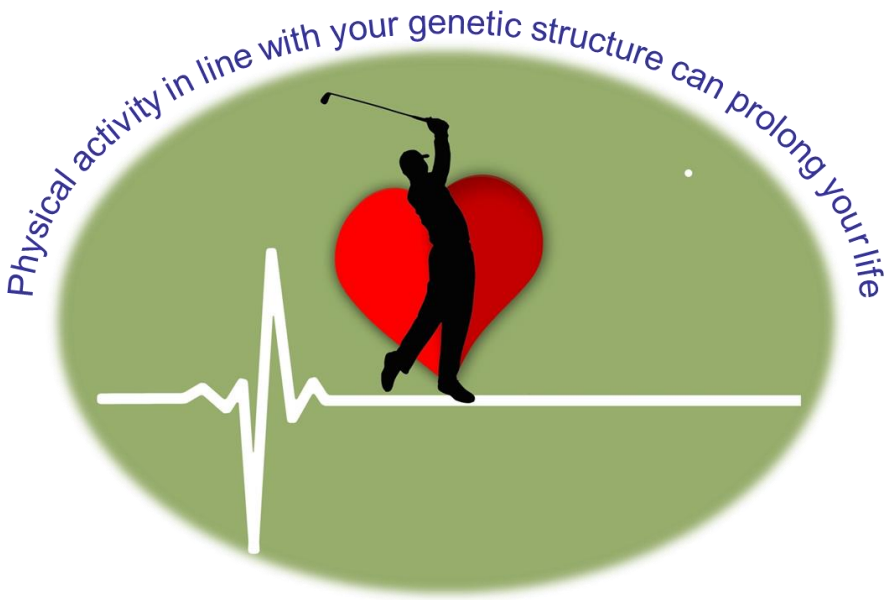
What should I do with these results?

Identifying risks related to physical activity should be followed by advice received from your fitness coach (or sports coach), your nutritionist or your doctor. Your coach is the most appropriate person who can correctly integrate the information provided by this package into an effective physical activity schedule. If certain metabolic disorders are already installed, these results can be used to alleviate such metabolic problems, in which case your doctor may also integrate this information.

SUMMARY

Your recommendations are the following:

Cardiac, vascular and respiratory functions	Genetic predisposition favoring sustained physical effort, without excessive accumulation of lactic acid. Average benefits (comparable to the average of the general population) on cardio-metabolic functions associated with moderate and repeated physical effort.
Muscle function	Normal sprint potential. Normal muscle strength capacity. Increased potential to improve physical performance in physically active individuals over 60 years of age.
Body weight	Average potential for weight gain (same as the average population potential). This information may be useful to those who practice sports or routine physical activities in order to manage body weight, as needed.
Metabolism	It is recommended to avoid physical effort of maximum intensity, daily and repeated. Practicing small and medium intensity physical activities is recommended for improving glucose and lipid metabolism. Maximum efforts can be achieved, but it is advisable to avoid these situations as far as possible.



The algorithms used in this package take into account the latest scientific findings published in specialized, peer reviewed, scientific journals. These algorithms are the intellectual property of Advanced Nutrigenomics. The genetic variations included in this package, as well as the nutrients for which personalized values are offered, are the result of continuous evaluation of existing published studies.

CARDIAC, VASCULAR AND RESPIRATORY FUNCTIONS

Test 90		
Locus	**Gene**	**Genotype**
rs1049434	SLC16A1	T/T

Comment
This genotype increases your endurance during physical activity.

The *SLC16A1* gene (*MCT1*) contributes to the control of lactic acid and pyruvic acid transport through cell membranes. T/T genotype carriers have an increased resistance to sustained physical effort (endurance).

Test 91 (haplotype PPARA)		
Locus	**Gene**	**Genotype**
rs135542	PPARA	C/C
rs135539	PPARA	C/C
rs4253728	PPARA	G/G
rs1800206	PPARA	C/C
rs4253778	PPARA	G/G
Haplotip H-23:		Absent

Comment
The absence of this haplotype results in average benefits (comparable to the average in the general population), in reducing cardiovascular risk, in the presence of moderate intensity physical activity.

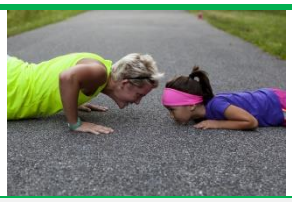
The *PPARA* gene controls the activity of peroxisomes involved in many metabolic processes, including cardiovascular and anti-inflammatory protection. The presence of the H-23 haplotype (CAGCG) is associated with a favorable, maximized cardiovascular risk reduction response in individuals who practice moderate and daily physical activity.

Conclusion

Genetic predisposition favoring sustained physical effort, without excessive accumulation of lactic acid.

Average benefits (comparable to the average of the general population) on cardio-metabolic functions associated with moderate and repeated physical effort.

MUSCLE FUNCTION



Test 92		
Locus	**Gene**	**Genotype**
rs1815739	ACTN3	T/C

Comment
This genotype does not negatively affect the ability for sprinting.

The *ACTN3* gene encodes and controls the synthesis of the protein known as alpha-actinin 3. This protein contributes to the ability of type II muscle fibers to contract rapidly during sprinting. Those who carry the genetic variation T in both copies of the gene (T/T genotype) have a reduced capacity for sprinting.

Test 93		
Locus	**Gene**	**Genotype**
rs12676	CHDH	C/C

Comment
This genotype does not affect muscle contraction (muscle strength).

The *CHDH* gene controls the conversion of choline into betaine, generating a large amount of ATP in the mitochondria. Individuals carrying the genetic variation A in both copies of the gene (A/A genotype) have mitochondria with altered structure, associated with a reduced capacity to generate the amount of ATP required for muscle contraction. This outcome might be improved by supplementation with choline and betaine.

Test 94		
Locus	**Gene**	**Genotype**
rs1799752	ACE	Del/Del

Comment
This genotype is associated with improved physical performance at older ages.

The *ACE* gene contributes to blood pressure control. Individuals over 60 years of age who carry the Del variation in both copies of the gene (Del/Del genotype) can benefit from a gradual improvement in physical performance, if they remain physically active. People of the same age, who carry the Del/In or In/In genotypes, can benefit from physical activity, but with less chance of improving these performances.

Conclusion

Normal sprint potential.
Normal muscle strength capacity.
Increased potential to improve physical performance in physically active individuals over 60 years of age.

BODY WEIGHT

Test 95		
Locus	**Gene**	**Genotype**
rs17817449	FTO	T/T

Comment
This genotype is not associated with predisposition to weight gain.

Test 96		
Locus	**Gene**	**Genotype**
rs1421085	FTO	T/T

Comment
This genotype is not associated with predisposition to weight gain.

The *FTO* gene helps control the hunger sensation from the hypothalamus as well as food preferences. G/G genotype (rs17817449) or C/C genotype (rs1421085) carriers have increased tendency to gain weight easier, coupled with increased calorie intake.

Conclusion

Average potential for weight gain (same as the average population potential).

This information may be useful to those who practice sports or routine physical activities in order to manage body weight, as needed.

METABOLISM

Test 97		
Locus	**Gene**	**Genotype**
rs1496653	UBE2E2	A/A
rs6795735	ADAMTS9-AS2	T/T
rs10842994	KLHDC5	C/T
rs2943640	IRS1	C/C
Scor genetic:		5

Comment

This score recommends avoiding physical effort of maximum intensity, daily and repeated.

This genetic score is a result of the interaction between certain genetic variations within genes involved in metabolic activity (especially carbohydrate metabolism), and the of physical activity. The score, ranging from 0 to 8, indicates the predisposition that certain physical activity type might be associated with a higher risk of metabolic disorders, such as increased insulin resistance and type 2 diabetes.

Conclusion

It is recommended to avoid physical effort of maximum intensity, daily and repeated. Practicing small and medium intensity physical activities is recommended for improving glucose and lipid metabolism. Maximum efforts can be achieved, but it is advisable to avoid these situations as far as possible.

Package 5. Other tests

This packkage is meant to inform you about certain genetic variations that may be known to be associated with the occurrence of certain diseases. The results of this package can not be considered as diagnostic tests. The existence of any of these variations does not mean that such a condition is already present, or that the occurrence of such a disease is inevitable. This package also identifies certain genetic variations that may interfere with certain drug treatments. Therefore, the tests of this package are not medical diagnostic tests. Only physicians are able to perform a medical diagnosis, taking into account, in addition to the existence of genetic variations, other factors such as family history, manifestations and symptoms, other medical analyzes, etc.

What are the benefits?

The onset of some diseases depends, in part, on the existence of genetic changes. Most of the time, however, these genetic changes are not enough for the onset of these conditions.

Knowing about the presence of genetic changes allows the physician not only to establish appropriate prevention against the disease onset, but provides also with essential information for the treatment of some diseases with genetic substrates. These tests may also provide important information regarding the efficacy of certain drug treatments. These results are for information purposes nly and cannot be considered as diagnostic tools.

What should I do with these results?

The results of this package should be interpreted by your doctor, who is the only able to interpret them correctly. Therefore, please inform your doctor about the results of this package. If there is any suspicion in regard to a particular genetic variation, it is necessary to confirm this result using a dedicated genetic diagnostic test.

Genotypes associated with drug response

ESTROGENS/ESTROGEN-CONTAINING CONTRACEPTIVES IN WOMEN

Test 98		
Locus	**Gene**	**Genotype**
rs1799963	F2	G/G

The *F2* gene (factor II, thrombin / prothrombin) helps control blood clotting. **Individuals carrying the genetic variation A (also known as genetic variation G20210A) have an increased risk of thrombosis (thrombophilia).** Women who carry this genetic variation, and who undergo estrogen treatments (including estrogen-containing contraceptives), have an increased risk of thrombosis as a side effect of these treatments.

Test 99		
Locus	**Gene**	**Genotype**
rs6025	F5	C/C

The F5 gene (factor V Leiden) helps to control blood coagulation. **Carriers of the T allele (also known as genetic variation R506Q) have an increased risk of thrombosis (thrombophilia)**. Women carrying this genetic variation, and following estrogen treatments (including estrogen-containing contraceptives), have an increased risk of thrombosis as a side effect of these treatments.

TREATMENT WITH THIOPURINES

Test 100		
Locus	**Gene**	**Genotype**
rs2647047	class HLA II	C/C

Comment
Genetic risk variant is ABSENT.

Test 101		
Locus	**Gene**	**Genotype**
rs7745656	class HLA II	G/T

Comment
Genetic risk variant is PRESENT.

Test 102		
Locus	**Gene**	**Genotype**
rs2647087	class HLA II	A/C

Comment
Genetic risk variant is PRESENT.

Test 103		
Locus	**Gene**	**Genotype**
rs6935723	class HLA II	T/C

Comment
Genetic risk variant is PRESENT.

Test 104		
Locus	**Gene**	**Genotype**
rs2647089	class HLA II	T/C

Comment
Genetic risk variant is PRESENT.

The HLA II genes encode proteins involved in the major histocompatibility complex II (MHC II), with roles in extracellular presentation of some antigens to T lymphocytes. This mechanism is involved in immune control. Alterations of this mechanism are also responsible for the onset of autoimmune diseases or reactions. In the case of people receiving thiopurine therapy, the presence of at least one of the above genetic variations significantly increases the risk of development secondary pancreatitis due to thiopurine therapy. Thus, carriers of these genetic variations have a risk of up to 17% for developing pancreatitis during treatment with tiopurine (between 21 and 27 days of treatment), when compared to the risk of those who do not have these genetic variations (4-7 %).

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Test 105 (haplotype TPMT)		
Locus	**Gene**	**Genotype**
rs1800462	TPMT	C/C
rs1800460	TPMT	C/C
rs1142345	TPMT	T/T
Identified haplotype:		*1/*1

Comment
This haplotype does not require modification of the generally recommended thiopurines dosage.

The *TPMT* gene controls the metabolism of thiopurines (inactivation by methylation). Individuals carrying certain genetic variations classified by certain haplotypes have a reduced metabolic capacity for these drugs and, consequently, an increased risk of complications (toxic side effects) such as myelosuppression, anemia, bleeding, leukopenia, and infections. In these situations, it is necessary to reduce thiopurine doses according to the recommendations for each treatment protocol applied.

Conclusion

It is recommended that thiopurine doses be adjusted according to the protocol applied and the type of genetic modification identified.

This test cannot detect haplotype *4 TPMT.

RESPONSE TO VITAMIN D IN ATOPIC DERMATITIS

Test 106 (haplotype CYP24A1)		
Locus	**Gene**	**Genotype**
rs2248359	CYP24A1	C/T
rs2296241	CYP24A1	G/A
Haplotype of risk:		Present

Comment
This haplotype is associated with severe atopic dermatitis or refractory to treatment.

The *CYP24A1* gene is involved in the metabolism of active vitamin D form. Individuals carrying CA or TA haplotypes, who are diagnosed with atopic dermatitis, can benefit from the addition of Vitamin D to the treatment regimen if the disease is severe or refractory to the previously applied treatment protocol.

Test 107 (haplotype CYP27B1)		
Locus	**Gene**	**Genotype**
rs703842	CYP27B1	G/G
rs10877012	CYP27B1	T/T
rs3782130	CYP27B1	C/C
rs4646536	CYP27B1	G/G
Haplotype AGGG:		Absent

Comment
The absence of a risk haplotype is not associated with severe atopic dermatitis or refractory to treatment.

The *CYP27B1* gene controls the activation of Vitamin D (calcitriol synthesis). Individuals carrying the AGGG haplotype, who are diagnosed with atopic dermatitis, may benefit from the addition of calcitriol to the treatment regimen if the form of the disease is severe or refractory to the previously applied treatment protocol.

Conclusion

It is advisable to add calcitriol to the treatment regimen for atopic dermatitis.

TREATMENT WITH METHOTREXATE

Test 108		
Locus	**Gene**	**Genotype**
rs1677693	DHFR	G/T

Comment
This genotype may interfere with standard doses of methotrexate. Treatment with lower doses may be advised.

Test 109		
Locus	**Gene**	**Genotype**
rs1643659	DHFR	T/C

Comment
This genotype may interfere with standard doses of methotrexate. Treatment with lower doses may be advised.

Test 110		
Locus	**Gene**	**Genotype**
rs1650694	DHFR	G/C

Comment
This genotype may be associated with resistance to methotrexate (acute lymphoblastic leukemia, ALL).

Test 111		
Locus	**Gene**	**Genotype**
rs408626	DHFR	T/C

Comment
This genotype is not associated with resistance to methotrexate (acute lymphoblastic leukemia, ALL).

Test 112		
Locus	**Gene**	**Genotype**
rs1105525	DHFR	C/C

Comment
This genotype is not associated with resistance to methotrexate (acute lymphoblastic leukemia, ALL).

Test 113		
Locus	**Gene**	**Genotype**
rs1650697	DHFR	G/G

Comment
This genotype is not associated with resistance to methotrexate (acute lymphoblastic leukemia, ALL).

Test 114		
Locus	**Gene**	**Genotype**
rs3045983	DHFR	In/In

Comment
This genotype is not associated with resistance to methotrexate (acute lymphoblastic leukemia, ALL).

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Test 115		
Locus	**Gene**	**Genotype**
rs1232027	DHFR	G/A

Comment
This genotype is associated with a better response to methotrexate treatment in psoriatic arthritis.

Test 116		
Locus	**Gene**	**Genotype**
rs7387	DHFR	ND

Comment
This genotype could not be determined.

The *DHFR* gene controls the synthesis of tetrahydrofolic acid from dihydrofolic acid. Carriers of specific genetic variations may have a different response to methotrexate treatment. Depending on your condition and the information your doctor considers relevant, these tests may help to make a therapeutic decision, modify the dose of methotrexate or administer alternative drugs.

Conclusion

Your doctor should be informed if you are taking a treatment containing methotrexate or before you have been prescribed such treatment. Only the doctor can decide how to use the information provided by these tests.

PYRIDOXINE TREATMENT IN HOMOCYSTEINURIA

Test 117		
Locus	**Gene**	**Genotype**
rs375846341	CBS	T/T

Comment
This genotype associates with adequate response to pyridoxine treatment in homocysteinuria.

The *CBS* gene controls the use of Vitamin B6 in the conversion of homocysteine to cystathionine. Carriers of the G/G genotype, who are suffering from homocysteinuria, do not respond adequately to pyridoxine treatment, whereas T/G genotype carriers may have a poor response to this treatment.

Conclusion

No changes are suggested to the pyridoxine treatment regimen for homocysteinuria.

WARFARIN SENSITIVITY

Test 118		
Locus	**Gene**	**Genotype**
rs9923231	VKORC1	C/C

Test 119		
Locus	**Gene**	**Genotype**
rs1799853	CYP2C9	C/C

Test 120		
Locus	**Gene**	**Genotype**
rs1057910	CYP2C9	A/A

The result of this test is a combination of genotypes that defines the therapeutic dose of varfarin (see below), in the absence of other contraindications.

The genotype for the rs9923231 locus is provided for the forward DNA strand. Therefore, the following results for this genotype are equivalent: C/C is equivalent to G/G on the reverse strand; C/T is equivalent to G/A on the reverse strand; T/T is equivalent to A/A on the reverse strand.

Results	
Gene	**Genotype / Haplotype**
VKORC1	C/C (G/G)
CYP2C9	CYP2C9 *1/*1

The *VKORC1* gene controls blood clotting due to Vitamin K activation. The *CYP2C9* gene controls the metabolism (inactivation) of warfarin. To find the recommended warfarin dose based on the result of this test, see the table below.

This table follows the PharmGKB recommendations for the personalization of coumarin agents (warfarin equivalent) based on genotypes VKORC1 and CYP2C9 (https://www.pharmgkb.org/molecule/PA451906). Doses are mg/day warfarin.

VKORC1	CYP2C9 *1/*1	CYP2C9 *1/*2	CYP2C9 *1/*3	CYP2C9 *2/*2	CYP2C9 *2/*3	CYP2C9 *3/*3
C/C (G/G)	5-7	5-7	3-4	3-4	3-4	0,5-2
C/T (G/A)	5-7	3-4	3-4	3-4	0,5-2	0,5-2
T/T (A/A)	3-4	3-4	0,5-2	0,5-2	0,5-2	0,5-2

Conclusion

The recommended dose of WARFARIN (Coumadin) is 5-7 mg/day.

Genotypes associated with some medial conditions

ACHONDROPLASIA

Test 121

Locus	Gene	Genotype	Reference	Mutation	Your result
rs28931614	FGFR3	G/G	G/G	A, C	Negative

The *FGFR3* gene controls bone growth by stimulating cartilage proliferation during the growth period. Individuals carrying a genetic variation A or C (rs28931614) will develop acondroplasia, starting with fetal life or early childhood. This mutation is responsible for approximately 98% of cases of acondroplasia. This mutation can be transmitted by either parent or may occur spontaneously. The existence of two mutations (in both copies of the gene) is incompatible with survival.

ASTHENOSPERMIA

Test 122

Locus	Gene	Genotype	Reference	Mutation	Your result
rs12676	CHDH	C/C	C/C	A	Negative

The *CHDH* gene controls the synthesis of betaine from the choline. This reaction is accompanied by the release of ATP (energy) required for normal sperm motility. Male individuals diagnosed with asthenospermia carrying the A/A genotype may benefit from improved sperm motility by addition of betaine, 5-methyltetrahydrofolate (5-MTHF) and Vitamin B12 to the treatment regimen.

Recommendation
This test is not relevant to you.

GAUCHER DISEASE

Test 123

Locus	Gene	Genotype	Reference	Mutation	Your result
rs76763715	GBA	T/T	T/T	C, G	Negative
rs421016	GBA	A/A	A/A	C, G	Negative

The *GBA* gene encodes for the beta-glucocerebrosidase enzyme, active in lysosomes, and which has the role of recycling some metabolites. Depending on the heterozygous or homozygous status for the above genetic variations, a person may be transmitter of these variations (parents) or may have Gaucher disease (typically homozygous or carriers of several genetic variations involved). These two variations, in various combinations or along with the presence of other mutations in the GBA gene, represent about 89% of the genetic causes of Gaucher disease. Analysis of these genetic variations should be performed by a geneticist.

BRCA1/BRCA2

Test 124

Locus	Gene	Genotype	Reference	Mutation	Your result
rs80357969	BRCA1	In/In	CT/CT (In/In)	- (Del 2 bp)	Negative
rs80356898	BRCA1	G/G	G/G	A	Negative
rs80357927	BRCA1	In/In	T/T (In/In)	- (Del)	Negative
rs80357468	BRCA1	C/C	C/C	T	Negative
rs80359874	BRCA1	In/In	In/In	- (Del 40 bp)	Negative
rs28897672	BRCA1	A/A	A/A	C	Negative
rs730881459	BRCA1	In/In	A/A (In/In)	- (Del)	Negative
rs80357526	BRCA1	In/In	In/In	- (Del 4 bp)	Negative
rs80357082	BRCA1	T/T	T/T	A	Negative
rs80358061	BRCA1	A/A	A/A	C	Negative
rs80358163	BRCA1	T/T	T/T	C	Negative
rs62625306	BRCA1	C/C	C/C	A, T	Negative
rs80357664	BRCA1	In/In	CT/CT (In/In)	- (Del 2 bp)	Negative
rs80357669	BRCA1	In/In	G/G (In/In)	- (Del)	Negative
rs80356925	BRCA1	G/G	G/G	C	Negative
rs80357971	BRCA1	In/In	TT/TT (In/In)	- (Del 2 bp)	Negative
rs80356978	BRCA1	C/C	C/C	A	Negative
rs80357661	BRCA1	In/In	In/In	- (Del 4 bp)	Negative
rs80357819	BRCA1	In/In	In/In	- (Del 5 bp)	Negative
rs80357115	BRCA1	A/A	A/A	C	Negative
rs273899692	BRCA1	AG/AG	AG/AG	TA	Negative
rs80356936	BRCA1	A/A	A/A	G	Negative
rs80357424	BRCA1	C/C	C/C	A	Negative
rs80357877	BRCA1	In/In	In/In	- (Del 11 bp)	Negative
rs80357509	BRCA1	In/In	T/T (In/In)	- (Del)	Negative
rs80357621	BRCA1	In/In	A/A (In/In)	- (Del)	Negative
rs62625307	BRCA1	G/G	G/G	A/A	Negative
rs80357797	BRCA1	Del/Del	Del/Del	+ (In 4 bp)	Negative
rs28897686	BRCA1	C/C	C/C	T	Negative
rs80357868	BRCA1	In/In	In/In	- (Del 4 bp)	Negative
rs80357848	BRCA1	Del/Del	Del/Del	+ T (In)	Negative
rs80357634	BRCA1	Del/Del	Del/Del	+ A (In)	Negative
rs80357711	BRCA1	In/In	T/T (In/In)	- (Del)	Negative
rs80358178	BRCA1	C/C	C/C	T	Negative
rs80357260	BRCA1	G/G	G/G	A	Negative
rs80356991	BRCA1	C/C	C/C	T	Negative

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Test 124

Locus	Gene	Genotype	Reference	Mutation	Your result
rs41293455	BRCA1	G/G	G/G	A	Negative
rs80358027	BRCA1	C/C	C/C	T	Negative
rs80357433	BRCA1	G/G	G/G	C	Negative
rs80356862	BRCA1	G/G	G/G	C	Negative
rs80359876	BRCA1	In/In	In/In	- (Del 19 bp)	Negative
rs55770810	BRCA1	G/G	G/G	T	Negative
rs41293459	BRCA1	C/C	C/C	T	Negative
rs28897696	BRCA1	G/G	G/G	T, A	Negative
rs80357872	BRCA1	In/In	G/G (In/In)	- (Del)	Negative
rs80357867	BRCA1	In/In	In/In	- (Del 4 bp)	Negative
rs80358004	BRCA1	C/C	C/C	A, G, T	Negative
rs80357462	BRCA1	G/G	G/G	C	Negative
rs80357123	BRCA1	G/G	G/G	A	Negative
rs397507246	BRCA1	Del/Del	Del/Del	+G (In)	Negative
rs80358150	BRCA1	C/C	C/C	G, T	Negative
rs80358099	BRCA1	C/C	C/C	A	Negative
rs41293463	BRCA1	A/A	A/A	C, T	Negative
rs786203663	BRCA1	CCACA/CCACA	CCACA/CCACA	TCACT	Negative
rs80358073	BRCA1	C/C	C/C	A, G, T	Negative
rs80356962	BRCA1	C/C	C/C	T	Negative
rs41293465	BRCA1	G/G	G/G	A	Negative
rs80357919	BRCA1	In/In	In/In	- (Del 4 bp)	Negative
rs80357670	BRCA1	In/In	AC/AC (In/In)	- (Del 2 bp)	Negative
rs397515635	BRCA2	Del/Del	Del/Del	+ (In 4 bp)	Negative
rs397507265	BRCA2	In/In	G/G (In/In)	- (Del)	Negative
rs80359277	BRCA2	In/In	In/In	- (Del 4 bp)	Negative
rs80359283	BRCA2	In/In	AG/AG (In/In)	- (Del 2 bp)	Negative
rs80358428	BRCA2	G/G	G/G	T	Negative
rs80358435	BRCA2	G/G	G/G	T	Negative
rs80358452	BRCA2	T/T	T/T	G	Negative
rs80359301	BRCA2	In/In	A/A (In/In)	- (Del)	Negative
rs80359302	BRCA2	In/In	In/In	- (Del 5 bp)	Negative
rs80358474	BRCA2	C/C	C/C	T	Negative
rs80359322	BRCA2	In/In	C/C (In/In)	- (Del)	Negative
rs80358494	BRCA2	C/C	C/C	T	Negative
rs397507285	BRCA2	T/T	T/T	G	Negative
rs80358515	BRCA2	C/C	C/C	T	Negative
rs398122752	BRCA2	In/In	In/In	- (Del 5 bp)	Negative
rs80359351	BRCA2	In/In	In/In	- (Del 4 bp)	Negative

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Test 124

Locus	Gene	Genotype	Reference	Mutation	Your result
rs80358533	BRCA2	A/A	A/A	T	Negative
rs80359372	BRCA2	In/In	In/In	- (Del 4 bp)	Negative
rs730881521	BRCA2	A/A	A/A	T	Negative
rs80359380	BRCA2	Del/Del	Del/Del	+ (In 2 bp)	Negative
rs80359391	BRCA2	In/In	TG/TG (In/In)	- (Del 2 bp)	Negative
rs746229647	BRCA2	In/In	TG/TG (In/In)	- (Del 2 bp)	Negative
rs80358638	BRCA2	G/G	G/G	T	Negative
rs276174843	BRCA2	CT/CT	CT/CT	DelCTInA	Negative
rs730881607	BRCA2	In/In	TT/TT (In/In)	- (Del 2 bp)	Negative
rs276174844	BRCA2	In/In	In/In	- (Del 5 bp)	Negative
rs80359444	BRCA2	In/In	In/In	- (Del 5 bp)	Negative
rs80359448	BRCA2	In/In	A/A (In/In)	- (Del)	Negative
rs80359449	BRCA2	In/In	In/In	- (Del 4 bp)	Negative
rs80359454	BRCA2	In/In	In/In	- (Del 4 bp)	Negative
rs80358692	BRCA2	A/A	A/A	T	Negative
rs80359461	BRCA2	In/In	A/A (In/In)	- (Del)	Negative
rs80359470	BRCA2	In/In	AA/AA (In/In)	- (Del)	Negative
rs80359473	BRCA2	In/In	In/In	- (Del 4 bp)	Negative
rs80358721	BRCA2	C/C	C/C	G	Negative
rs80359480	BRCA2	Del/Del	Del/Del	+A (In)	Negative
rs80359494	BRCA2	In/In	In/In	- (Del 4 bp)	Negative
rs80359499	BRCA2	Del/Del	Del/Del	+T (In)	Negative
rs770318608	BRCA2	In/In	In/In	- (Del 4 bp)	Negative
rs80358783	BRCA2	A/A	A/A	T	Negative
rs80359525	BRCA2	In/In	In/In	- (Del 5 bp)	Negative
rs80359526	BRCA2	In/In	In/In	- (Del 4 bp)	Negative
rs41293497	BRCA2	C/C	C/C	A, G, T	Negative
rs80359533	BRCA2	In/In	AT/AT (In/In)	- (Del 2 bp)	Negative
rs80359538	BRCA2	In/In	In/In	- (Del 4 bp)	Negative
rs80359541	BRCA2	In/In	C/C (In/In)	- (Del)	Negative
rs80359543	BRCA2	In/In	In/In	- (Del 4 bp)	Negative
rs80359550	BRCA2	In/In	T/T (In/In)	- (Del)	Negative
rs80359555	BRCA2	In/In	In/In	- (Del 5 bp)	Negative
rs80359558	BRCA2	In/In	In/In	- (Del 5 bp)	Negative
rs276174868	BRCA2	GCA/GCA	GCA/GCA	DelGCAInC	Negative
rs11571658	BRCA2	In/In	TT/TT (In/In)	- (Del 2 bp)	Negative
rs81002899	BRCA2	T/T	T/T	C, G	Negative
rs80359577	BRCA2	Del/Del	Del/Del	+A (In)	Negative
rs80359584	BRCA2	In/In	In/In	- (Del 5 bp)	Negative

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Test 124

Locus	Gene	Genotype	Reference	Mutation	Your result
rs80359590	BRCA2	Del/Del	Del/Del	+T (In)	Negative
rs80359598	BRCA2	In/In	In/In	- (Del 4 bp)	Negative
rs80359604	BRCA2	In/In	GT/GT (In/In)	- (Del 2 bp)	Negative
rs730881601	BRCA2	Del/Del	Del/Del	+ (In 4 bp)	Negative
rs80358920	BRCA2	C/C	C/C	T	Negative
rs28897743	BRCA2	G/G	G/G	A	Negative
rs80359636	BRCA2	In/In	CT/CT (In/In)	- (Del 2 bp)	Negative
rs80359647	BRCA2	Del/Del	Del/Del	+G (In)	Negative
rs80359671	BRCA2	In/In	In/In	- (Del 5 bp)	Negative
rs80359677	BRCA2	In/In	AG/AG (In/In)	- (Del 2 bp)	Negative
rs80359027	BRCA2	G/G	G/G	A	Negative
rs80359035	BRCA2	C/C	C/C	A, T	Negative
rs41293511	BRCA2	G/G	G/G	C	Negative
rs41293513	BRCA2	A/A	A/A	C	Negative
rs730881581	BRCA2	G/G	G/G	A	Negative
rs80359705	BRCA2	In/In	C/C (In/In)	- (Del)	Negative
rs81002837	BRCA2	G/G	G/G	A, T	Negative
rs276174907	BRCA2	TAG/TAG	TAG/TAG	DelTAGInAA	Negative
rs81002798	BRCA2	G/G	G/G	A, T	Negative
rs276174914	BRCA2	A..T/A..T	A..T/A..T	Del9In10	Negative
rs81002862	BRCA2	A/A	A/A	G	Negative
rs80359752	BRCA2	Del/Del	Del/Del	+A (In)	Negative
rs81002889	BRCA2	G/G	G/G	A, C	Negative
rs80359200	BRCA2	C/C	C/C	G	Negative

The *BRCA1* and *BRCA2* genes control the process of repairing DNA replication errors. Numerous genetic variations have been found in the structure of these genes, many of which are associated with various forms of cancer, or causing various forms of cancer.

If you have a POSITIVE result for any of the above mutations, you should ask your doctor to establish a strategy to prevent and reduce the risk of cancer. Additional, more extensive, genetic testing may be required.

ALPHA-1 ANTITRYPSIN DEFICIENCY

Test 125

Locus	Gene	Genotype	Reference	Mutation	Your result
rs28929474	SERPINA1	C/C	C/C	T	Negative
rs17580	SERPINA1	T/T	T/T	A	Negative

The *SERPINA1* gene encodes and controls the synthesis of a protein, alpha-1 antitrypsin, which limits the action of an enzyme, neutrophil-elastase. Normally, neutrophil-elastase is released by leukocytes to fight infections in tissues, including the lungs and the liver. Deficiency of alpha-1 antitrypsin causes the activation and action of neutrophil-elastase to be exaggerated, leading to diseases affecting various organs.

rs28929474 — For this locus, a POSITIVE result might be associated with severe deficiency of alpha-1 antitrypsin, causing pulmonary emphysema and hepatic impairment. People with this mutation will always transmit this mutation to their children. This mutation is also associated with liver complications in people diagnosed with cystic fibrosis (see below). A CARRIER result might indicate that these people have a 50% chance of transmitting the mutation to their children. A CARRIER of this mutation is also associated with an increased risk of granulomatosis with polyangiitis.

rs17580 — For this locus, a POSITIVE result might be associated with mild deficiency of alpha-1 antitrypsin, associated with an increased risk of chronic obstructive pulmonary disease (COPD). People with a POSITIVE result will always transmit this mutation to their children. A CARRIER result means that these people have a 50% chance of transmitting the mutation to their children.

If there is a positive/carrier result for any of the above mutations, you should ask your doctor for a strategy to prevent and reduce the risk of lung or liver damage. Additional genetic testing may be required.

BIOTINIDASE DEFICIENCY

Test 126

Locus	Gene	Genotype	Reference	Mutation	Your result
rs80338685	BTD	A/A	A/A	C	Negative
rs80338686	BTD	C/C	C/C	T	Negative
rs13078881	BTD	G/G	G/G	C	Negative
rs13073139	BTD	G/G	G/G	A	Negative

The *BTD* gene controls the recycling of biotin (vitamin B7, vitamin H), ie the release of biotin from food proteins. The free form of biotin is then used in various metabolic processes that contribute to the metabolism of proteins, fatty acids and carbohydrates. Individuals carrying one or more mutations (POSITIVE result) may suffer, with varying degrees of severity, from biotinidase deficiency, a disease that begins to manifest in the newborn or small child. Detected on time, this disease can be successfully treated using biotin.

If there is a POSITIVE result for any of the above mutations, you should ask your doctor for a strategy to prevent or reduce the biotinidase deficiency. Additional genetic testing or other biochemical testing may be required.

FACTOR II DEFICIENCY (PROTHROMBIN)

Test 127

Locus	Gene	Genotype	Reference	Mutation	Your result
rs1799963	F2	G/G	G/G	A	Negative

The *F2* gene (factor II, thrombin/prothrombin) helps control blood clotting. Individuals carrying the genetic variation A (also known as genetic variation G20210A) have an increased risk of thrombosis (thrombophilia). A POSITIVE result may indicate increased risk of thrombophilia.

If there is a POSITIVE result for the above mutation, you should ask your doctor for a strategy to prevent or reduce the manifestations associated with thrombophilia. Additional genetic testing and other tests may be required.

FACTOR V DEFICIENCY (LEIDEN)

Test 128

Locus	Gene	Genotype	Reference	Mutation	Your result
rs6025	F5	C/C	C/C	T	Negative

The *F5* gene (factor V Leiden) helps control blood coagulation. T allele carriers (also known as genetic variation R506Q) have an increased risk of thrombosis (thrombophilia). A POSITIVE result indicates increased risk of thrombophilia.

If there is a POSITIVE result for the above mutation, you should ask your doctor for a strategy to prevent or reduce the manifestations associated with thrombophilia. Additional genetic testing and other tests may be required.

FAMILIAL MEDITERANEAN FEVER

Test 129

Locus	Gene	Genotype	Reference	Mutation	Your result
rs28940578	MEFV	C/C	C/C	T	Negative

The *MEFV* gene controls the synthesis of a protein (pyrin/marenostrin) that is involved in the control of inflammatory processes. Usually, carriers of the T/T genotype are those who suffer from this condition. In rare cases, due to the co-dominance process, some carriers of the C/T genotype may also manifest this condition.

If there is a POSITIVE result for the above mutation, you should ask your doctor for a strategy to prevent or reduce the manifestations associated with familial mediteranean fever. Additional genetic testing and other tests may be required.

CYSTIC FIBROSIS

Test 130

Locus	Gene	Genotype	Reference	Mutation	Your result
rs113993960	CFTR	In/In	CTT/CTT (In/In)	- (Del 3 bp)	Negative

The *CFTR* gene controls exocrine gland excretion (mucus production, sweating, digestive enzymes, etc.). Individuals with a POSITIVE result (homozygous for deletion) are, usually, diagnosed with cystic fibrosis, this mutation being responsible for 70% of cases of cystic fibrosis. People with a genetic diagnosis of CARRIER (heterozygotes) are generally unaffected, but can transmit this mutation to their children. In rare cases, people who are heterozygous for this mutation may suffer from cystic fibrosis if this mutation is accompanied by other mutations.

If there is a POSITIVE result for the above mutation, you should ask your doctor for a strategy to prevent or reduce the manifestations associated with cystic fibrosis. Additional genetic testing and other tests may be required.

HEREDITARY HEMOCHROMATOSIS

Test 131

Locus	Gene	Genotype	Reference	Mutation	Your result
rs1799945	HFE	C/C	C/C	G	Negative
rs1800730	HFE	A/A	A/A	T	Negative
rs1800562	HFE	G/G	G/G	A	Negative

The *HFE* gene helps control the circulation and distribution of iron in the body. Persons carrying any of the several genetic variations in this gene are at increased risk or may develop hereditary hemochromatosis, depending on the location of these genetic variations and the presence of one or more variations. The onset of this condition depends, in part, on the amount of iron intake from foods as well as the degree of exposure to excess iron. Therefore, a positive disease diagnosis in general can not be determined solely on the basis of genetic analysis. A POSITIVE result indicates, in this context, the possibility of an increased risk of hereditary hemochromatosis, and may contribute to completing the information required to determine a medical diagnosis.

If there is a POSITIVE result for any of the above mutations, you should ask your doctor for a strategy to prevent or reduce the manifestations associated with hemochromatosis. Additional genetic testing and other tests may be required.

HOMOCYSTINURIA

Test 132

Locus	Gene	Genotype	Reference	Mutation	Your result
rs375846341	CBS	T/T	T/T	G	Negative

The *CBS* gene controls the use of Vitamin B6 in the metabolism of homocysteine to cystathionine. Carriers of the genetic variation G have an increased risk of developing homocystinuria. A POSITIVE result may indicate an increased risk of developing this condition.

If there is a POSITIVE result for the above mutation, you should ask your doctor for a strategy to prevent or reduce the manifestations associated with homocystinuria. Additional genetic testing and other tests may be required.

CONGENITAL LACTASE DEFICIENCY

Test 133

Locus	Gene	Genotype	Reference	Mutation	Your result
rs121908936	LCT	A/A	A/A	T	Negative

The *LCT* gene controls the process of hydrolysis ("digestion") of lactose. A parent, carrier for the genetic variation T (genotype A/T), can transmit it to his or her child. If the newborn has two genetic variations T (genotype T/T), he or she may develop congenital alactasia. A POSITIVE result indicates the presence of two copies of the gene containing the genetic variation T, which may be accompanied by the manifestation of congenital alactasia in the newborn. A CARRIER result indicates the presence of a copy of the gene containing the genetic variation T. The carrier does not manifest the disease but can transmit this genetic variation to his or her children.

If there is a POSITIVE result for the above mutation, you should ask your doctor for a strategy to prevent or reduce the manifestations associated with congenital alactasia. Additional genetic testing and other tests may be required.

LACTOSE INTOLERANCE

Test 134

Locus	Gene	Genotype	Reference	Mutation	Your result
rs4988235	MCM6	G/G	A/A	G	POSITIVE
rs182549	MCM6	C/C	T/T	C	POSITIVE

The *MCM6* gene controls the expression of the *LCT* gene. *LCT* controls lactase synthesis, an enzyme required to digest milk containing lactose. Carriers of one or more genetic variations in the *MCM6* gene may develop (especially if they are homozygous for at least one of these genetic variants: G/G or C/C) lactose intolerance, which generally begins to manifest at the end of the childhood or in adulthood. A POSITIVE result indicates a high probability that the person will develop lactose intolerance during his or her lifetime. A CARRIER result is generally not accompanied by manifestations of lactose intolerance, but the person could transmit this genetic variation to his/her children. Lactose intolerance can be easily prevented by limiting drastically or completely the consumption of unfermented milk containing lactose. Fermented milk products (fermented cheese, yoghurt, beaten milk, kefir, etc.) or milk without lactose can be consumed.

If there is a POSITIVE result for one of the genetic variations above, you should ask your nutritionist to establish a list of foods that should be avoided, and to provide alternative foods.

THYROID VOLUME

Test 135

Locus	Gene	Genotype	Reference	Mutation	Your result
rs1354920	FAM227B	T/C	C/C	T	POSITIVE
rs17767491	LOC105371356	A/G	A/A	G	POSITIVE
rs12091047	CAPZB	C/C	C/C	T	Negative

The presence of genetic variations in any of the above genes is associated with an increased risk of changes in thyroid volume and function, accompanied by changes in hormones and antibodies that are either secreted by the thyroid or contribute to thyroid function. A POSITIVE result indicates an increased risk of changes in thyroid volume and function. For information purposes, the table below shows the endocrine changes associated with these genetic variations (mean values relative to mean values in the general population of European origin). This information may be useful to the endocrinologist if you are diagnosed with thyroid disorders. The table indicates the direction (positive or negative, +/-) and the mean amplitude of these changes in the case of a POSITIVE result for that genetic variation.

Locus	TSH	anti-TPO	fT3	fT4
rs1354920	+ 4,7%	+ 5,8%	+ 5,9%	+ 5,9%
rs17767491	+ 5,3%	+ 6,4%	+ 6,3%	+ 6,5%
rs12091047	- 5,1%	- 5,8%	- 5,7%	- 5,8%

If there is a POSITIVE result for any of the above variations, you should ask your doctor for a strategy to prevent or reduce the manifestations associated with thyroid-related problems. Additional genetic testing and other tests may be required.

Upper tolerable limits

The table below indicates the maximum daily intake of nutrients for adults, based on age, gender and physiological status. Except for doctor's recommendations, these limits should not be exceeded.

NUTRIENT	UNITS	MEN	WOMEN	PREGNANCY	LACTATION
Vitamin A	µg/d	3000	3000	3000	3000
Vitamin C	mg/d	2000	2000	2000	2000
Vitamin D	µg/d	100	100	100	100
Vitamin E	mg/d	1000	1000	1000	1000
Vitamin K	µg/d	ND	ND	ND	ND
Thiamin	mg/d	ND	ND	ND	ND
Riboflavin	mg/d	ND	ND	ND	ND
Niacin	mg/d	35	35	35	35
Vitamin B6	mg/d	100	100	100	100
Folates	µg/d	1000	1000	1000	1000
Vitamin B12	µg/d	ND	ND	ND	ND
Pantothenic acid	mg/d	ND	ND	ND	ND
Betaine	mg/d	ND	ND	ND	ND
Biotin	µg/d	ND	ND	ND	ND
Cholin	mg/d	3500	3500	3500	3500
Calcium	mg/d	2500 (<50 yo) 2000 (>50 yo)	2500 (<50 yo) 2000 (>50 yo)	2500	2500
Chromium	µg/d	ND	ND	ND	ND
Copper	µg/d	10000	10000	10000	10000
Iron	mg/d	45	45	45	45
Fluoride	mg/d	10	10	10	10
Phosphorus	mg/d	4000 (<70 yo) 3000 (>70 yo)	4000 (<70 yo) 3000 (>70 yo)	3500	4000
Iodine	µg/d	1100	1100	1100	1100
*Magnesium	mg/d	350	350	350	350
Manganese	mg/d	11	11	11	11
Molibdenum	µg/d	2000	2000	2000	2000
Selenium	µg/d	400	400	400	400
Zinc	mg/d	40	40	40	40
Sodium	g/d	2,3	2,3	2,3	2,3
Chloride	g/d	3,6	3,6	3,6	3,6

* The upper limit for Magnesium is the contribution of supplements and medicines, and does not reflect the contribution of food and water.

ND = not determined

Conversion formulas

Nutrient	IU → µg or mg	Equivalents → µg or mg
Vitamin A	1 IU = 0.3 µg retinol 1 IU = 0.6 µg beta-caroten	1 µg RE = 1 µg retinol 1 µg RE = 2 µg beta-caroten (supplements) 1 µg RE = 12 µg beta-caroten (foods) 1 µg RE = 24 µg alpha-caroten 1 µg RE = 24 µg beta-chryptoxanthin
Vitamin E	1 IU = 0.67 mg *d*-alpha-tocoferol (natural) 1 IU = 0.9 mg *dl*-alpha-tocopherol (synthetic)	1 mg Vitamin E (alpha-tocoferol) = 1 mg natural alfa-tocoferol 1 mg Vitamin E (alpha-tocopherol) = 0.5 mg synthetic alpha-tocopherol
Vitamin D	1 IU = 0.025 µg	1 IU = 0.025 µg
Folates		1 µg DFE = 1 µg natural folates 1 µg DFE = 0.6 µg folic acid (in supplements or fortified foods with folic acid)
Niacin		1 mg NE = 1 mg niacinamide 1 mg NE = 1 mg inositole hexanicotinate 1 mg NE = 1 mg niacin 1 mg NE = 60 mg tryptophan

Selected references

The following databases can be useful to specialistsin order to learn more about the frequency, structure and association of genetic variations with certain conditions, and about existing treatment alternatives:

dbSNP – database containing the localization, frequency and structure of localized genetic variations (https://www.ncbi.nlm.nih.gov/projects/SNP/).

ClinVar – a database associating pathogenic genetic variations with details of pathogenicity and current scientific evidence (https://www.ncbi.nlm.nih.gov/clinvar/).

PharmGKB – database indicating the interactions between genetic variations and drugs (https://www.pharmgkb.org/).

GeneCards – provides information on the role of genes amd encoded proteins (http://www.genecards.org/).

Specific Genetic Disorders – provides diagnostic and treatment information for rare diseases with genetic aetiology (https://www.genome.gov/10001204/).

Susan G Komen Foundation – provides information on the role of BRCA1/BRCA2 mutations in the pathogenesis of cancers in women and men (http://ww5.komen.org/BreastCancer/InheritedGeneticMutations.html).

The list of references below is a selection of the studies and information used to compile this report. This list does not represent the entire set of information that was used to generate this report, but only to the extent that it may be useful to the professionals.

1997. *Dietary Reference Intakes for Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride.* Washington (DC).

1998. *Dietary Reference Intakes for Thiamin, Riboflavin, Niacin, Vitamin B6, Folate, Vitamin B12, Pantothenic Acid, Biotin, and Choline.* Washington (DC).

2000. *Dietary Reference Intakes for Vitamin C, Vitamin E, Selenium, and Carotenoids.* Washington (DC).

2001. *Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc.* Washington (DC).

AL-SHAKFA, F., DULUCQ, S., BRUKNER, I., MILACIC, I., ANSARI, M., BEAULIEU, P., MOGHRABI, A., LAVERDIERE, C., SALLAN, S. E., SILVERMAN, L. B., NEUBERG, D., KUTOK, J. L., SINNETT, D. & KRAJINOVIC, M. 2009. DNA variants in region for noncoding interfering transcript of dihydrofolate reductase gene and outcome in childhood acute lymphoblastic leukemia. *Clin Cancer Res,* 15**,** 6931-8.

AMES, B. N., ELSON-SCHWAB, I. & SILVER, E. A. 2002. High-dose vitamin therapy stimulates variant enzymes with decreased coenzyme binding affinity (increased K(m)): relevance to genetic disease and polymorphisms. *Am J Clin Nutr,* 75**,** 616-58.

AMEUR, A., ENROTH, S., JOHANSSON, A., ZABOLI, G., IGL, W., JOHANSSON, A. C., RIVAS, M. A., DALY, M. J., SCHMITZ, G., HICKS, A. A., MEITINGER, T., FEUK, L., VAN DUIJN, C., OOSTRA, B., PRAMSTALLER, P. P., RUDAN, I., WRIGHT, A. F., WILSON, J. F., CAMPBELL, H. & GYLLENSTEN, U. 2012. Genetic adaptation of fatty-acid metabolism: a human-specific haplotype increasing the biosynthesis of long-chain omega-3 and omega-6 fatty acids. *Am J Hum Genet,* 90**,** 809-20.

ASKARI, B. S. & KRAJINOVIC, M. 2010. Dihydrofolate reductase gene variations in susceptibility to disease and treatment outcomes. *Curr Genomics,* 11**,** 578-83.

BAFFOUR-AWUAH, N. Y., FLEET, S., MONTGOMERY, R. K., BAKER, S. S., BUTLER, J. L., CAMPBELL, C., TISCHFIELD, S., MITCHELL, P. D., ALLENDE-RICHTER, S., MOON, J. E., FISHMAN, L., BOUSVAROS, A., FOX, V., KUOKKANEN, M., GRAND, R. J. & HIRSCHHORN, J. N. 2015. Functional significance of single nucleotide polymorphisms in the lactase gene in diverse US patients and evidence for a novel lactase persistence allele at -13909 in those of European ancestry. *J Pediatr Gastroenterol Nutr,* 60**,** 182-91.

BOHME, M., GRALLERT, H., KLAPPER, M., GIEGER, C., FISCHER, A., HEID, I., WICHMANN, H. E., DORING, F. & ILLIG, T. 2009. Association between functional FABP2 promoter haplotypes and body mass index: analyses of 8072 participants of the KORA cohort study. *Mol Nutr Food Res,* 53**,** 681-5.

BOREL, P., LIETZ, G., GONCALVES, A., SZABO DE EDELENYI, F., LECOMPTE, S., CURTIS, P., GOUMIDI, L., CASLAKE, M. J., MILES, E. A., PACKARD, C., CALDER, P. C., MATHERS, J. C., MINIHANE, A. M., TOURNIAIRE, F., KESSE-GUYOT, E., GALAN, P., HERCBERG, S., BREIDENASSEL, C., GONZÁLEZ GROSS, M., MOUSSA, M., MEIRHAEGHE, A. & REBOUL, E. 2013. CD36 and SR-BI Are Involved in Cellular Uptake of Provitamin A Carotenoids by Caco-2 and HEK Cells, and Some of Their Genetic Variants Are Associated with Plasma Concentrations of These Micronutrients in Humans. *The Journal of Nutrition,* 143**,** 448-456.

BUFORD, T. W., HSU, F. C., BRINKLEY, T. E., CARTER, C. S., CHURCH, T. S., DODSON, J. A., GOODPASTER, B. H., MCDERMOTT, M. M., NICKLAS, B. J., YANK, V., JOHNSON, J. A., PAHOR, M. & GROUP, L. R. 2014. Genetic influence on exercise-induced changes in physical function among mobility-limited older adults. *Physiol Genomics,* 46**,** 149-58.

CHANDRAN, V., SIANNIS, F., RAHMAN, P., PELLETT, F. J., FAREWELL, V. T. & GLADMAN, D. D. 2010. Folate pathway enzyme gene polymorphisms and the efficacy and toxicity of methotrexate in psoriatic arthritis. *J Rheumatol,* 37**,** 1508-12.

CHANG, M. H., YESUPRIYA, A., NED, R. M., MUELLER, P. W. & DOWLING, N. F. 2010. Genetic variants associated with fasting blood lipids in the U.S. population: Third National Health and Nutrition Examination Survey. *BMC Med Genet,* 11**,** 62.

DA COSTA, K.-A., CORBIN, K. D., NICULESCU, M. D., GALANKO, J. A. & ZEISEL, S. H. 2014. Identification of new genetic polymorphisms that alter the dietary requirement for choline and vary in their distribution across ethnic and racial groups. *The FASEB Journal,* 28**,** 2970-2978.

DA ROCHA, T. J., KORB, C., SCHUCH, J. B., BAMBERG, D. P., DE ANDRADE, F. M. & FIEGENBAUM, M. 2014. SLC30A3 and SEP15 gene polymorphisms influence the serum concentrations of zinc and selenium in mature adults. *Nutr Res,* 34**,** 742-8.

DOKTER, E. M., VAN ROOIJ, I. A., WIJERS, C. H., GROOTHUISMINK, J. M., VAN DER BIEZEN, J. J., FEITZ, W. F., ROELEVELD, N. & VAN DER ZANDEN, L. F. 2016. Interaction between MTHFR 677C>T and periconceptional folic acid supplementation in the risk of Hypospadias. *Birth Defects Res A Clin Mol Teratol,* 106**,** 275-84.

DUELL, E. J., LUJAN-BARROSO, L., LLIVINA, C., MUNOZ, X., JENAB, M., BOUTRON-RUAULT, M. C., CLAVEL-CHAPELON, F., RACINE, A., BOEING, H., BUIJSSE, B., CANZIAN, F., JOHNSON, T., DALGARD, C., OVERVAD, K., TJONNELAND, A., OLSEN, A., SANCHEZ, S. C., SANCHEZ-CANTALEJO, E., HUERTA, J. M., ARDANAZ, E., DORRONSORO, M., KHAW, K. T., TRAVIS, R. C., TRICHOPOULOU, A., TRICHOPOULOS, D., RAFNSSON, S., PALLI, D., SACERDOTE, C., TUMINO, R., PANICO, S., GRIONI, S., BUENO-DE-MESQUITA, H. B., ROS, M. M., NUMANS, M. E., PEETERS, P. H., JOHANSEN, D., LINDKVIST, B., JOHANSSON, M., JOHANSSON, I., SKEIE, G., WEIDERPASS, E., DUARTE-SALLES, T., STENLING, R., RIBOLI, E., SALA, N. & GONZALEZ, C. A. 2013. Vitamin C transporter gene (SLC23A1 and SLC23A2) polymorphisms, plasma vitamin C levels, and gastric cancer risk in the EPIC cohort. *Genes Nutr,* 8**,** 549-60.

DUELL, E. J., SALA, N., TRAVIER, N., MUÑOZ, X., BOUTRON-RUAULT, M. C., CLAVEL-CHAPELON, F., BARRICARTE, A., ARRIOLA, L., NAVARRO, C., SÁNCHEZ-CANTALEJO, E., QUIRÓS, J. R., KROGH, V., VINEIS, P., MATTIELLO, A., TUMINO, R., KHAW, K.-T., WAREHAM, N., ALLEN, N. E., PEETERS, P. H., NUMANS, M. E., BUENO-DE-MESQUITA, H. B., VAN OIJEN, M. G. H., BAMIA, C., BENETOU, V., TRICHOPOULOS, D., CANZIAN, F., KAAKS, R., BOEING, H., BERGMANN, M. M., LUND, E., EHRNSTRÖM, R., JOHANSEN, D., HALLMANS, G., STENLING, R., TJØNNELAND, A., OVERVAD, K., OSTERGAARD, J. N., FERRARI, P., FEDIRKO, V., JENAB, M., NESI, G., RIBOLI, E. & GONZÁLEZ, C. A. 2012. Genetic variation in alcohol dehydrogenase (ADH1A, ADH1B, ADH1C, ADH7) and aldehyde dehydrogenase (ALDH2), alcohol consumption and gastric cancer risk in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort. *Carcinogenesis,* 33**,** 361-367.

DULUCQ, S., ST-ONGE, G., GAGNE, V., ANSARI, M., SINNETT, D., LABUDA, D., MOGHRABI, A. & KRAJINOVIC, M. 2008. DNA variants in the dihydrofolate reductase gene and outcome in childhood ALL. *Blood,* 111**,** 3692-700.

EFSA PANEL ON DIETETIC PRODUCTS, N. & ALLERGIES 2011. Scientific Opinion on the substantiation of health claims related to betaine and contribution to normal homocysteine metabolism (ID 4325) pursuant to Article 13(1) of Regulation (EC) No 1924/2006. *EFSA Journal,* 9**,** n/a-n/a.

EL-SOHEMY, A., CORNELIS, M. C., KABAGAMBE, E. K. & CAMPOS, H. 2007. Coffee, CYP1A2 genotype and risk of myocardial infarction. *Genes Nutr,* 2**,** 155-6.

FEDOTOVSKAYA, O. N., MUSTAFINA, L. J., POPOV, D. V., VINOGRADOVA, O. L. & AHMETOV, II 2014. A common polymorphism of the MCT1 gene and athletic performance. *Int J Sports Physiol Perform,* 9**,** 173-80.

FRADIN, D. & BOUGNERES, P. 2007. Three common intronic variants in the maternal and fetal thiamine pyrophosphokinase gene (TPK1) are associated with birth weight. *Ann Hum Genet,* 71**,** 578-85.

GAFFNEY-STOMBERG, E., LUTZ, L. J., SHCHERBINA, A., RICKE, D. O., PETROVICK, M., CROPPER, T. L., CABLE, S. J. & MCCLUNG, J. P. 2016. Association Between Single Gene Polymorphisms and Bone Biomarkers and Response to Calcium and Vitamin D Supplementation in Young Adults Undergoing Military Training. *J Bone Miner Res*.

GARCIA-MINGUILLAN, C. J., FERNANDEZ-BALLART, J. D., CERUELO, S., RIOS, L., BUENO, O., BERROCAL-ZARAGOZA, M. I., MOLLOY, A. M., UELAND, P. M., MEYER, K. & MURPHY, M. M. 2014. Riboflavin status modifies the effects of methylenetetrahydrofolate reductase (MTHFR) and methionine synthase reductase (MTRR) polymorphisms on homocysteine. *Genes Nutr,* 9**,** 435.

GIACCONI, R., KANONI, S., MECOCCI, P., MALAVOLTA, M., RICHTER, D., PIERPAOLI, S., COSTARELLI, L., CIPRIANO, C., MUTI, E., MANGIALASCHE, F., PIACENZA, F., TESEI, S., GALEAZZI, R., THEODORAKI, E. V., LATTANZIO, F., DEDOUSSIS, G. & MOCCHEGIANI, E. 2010. Association of MT1A haplotype with cardiovascular disease and antioxidant enzyme defense in elderly Greek population: comparison with an Italian cohort. *J Nutr Biochem,* 21**,** 1008-14.

GICHOHI-WAINAINA, W. N., TOWERS, G. W., SWINKELS, D. W., ZIMMERMANN, M. B., FESKENS, E. J. & MELSE-BOONSTRA, A. 2015a. Erratum to: Inter-ethnic differences in genetic variants within the transmembrane protease, serine 6 (TMPRSS6) gene associated with iron status indicators: a systematic review with meta-analyses. *Genes Nutr,* 10**,** 457.

GICHOHI-WAINAINA, W. N., TOWERS, G. W., SWINKELS, D. W., ZIMMERMANN, M. B., FESKENS, E. J. & MELSE-BOONSTRA, A. 2015b. Inter-ethnic differences in genetic variants within the transmembrane protease, serine 6 (TMPRSS6) gene associated with iron status indicators: a systematic review with meta-analyses. *Genes Nutr,* 10**,** 442.

GIRARDI, A., MARTINELLI, M., CURA, F., PALMIERI, A., CARINCI, F., SESENNA, E. & SCAPOLI, L. 2014. RFC1 and non-syndromic cleft lip with or without cleft palate: an association based study in Italy. *J Craniomaxillofac Surg,* 42**,** 1503-5.

GLYNN, R. J., RIDKER, P. M., GOLDHABER, S. Z., ZEE, R. Y. & BURING, J. E. 2007. Effects of random allocation to vitamin E supplementation on the occurrence of venous thromboembolism: report from the Women's Health Study. *Circulation,* 116**,** 1497-503.

HALDER, I., CHAMPLIN, J., SHEU, L., GOODPASTER, B. H., MANUCK, S. B., FERRELL, R. E. & MULDOON, M. F. 2014. PPARalpha gene polymorphisms modulate the association between physical activity and cardiometabolic risk. *Nutr Metab Cardiovasc Dis,* 24**,** 799-805.

HALLAU, J., HAMANN, L., SCHUMANN, R. R., WORM, M. & HEINE, G. 2016. A Promoter Polymorphism of the Vitamin D Metabolism Gene Cyp24a1 is Associated with Severe Atopic Dermatitis in Adults. *Acta Derm Venereol,* 96**,** 169-72.

HARBRON, J., VAN DER MERWE, L., ZAAHL, M. G., KOTZE, M. J. & SENEKAL, M. 2014. Fat mass and obesity-associated (FTO) gene polymorphisms are associated with physical activity, food intake, eating behaviors, psychological health, and modeled change in body mass index in overweight/obese Caucasian adults. *Nutrients,* 6**,** 3130-52.

HEAP, G. A., WEEDON, M. N., BEWSHEA, C. M., SINGH, A., CHEN, M., SATCHWELL, J. B., VIVIAN, J. P., SO, K., DUBOIS, P. C., ANDREWS, J. M., ANNESE, V., BAMPTON, P., BARNARDO, M., BELL, S., COLE, A., CONNOR, S. J., CREED, T., CUMMINGS, F. R., D'AMATO, M., DANESHMEND, T. K., FEDORAK, R. N., FLORIN, T. H., GAYA, D. R., GREIG, E., HALFVARSON, J., HART, A., IRVING, P. M., JONES, G., KARBAN, A., LAWRANCE, I. C., LEE, J. C., LEES, C., LEV-TZION, R., LINDSAY, J. O., MANSFIELD, J., MAWDSLEY, J., MAZHAR, Z., PARKES, M., PARNELL, K., ORCHARD, T. R., RADFORD-SMITH, G., RUSSELL, R. K., REFFITT, D., SATSANGI, J., SILVERBERG, M. S., STURNIOLO, G. C., TREMELLING, M., TSIANOS, E. V., VAN HEEL, D. A., WALSH, A., WATERMEYER, G., WEERSMA, R. K., ZEISSIG, S., ROSSJOHN, J., HOLDEN, A. L., INTERNATIONAL SERIOUS ADVERSE EVENTS, C., GROUP, I. B. D. P. S. & AHMAD, T. 2014. HLA-DQA1-HLA-DRB1 variants confer susceptibility to pancreatitis induced by thiopurine immunosuppressants. *Nat Genet,* 46**,** 1131-4.

HOLM, P. I., HUSTAD, S., UELAND, P. M., VOLLSET, S. E., GROTMOL, T. & SCHNEEDE, J. 2007. Modulation of the homocysteine-betaine relationship by methylenetetrahydrofolate reductase 677 C->t genotypes and B-vitamin status in a large-scale epidemiological study. *J Clin Endocrinol Metab,* 92**,** 1535-41.

INAMORI, T., GODA, T., KASEZAWA, N. & YAMAKAWA-KOBAYASHI, K. 2013. The combined effects of genetic variation in the SIRT1 gene and dietary intake of n-3 and n-6 polyunsaturated fatty acids on serum LDL-C and HDL-C levels: a population based study. *Lipids Health Dis,* 12**,** 4.

JOHNSON, J. A., GONG, L., WHIRL-CARRILLO, M., GAGE, B. F., SCOTT, S. A., STEIN, C. M., ANDERSON, J. L., KIMMEL, S. E., LEE, M. T., PIRMOHAMED, M., WADELIUS, M., KLEIN, T. E., ALTMAN, R. B. & CLINICAL PHARMACOGENETICS IMPLEMENTATION, C. 2011. Clinical Pharmacogenetics Implementation Consortium Guidelines for CYP2C9 and VKORC1 genotypes and warfarin dosing. *Clin Pharmacol Ther,* 90**,** 625-9.

JOHNSON, W. G., SCHOLL, T. O., SPYCHALA, J. R., BUYSKE, S., STENROOS, E. S. & CHEN, X. 2005. Common dihydrofolate reductase 19-base pair deletion allele: a novel risk factor for preterm delivery. *Am J Clin Nutr,* 81**,** 664-8.

KALANTARIAN, S., RIMM, E. B., HERRINGTON, D. M. & MOZAFFARIAN, D. 2014. Dietary macronutrients, genetic variation, and progression of coronary atherosclerosis among women. *Am Heart J,* 167**,** 627-635 e1.

KANONI, S., DEDOUSSIS, G. V., HERBEIN, G., FULOP, T., VARIN, A., JAJTE, J., RINK, L., MONTI, D., MARIANI, E., MALAVOLTA, M., GIACCONI, R., MARCELLINI, F. & MOCCHEGIANI, E. 2010. Assessment of gene-nutrient interactions on inflammatory status of the elderly with the use of a zinc diet score--ZINCAGE study. *J Nutr Biochem,* 21**,** 526-31.

KAPUR, K., JOHNSON, T., BECKMANN, N. D., SEHMI, J., TANAKA, T., KUTALIK, Z., STYRKARSDOTTIR, U., ZHANG, W., MAREK, D., GUDBJARTSSON, D. F., MILANESCHI, Y., HOLM, H., DIIORIO, A., WATERWORTH, D., LI, Y., SINGLETON, A. B., BJORNSDOTTIR, U. S., SIGURDSSON, G., HERNANDEZ, D. G., DESILVA, R., ELLIOTT, P., EYJOLFSSON, G. I., GURALNIK, J. M., SCOTT, J., THORSTEINSDOTTIR, U., BANDINELLI, S., CHAMBERS, J., STEFANSSON, K., WAEBER, G., FERRUCCI, L., KOONER, J. S., MOOSER, V., VOLLENWEIDER, P., BECKMANN, J. S., BOCHUD, M. & BERGMANN, S. 2010. Genome-wide meta-analysis for serum calcium identifies significantly associated SNPs near the calcium-sensing receptor (CASR) gene. *PLoS Genet,* 6**,** e1001035.

KLIMENTIDIS, Y. C., CHEN, Z., ARORA, A. & HSU, C. H. 2014. Association of physical activity with lower type 2 diabetes incidence is weaker among individuals at high genetic risk. *Diabetologia,* 57**,** 2530-4.

KOHLMEIER, M., DA COSTA, K. A., FISCHER, L. M. & ZEISEL, S. H. 2005. Genetic variation of folate-mediated one-carbon transfer pathway predicts susceptibility to choline deficiency in humans. *Proc Natl Acad Sci U S A,* 102**,** 16025-30.

LECOMPTE, S., SZABO DE EDELENYI, F., GOUMIDI, L., MAIANI, G., MOSCHONIS, G., WIDHALM, K., MOLNAR, D., KAFATOS, A., SPINNEKER, A., BREIDENASSEL, C., DALLONGEVILLE, J., MEIRHAEGHE, A. & BOREL, P. 2011. Polymorphisms in the CD36/FAT gene are associated with plasma vitamin E concentrations in humans. *Am J Clin Nutr,* 93**,** 644-51.

LEVINE, A. J., FIGUEIREDO, J. C., LEE, W., CONTI, D. V., KENNEDY, K., DUGGAN, D. J., POYNTER, J. N., CAMPBELL, P. T., NEWCOMB, P., MARTINEZ, M. E., HOPPER, J. L., LE MARCHAND, L., BARON, J. A., LIMBURG, P. J., ULRICH, C. M. & HAILE, R. W. 2010. A candidate gene study of folate-associated one carbon metabolism genes and colorectal cancer risk. *Cancer Epidemiol Biomarkers Prev,* 19**,** 1812-21.

LINNEBANK, M., JANOSIK, M., KOZICH, V., PRONICKA, E., KUBALSKA, J., SOKOLOVA, J., LINNEBANK, A., SCHMIDT, E., LEYENDECKER, C., KLOCKGETHER, T., KRAUS, J. P. & KOCH, H. G. 2004. The cystathionine β-synthase (CBS) mutation c.1224-2A>C in Central Europe: Vitamin B6 nonresponsiveness and a common ancestral haplotype. *Human Mutation,* 24**,** 352-353.

LOOS, R. J., HAGBERG, J. M., PERUSSE, L., ROTH, S. M., SARZYNSKI, M. A., WOLFARTH, B., RANKINEN, T. & BOUCHARD, C. 2015. Advances in exercise, fitness, and performance genomics in 2014. *Med Sci Sports Exerc,* 47**,** 1105-12.

MCCULLOUGH, M. L., STEVENS, V. L., DIVER, W. R., FEIGELSON, H. S., RODRIGUEZ, C., BOSTICK, R. M., THUN, M. J. & CALLE, E. E. 2007. Vitamin D pathway gene polymorphisms, diet, and risk of postmenopausal breast cancer: a nested case-control study. *Breast Cancer Res,* 9**,** R9.

MEPLAN, C., CROSLEY, L. K., NICOL, F., BECKETT, G. J., HOWIE, A. F., HILL, K. E., HORGAN, G., MATHERS, J. C., ARTHUR, J. R. & HESKETH, J. E. 2007. Genetic polymorphisms in the human selenoprotein P gene determine the response of selenoprotein markers to selenium supplementation in a gender-specific manner (the SELGEN study). *FASEB J,* 21**,** 3063-74.

MEYER, T. E., VERWOERT, G. C., HWANG, S. J., GLAZER, N. L., SMITH, A. V., VAN ROOIJ, F. J., EHRET, G. B., BOERWINKLE, E., FELIX, J. F., LEAK, T. S., HARRIS, T. B., YANG, Q., DEHGHAN, A., ASPELUND, T., KATZ, R., HOMUTH, G., KOCHER, T., RETTIG, R., RIED, J. S., GIEGER, C., PRUCHA, H., PFEUFER, A., MEITINGER, T., CORESH, J., HOFMAN, A., SARNAK, M. J., CHEN, Y. D., UITTERLINDEN, A. G., CHAKRAVARTI, A., PSATY, B. M., VAN DUIJN, C. M., KAO, W. H., WITTEMAN, J. C., GUDNASON, V., SISCOVICK, D. S., FOX, C. S., KOTTGEN, A., GENETIC FACTORS FOR OSTEOPOROSIS, C., META ANALYSIS OF, G. & INSULIN RELATED TRAITS, C. 2010. Genome-wide association studies of serum magnesium, potassium, and sodium concentrations identify six Loci influencing serum magnesium levels. *PLoS Genet,* 6.

MILLS, J. L., FAN, R., BRODY, L. C., LIU, A., UELAND, P. M., WANG, Y., KIRKE, P. N., SHANE, B. & MOLLOY, A. M. 2014. Maternal choline concentrations during pregnancy and choline-related genetic variants as risk factors for neural tube defects. *Am J Clin Nutr,* 100**,** 1069-74.

MINOURA, A., WANG, D. H., SATO, Y., ZOU, Y., SAKANO, N., KUBO, M., TAKEMOTO, K., MASATOMI, C. & OGINO, K. 2014. Association of dietary fat and carbohydrate consumption and predicted ten-year risk for developing coronary heart disease in a general Japanese population. *Acta Med Okayama,* 68**,** 129-35.

MORENO-LUNA, R., PEREZ-JIMENEZ, F., MARIN, C., PEREZ-MARTINEZ, P., GOMEZ, P., JIMENEZ-GOMEZ, Y., DELGADO-LISTA, J., MORENO, J. A., TANAKA, T., ORDOVAS, J. M. & LOPEZ-MIRANDA, J. 2007. Two independent apolipoprotein A5 haplotypes modulate postprandial lipoprotein metabolism in a healthy Caucasian population. *J Clin Endocrinol Metab,* 92**,** 2280-5.

MOSTOWSKA, A., BIEDZIAK, B., DUNIN-WILCZYNSKA, I., KOMOROWSKA, A. & JAGODZINSKI, P. P. 2011. Polymorphisms in CHDH gene and the risk of tooth agenesis. *Birth Defects Res A Clin Mol Teratol,* 91**,** 169-76.

MOSTOWSKA, A., HOZYASZ, K. K., BIEDZIAK, B., MISIAK, J. & JAGODZINSKI, P. P. 2010a. Polymorphisms located in the region containing BHMT and BHMT2 genes as maternal protective factors for orofacial clefts. *Eur J Oral Sci,* 118**,** 325-32.

MOSTOWSKA, A., HOZYASZ, K. K., WOJCICKI, P., DZIEGELEWSKA, M. & JAGODZINSKI, P. P. 2010b. Associations of folate and choline metabolism gene polymorphisms with orofacial clefts. *J Med Genet,* 47**,** 809-15.

NILSSON, T. K., BOTTIGER, A. K., HENRIQUEZ, P. & SERRA MAJEM, L. 2014. MTHFR polymorphisms and serum cobalamin affect plasma homocysteine concentrations differentially in females and males. *Mol Med Rep,* 10**,** 2706-12.

NIMPTSCH, K., NIETERS, A., HAILER, S., WOLFRAM, G. & LINSEISEN, J. 2009. The association between dietary vitamin K intake and serum undercarboxylated osteocalcin is modulated by vitamin K epoxide reductase genotype. *Br J Nutr,* 101**,** 1812-20.

NISSEN, J., RASMUSSEN, L. B., RAVN-HAREN, G., ANDERSEN, E. W., HANSEN, B., ANDERSEN, R., MEJBORN, H., MADSEN, K. H. & VOGEL, U. 2014. Common variants in CYP2R1 and GC genes predict vitamin D concentrations in healthy Danish children and adults. *PLoS One,* 9**,** e89907.

NORMAN, B., ESBJORNSSON, M., RUNDQVIST, H., OSTERLUND, T., GLENMARK, B. & JANSSON, E. 2014. ACTN3 genotype and modulation of skeletal muscle response to exercise in human subjects. *J Appl Physiol (1985),* 116**,** 1197-203.

O'SEAGHDHA, C. M., YANG, Q., GLAZER, N. L., LEAK, T. S., DEHGHAN, A., SMITH, A. V., KAO, W. H., LOHMAN, K., HWANG, S. J., JOHNSON, A. D., HOFMAN, A., UITTERLINDEN, A. G., CHEN, Y. D., CONSORTIUM, G., BROWN, E. M., SISCOVICK, D. S., HARRIS, T. B., PSATY, B. M., CORESH, J., GUDNASON, V., WITTEMAN, J. C., LIU, Y. M., KESTENBAUM, B. R., FOX, C. S. & KOTTGEN, A. 2010. Common variants in the calcium-sensing receptor gene are associated with total serum calcium levels. *Hum Mol Genet,* 19**,** 4296-303.

PANGILINAN, F., MOLLOY, A. M., MILLS, J. L., TROENDLE, J. F., PARLE-MCDERMOTT, A., KAY, D. M., BROWNE, M. L., MCGRATH, E. C., ABAAN, H. O., SUTTON, M., KIRKE, P. N., CAGGANA, M., SHANE, B., SCOTT, J. M. & BRODY, L. C. 2014. Replication and exploratory analysis of 24 candidate risk polymorphisms for neural tube defects. *BMC Med Genet,* 15**,** 102.

PANGILINAN, F., MOLLOY, A. M., MILLS, J. L., TROENDLE, J. F., PARLE-MCDERMOTT, A., SIGNORE, C., O'LEARY, V. B., CHINES, P., SEAY, J. M., GEILER-SAMEROTTE, K., MITCHELL, A., VANDERMEER, J. E., KREBS, K. M., SANCHEZ, A., CORNMAN-HOMONOFF, J., STONE, N., CONLEY, M., KIRKE, P. N., SHANE, B., SCOTT, J. M. & BRODY, L. C. 2012. Evaluation of common genetic variants in 82 candidate genes as risk factors for neural tube defects. *BMC Medical Genetics,* 13**,** 62.

PARLE-MCDERMOTT, A., PANGILINAN, F., O'BRIEN, K. K., MILLS, J. L., MAGEE, A. M., TROENDLE, J., SUTTON, M., SCOTT, J. M., KIRKE, P. N., MOLLOY, A. M. & BRODY, L. C. 2009. A common variant in MTHFD1L is associated with neural tube defects and mRNA splicing efficiency. *Hum Mutat,* 30**,** 1650-6.

QI, L., SHEN, H., LARSON, I., SCHAEFER, E. J., GREENBERG, A. S., TREGOUET, D. A., CORELLA, D. & ORDOVAS, J. M. 2004. Gender-specific association of a perilipin gene haplotype with obesity risk in a white population. *Obes Res,* 12**,** 1758-65.

RELLING, M. V., GARDNER, E. E., SANDBORN, W. J., SCHMIEGELOW, K., PUI, C. H., YEE, S. W., STEIN, C. M., CARRILLO, M., EVANS, W. E., HICKS, J. K., SCHWAB, M., KLEIN, T. E. & CLINICAL PHARMACOGENETICS IMPLEMENTATION, C. 2013. Clinical pharmacogenetics implementation consortium guidelines for thiopurine methyltransferase genotype and thiopurine dosing: 2013 update. *Clin Pharmacol Ther,* 93**,** 324-5.

RELLING, M. V., GARDNER, E. E., SANDBORN, W. J., SCHMIEGELOW, K., PUI, C. H., YEE, S. W., STEIN, C. M., CARRILLO, M., EVANS, W. E., KLEIN, T. E. & CLINICAL PHARMACOGENETICS IMPLEMENTATION, C. 2011. Clinical Pharmacogenetics Implementation Consortium guidelines for thiopurine methyltransferase genotype and thiopurine dosing. *Clin Pharmacol Ther,* 89**,** 387-91.

ROSS, A. C. 2011. The 2011 report on dietary reference intakes for calcium and vitamin D. *Public Health Nutr,* 14**,** 938-9.

SALOPURO, T., PULKKINEN, L., LINDSTROM, J., KOLEHMAINEN, M., TOLPPANEN, A. M., ERIKSSON, J. G., VALLE, T. T., AUNOLA, S., ILANNE-PARIKKA, P., KEINANEN-KIUKAANNIEMI, S., TUOMILEHTO, J., LAAKSO, M. & UUSITUPA, M. 2009. Variation in the UCP2 and UCP3 genes associates with abdominal obesity and serum lipids: the Finnish Diabetes Prevention Study. *BMC Med Genet,* 10**,** 94.

SHARMA, S., DAS, M., KUMAR, A., MARWAHA, V., SHANKAR, S., SINGH, P., RAGHU, P., ANEJA, R., GROVER, R., ARYA, V., DHIR, V., GUPTA, R., KUMAR, U., JUYAL, R. C. & K, T. B. 2009. Purine biosynthetic pathway genes and methotrexate response in rheumatoid arthritis patients among north Indians. *Pharmacogenet Genomics,* 19**,** 823-8.

SHAW, G. M., CARMICHAEL, S. L., YANG, W., SELVIN, S. & SCHAFFER, D. M. 2004. Periconceptional dietary intake of choline and betaine and neural tube defects in offspring. *Am J Epidemiol,* 160**,** 102-9.

SONG, Y., HSU, Y. H., NIU, T., MANSON, J. E., BURING, J. E. & LIU, S. 2009. Common genetic variants of the ion channel transient receptor potential membrane melastatin 6 and 7 (TRPM6 and TRPM7), magnesium intake, and risk of type 2 diabetes in women. *BMC Med Genet,* 10**,** 4.

SORENSEN, E., RIGAS, A. S., THORNER, L. W., BURGDORF, K. S., PEDERSEN, O. B., PETERSEN, M. S., HJALGRIM, H., ERIKSTRUP, C. & ULLUM, H. 2016. Genetic factors influencing ferritin levels in 14,126 blood donors: results from the Danish Blood Donor Study. *Transfusion,* 56**,** 622-7.

SUSSWEIN, L. R., MARSHALL, M. L., NUSBAUM, R., VOGEL POSTULA, K. J., WEISSMAN, S. M., YACKOWSKI, L., VACCARI, E. M., BISSONNETTE, J., BOOKER, J. K., CREMONA, M. L., GIBELLINI, F., MURPHY, P. D., PINEDA-ALVAREZ, D. E., POLLEVICK, G. D., XU, Z., RICHARD, G., BALE, S., KLEIN, R. T., HRUSKA, K. S. & CHUNG, W. K. 2016. Pathogenic and likely pathogenic variant prevalence among the first 10,000 patients referred for next-generation cancer panel testing. *Genetics in Medicine,* 18**,** 823-832.

TANAKA, T., ROY, C. N., YAO, W., MATTEINI, A., SEMBA, R. D., ARKING, D., WALSTON, J. D., FRIED, L. P., SINGLETON, A., GURALNIK, J., ABECASIS, G. R., BANDINELLI, S., LONGO, D. L. & FERRUCCI, L. 2010. A genome-wide association analysis of serum iron concentrations. *Blood,* 115**,** 94-6.

TEUMER, A., RAWAL, R., HOMUTH, G., ERNST, F., HEIER, M., EVERT, M., DOMBROWSKI, F., VOLKER, U., NAUCK, M., RADKE, D., ITTERMANN, T., BIFFAR, R., DORING, A., GIEGER, C., KLOPP, N., WICHMANN, H. E., WALLASCHOFSKI, H., MEISINGER, C. & VOLZKE, H. 2011. Genome-wide association study identifies four genetic loci associated with thyroid volume and goiter risk. *Am J Hum Genet,* 88**,** 664-73.

VANDE LOOCK, K., BOTSIVALI, M., ZANGOGIANNI, M., ANDERSON, D., BAUMGARTNER, A., FTHENOU, E., CHATZI, L., MARCOS, R., AGRAMUNT, S., NAMORK, E., GRANUM, B., KNUDSEN, L. E., NIELSSEN, J. K., MELTZER, H. M., HAUGEN, M., KYRTOPOULOS, S. A., DECORDIER, I., PLAS, G., ROELANTS, M., MERLO, F., KLEINJANS, J., KOGEVINAS, M. & KIRSCH-VOLDERS, M. 2014. The effect of dietary estimates calculated using food frequency questionnaires on micronuclei formation in European pregnant women: a NewGeneris study. *Mutagenesis,* 29**,** 393-400.

VERLENGIA, R., REBELO, A. C., CRISP, A. H., KUNZ, V. C., DOS SANTOS CARNEIRO CORDEIRO, M. A., HIRATA, M. H., CRESPO HIRATA, R. D. & SILVA, E. 2014. Lack of Association Between ACE Indel Polymorphism and Cardiorespiratory Fitness in Physically Active and Sedentary Young Women. *Asian J Sports Med,* 5**,** e22768.

WANG, B. J., LIU, M. J., WANG, Y., DAI, J. R., TAO, J. Y., WANG, S. N., ZHONG, N. & CHEN, Y. 2015. Association between SNPs in genes involved in folate metabolism and preterm birth risk. *Genet Mol Res,* 14**,** 850-9.

WILTINK, R. C., KRUIJSHAAR, M. E., VAN MINKELEN, R., ONKENHOUT, W., VERHEIJEN, F. W., KEMPER, E. A., VAN SPRONSEN, F. J., VAN DER PLOEG, A. T., NIEZEN-KONING, K. E., SARIS, J. J. & WILLIAMS, M. 2016. Neonatal screening for profound biotinidase deficiency in the Netherlands: consequences and considerations. *Eur J Hum Genet,* 24**,** 1424-9.

WOLF, B. 1993. Biotinidase Deficiency. *In:* PAGON, R. A., ADAM, M. P., ARDINGER, H. H., WALLACE, S. E., AMEMIYA, A., BEAN, L. J. H., BIRD, T. D., FONG, C. T., MEFFORD, H. C., SMITH, R. J. H. & STEPHENS, K. (eds.) *GeneReviews(R).* Seattle (WA).

XU, X., GAMMON, M. D., WETMUR, J. G., RAO, M., GAUDET, M. M., TEITELBAUM, S. L., BRITTON, J. A., NEUGUT, A. I., SANTELLA, R. M. & CHEN, J. 2007. A functional 19-base pair deletion polymorphism of dihydrofolate reductase (DHFR) and risk of breast cancer in multivitamin users. *Am J Clin Nutr,* 85**,** 1098-102.

ZHENG, J. S., ARNETT, D. K., PARNELL, L. D., SMITH, C. E., LI, D., BORECKI, I. B., TUCKER, K. L., ORDOVAS, J. M. & LAI, C. Q. 2013. Modulation by dietary fat and carbohydrate of IRS1 association with type 2 diabetes traits in two populations of different ancestries. *Diabetes Care,* 36**,** 2621-7.

ZILLIKENS, M. C., VAN MEURS, J. B., SIJBRANDS, E. J., RIVADENEIRA, F., DEHGHAN, A., VAN LEEUWEN, J. P., HOFMAN, A., VAN DUIJN, C. M., WITTEMAN, J. C., UITTERLINDEN, A. G. & POLS, H. A. 2009. SIRT1 genetic variation and mortality in type 2 diabetes: interaction with smoking and dietary niacin. *Free Radic Biol Med,* 46**,** 836-41.

ZINCK, J. W., DE GROH, M. & MACFARLANE, A. J. 2015. Genetic modifiers of folate, vitamin B-12, and homocysteine status in a cross-sectional study of the Canadian population. *Am J Clin Nutr,* 101**,** 1295-304.

MAKO GENOMICS

PGx Comprehensive Report

PATIENT: Gene Omics2

DOB:	1/1/1935	**SPECIMEN TYPE:**	Buccal Swab	**RECEIVED DATE:**	12/30/2016
GENDER:	Male	**COLLECTION DATE:**	1/18/2017	**REPORT GENERATED:**	10/19/2017
ETHNICITY:		**ACCESSION #:**	P1777777	**FACILITY/CLINIC:**	PGX HOUSE ACCOUNT
		ICD-10:	None Specified	**ORDERING PHYSICIAN:**	

TEST DETAILS SUMMARY

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*1	Normal Metabolizer
CYP2C19	*1/*17	Rapid Metabolizer
CYP3A5	*3/*3	Poor Metabolizer
CYP3A4	*1/*1	Normal Metabolizer
VKORC1	-1639G>A G/G	Low Warfarin Sensitivity
Apolipoprotein E	ε3/ε4	Altered APOE function
CYP2D6	*1/*4 XN	Ultra-Rapid or Normal Metabolizer
CYP2B6	*1/*1	Normal Metabolizer
CYP1A2	*1A/*1F	Normal Metabolizer - Higher Inducibility
SLCO1B1	521T>C T/T	Normal Function
COMT	Val158Met G/G	High/Normal COMT Activity
OPRM1	A118G A/G	Altered OPRM1 Function
UGT2B15	*1/*2	Intermediate Metabolizer
MTHFR	1298A>C AA 677C>T CC	No Increased Risk of Hyperhomocysteinemia
MTHFR	677C>T CC	Normal MTHFR Activity
Factor II Factor V Leiden	20210G>A GG 1691G>A GG	No Increased Risk of Thrombosis

*Comprehensive Test Detail information available at end of the report

CURRENT MEDICATIONS SUMMARY

Medications Outside the Scope of the Report: Allegra, Lisinopril, Loratadine

SAFE TO USE AS DIRECTED

Adderall (Amphetamine)
Ibuprofen (Advil, Motrin)
Warfarin (Coumadin)

USE MEDICATIONS WITH CAUTION

Omeprazole (Prilosec)
Prilosec (Omeprazole)
Zoloft (Sertraline)

CAUTION CONSIDER ALTERNATIVES

*Guidance for additional medications available in Potentially Impacted Medications section

Current Patient Medications

Allegra, Lisinopril, Loratadine, Omeprazole, Warfarin, Ibuprofen, Zoloft, Adderall, Prilosec

Omeprazole
Prilosec

Insufficient Response to Omeprazole (CYP2C19: Rapid Metabolizer) — ACTIONABLE

- Helicobacter pylori eradication: increase dose by 100-200% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase of 100-200%.

Prilosec
Omeprazole

Insufficient Response to Omeprazole (CYP2C19: Rapid Metabolizer) — ACTIONABLE

- Helicobacter pylori eradication: increase dose by 100-200% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase of 100-200%.

Zoloft
Sertraline

Possible Reduced Response to Sertraline (CYP2C19: Rapid Metabolizer) — INFORMATIVE

Sertraline can be prescribed at standard label-recommended dosage and administration. If patient does not respond to recommended maintenance dosing, consider an alternative medication.

Adderall
Amphetamine

Good Response to Amphetamine salts (COMT: High/Normal COMT Activity) — INFORMATIVE

The patient's genotype result predicts a higher likelihood of response to amphetamine stimulants. Amphetamines should be administered at the lowest effective dose, and dosage should be individually adjusted.

Ibuprofen
Advil, Motrin

Normal Sensitivity to Ibuprofen (CYP2C9: Normal Metabolizer) — INFORMATIVE

Individuals with a normal CYP2C9 activity (i.e normal metabolizers) can be prescribed ibuprofen according to standard label recommended-dosage and administration.

Warfarin
Coumadin

Less than normal Sensitivity to Warfarin (CYP2C9 *1/*1 VKORC1 -1639G>A G/G) — ACTIONABLE

Initiation Therapy: a dose increase may be required. Consider using the following warfarin dose range as provided in the FDA-approved label: **5-7 mg/day.** OR consider using a personalized dose calculated by a pharmacogenetic algorithm. The estimated time to reach steady state is 4-5 days.

Medications outside the scope of the report: Allegra, Lisinopril, Loratadine

A medication has potentially reduced efficacy, increased toxicity or the patient has an increased risk for the indicated condition.

Guidelines exist for adjusting dosage, increased vigilance or the patient has a moderate risk for the indicated condition.

The medication can be prescribed according to standard regimens or the patient's risk for the indicated condition is not increased.

ACTIONABLE — Recommendations based upon publications by international pharmacogenetic expert groups, consortia or regulatory bodies (CPIC, DPWG, FDA. EMA). Recommendations are suitable for implementation in a clinical setting. Guidelines may change as knowledge arises.

INFORMATIVE — There are insufficient or contradictory findings documenting the impact of a given genetic polymorphism or drug interaction. Recommendations are informative and implementation in a clinical setting is optional.

Risk Management

Type III Hyperlipoproteinemia

Not Associated with Type III Hyperlipoproteinemia

The patient is positive for the APOE c.388 T>C (Cys130Arg) mutation and negative for the APOE c.526 C>T (Arg176Cys) mutation. The patient's genotype is ε3/ε4 (frequency: 15-28%).
The APOE E3 is the normal APOE. The APOE E4 confers a limitation of HDL binding to its receptor, and is associated with increased plasma cholesterol, LDL, and triglycerides. Individuals that are heterozygous for this allele may have higher total cholesterol levels and elevated LDL cholesterol levels. The APOE ε3/ε4 genotype is associated with an increased risk for developing atherosclerosis and cardiovascular disease.
Consider dietary adjustments (very low fat diet) and lipid-lowering therapy based on lipid profiles and other risk factors.

Hyperhomocysteinemia - Depression

No Increased Risk of Hyperhomocysteinemia

The patient does not carry the MTHFR C677T variant. MTHFR enzyme activity is normal.
Patients diagnosed with depression often have low folate levels and homocysteine is a highly sensitive marker of folate status. Functional folate deficiency is indicated by elevated homocysteine. With a normal MTHFR activity, this patient can process folate normally and is unlikely to have elevated plasma levels of homocysteine.
Patients diagnosed with depression: as lower folate levels are associated with poorer antidepressant response, and baseline levels of folate within the normal range predict antidepressant response, testing for homocysteine levels and serum folate levels may be informative for this patient before prescribing methylfolate as an antidepressant-augmenting agent.

Thrombophilia

No Increased Risk of Thrombosis

The patient does not carry the Factor V Leiden G1691A mutation or Factor II G20210A mutation (wild-type).
The patient's risk of thrombosis is not increased (average risk of clotting is about 1 in 1000 for anyone in a year). However, because this test cannot find all of the inherited reasons for abnormal clotting, other factors may affect this risk assessment.
Unless other genetic and/or circumstantial risk factors are present (e.g., smoking or obesity...), estrogen-containing contraceptive and hormone replacement therapy can be used by the patient.

Hyperhomocysteinemia - Thrombosis

No Increased Risk of Hyperhomocysteinemia

The patient does not carry the MTHFR C677T or MTHFR A1298C mutation (wild-type). MTHFR enzyme activity is normal.
With a normal MTHFR activity, this patient is unlikely to have elevated plasma levels of homocysteine, which is a known risk factor for cardiovascular diseases and thrombosis. Unless other risk factors are present, the patient is not expected to have an increased risk for venous thromboembolism (VTE).
MTHFR enzyme activity is normal.

Potentially Impacted Medications

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Anticancer Agents	**Antifolates**	Methotrexate (Trexall)		
Cardiovascular	**Angiotensin II Receptor Antagonists**	Azilsartan (Edarbi, Edarbyclor) Candesartan (Atacand) Eprosartan (Teveten) Irbesartan (Avapro) Losartan (Cozaar, Hyzaar) Olmesartan (Benicar) Telmisartan (Micardis) Valsartan (Diovan, Entresto)		
	Antianginal Agents	Ranolazine (Ranexa)		
	Antiarrhythmics		Mexiletine (Mexitil) Propafenone (Rythmol)	Flecainide (Tambocor)
	Anticoagulants	Apixaban (Eliquis) Dabigatran Etexilate (Pradaxa) Edoxaban (Savaysa) Fondaparinux (Arixtra) Rivaroxaban (Xarelto) Warfarin (Coumadin)		
	Antiplatelets	Prasugrel (Effient) Ticagrelor (Brilinta) Vorapaxar (Zontivity)	Clopidogrel (Plavix)	
	Beta Blockers	Atenolol (Tenormin) Bisoprolol (Zebeta) Carvedilol (Coreg) Labetalol (Normodyne, Trandate) Nebivolol (Bystolic) Propranolol (Inderal) Timolol (Timoptic)		Metoprolol (Lopressor)
	Diuretics	Torsemide (Demadex)		
	Statins	Atorvastatin (Lipitor) Fluvastatin (Lescol) Lovastatin (Mevacor, Altoprev, Advicor) Pitavastatin (Livalo) Pravastatin (Pravachol) Rosuvastatin (Crestor) Simvastatin (Zocor)		
Diabetes	**Meglitinides**	Nateglinide (Starlix) Repaglinide (Prandin, Prandimet)		
	Sulfonylureas	Chlorpropamide (Diabenese) Glimepiride (Amaryl) Glipizide (Glucotrol) Glyburide (Micronase) Tolbutamide (Orinase)		

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Gastrointestinal	Antiemetics	Aprepitant (Emend-oral) Dronabinol (Marinol) Fosaprepitant (Emend-i.v) Granisetron (Sancuso, Sustol) Metoclopramide (Reglan) Rolapitant (Varubi)	Dolasetron (Anzemet) Netupitant-Palonosetron (Akynzeo) Palonosetron (Aloxi)	Ondansetron (Zofran, Zuplenz)
	Proton Pump Inhibitors	Rabeprazole (Aciphex)	Dexlansoprazole (Dexilant, Kapidex) Esomeprazole (Nexium) Lansoprazole (Prevacid) Omeprazole (Prilosec) Pantoprazole (Protonix)	
Infections	Antifungals	Amphotericin B (AmBisome, Abelcet) Anidulafungin (Eraxis) Caspofungin (Cancidas) Fluconazole (Diflucan) Isavuconazonium (Cresemba) Itraconazole (Sporanox) Micafungin (Mycamine) Posaconazole (Noxafil)		Voriconazole (Vfend)
	Anti-HIV Agents	Dolutegravir (Tivicay, Triumeq) Raltegravir (Isentress, Dutrebis)		
	Antimalarials	Proguanil (Malarone)		
Pain	Fibromyalgia Agents	Milnacipran (Savella)		
	Muscle Relaxants	Cyclobenzaprine (Flexeril, Amrix) Metaxalone (Skelaxin) Methocarbamol (Robaxin)	Carisoprodol (Soma) Tizanidine (Zanaflex)	
	NSAIDs	Celecoxib (Celebrex) Diclofenac (Voltaren) Flurbiprofen (Ansaid) Ibuprofen (Advil, Motrin) Indomethacin (Indocin) Ketoprofen (Orudis) Ketorolac (Toradol) Meloxicam (Mobic) Nabumetone (Relafen) Naproxen (Aleve) Piroxicam (Feldene) Sulindac (Clinoril)		
	Opioids	Alfentanil (Alfenta) Buprenorphine (Butrans, Buprenex) Hydromorphone (Dilaudid, Exalgo) Levorphanol (Levo Dromoran) Meperidine (Demerol) Methadone (Dolophine) Oxymorphone (Opana, Numorphan) Sufentanil (Sufenta) Tapentadol (Nucynta)	Dihydrocodeine (Synalgos-DC) Fentanyl (Actiq) Hydrocodone (Vicodin) Morphine (MS Contin) Oxycodone (Percocet, Oxycontin)	Codeine (Codeine; Fioricet with Codeine) Tramadol (Ultram)
	Antiaddictives	Bupropion (Wellbutrin, Zyban, Aplenzin, Contrave) Naltrexone (Vivitrol, Contrave)		

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Psychotropic	Anti-ADHD Agents	Amphetamine (Adderall, Evekeo) Dexmethylphenidate (Focalin) Dextroamphetamine (Dexedrine) Guanfacine (Intuniv) Lisdexamfetamine (Vyvanse) Methylphenidate (Ritalin, Aptensio XR, Concerta, Metadate ER, Quillivant ER)	Clonidine (Kapvay)	Atomoxetine (Strattera)
	Anticonvulsants	Brivaracetam (Briviact) Cannabidiol (Epidiolex) Carbamazepine (Tegretol, Carbatrol, Epitol) Eslicarbazepine (Aptiom) Ethosuximide (Zarontin) Ezogabine (Potiga) Felbamate (Felbatol) Fosphenytoin (Cerebyx) Gabapentin (Neurontin) Lacosamide (Vimpat) Lamotrigine (Lamictal) Levetiracetam (Keppra) Oxcarbazepine (Trileptal, Oxtellar XR) Perampanel (Fycompa) Phenobarbital (Luminal) Phenytoin (Dilantin) Pregabalin (Lyrica) Primidone (Mysoline) Rufinamide (Banzel) Stiripentol (Diacomit) Tiagabine (Gabitril) Topiramate (Topamax) Valproic Acid (Depakote, Depakene) Vigabatrin (Sabril) Zonisamide (Zonegran)		
	Antidementia Agents	Galantamine (Razadyne) Memantine (Namenda)	Donepezil (Aricept)	
	Antidepressants	Desvenlafaxine (Pristiq) Duloxetine (Cymbalta) Fluoxetine (Prozac, Sarafem) Levomilnacipran (Fetzima) Mirtazapine (Remeron) Nefazodone (Serzone) Trazodone (Oleptro) Vilazodone (Viibryd) Vortioxetine (Trintellix)	Amoxapine (Amoxapine) Fluvoxamine (Luvox) Maprotiline (Ludiomil) Sertraline (Zoloft)	Amitriptyline (Elavil) Citalopram (Celexa) Clomipramine (Anafranil) Desipramine (Norpramin) Doxepin (Silenor) Escitalopram (Lexapro) Imipramine (Tofranil) Nortriptyline (Pamelor) Paroxetine (Paxil, Brisdelle) Protriptyline (Vivactil) Trimipramine (Surmontil) Venlafaxine (Effexor)

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
	Antipsychotics	Aripiprazole (Abilify, Aristada) Asenapine (Saphris) Brexpiprazole (Rexulti) Cariprazine (Vraylar) Iloperidone (Fanapt) Loxapine (Loxitane, Adasuve) Lurasidone (Latuda) Paliperidone (Invega) Pimavanserin (Nuplazid) Quetiapine (Seroquel) Thioridazine (Mellaril) Thiothixene (Navane) Trifluoperazine (Stelazine) Ziprasidone (Geodon)	Chlorpromazine (Thorazine) Clozapine (Clozaril) Fluphenazine (Prolixin) Olanzapine (Zyprexa) Perphenazine (Trilafon) Pimozide (Orap)	Haloperidol (Haldol) Risperidone (Risperdal)
	Benzodiazepines	Alprazolam (Xanax) Clobazam (Onfi) Clonazepam (Klonopin)	Diazepam (Valium) Lorazepam (Ativan) Oxazepam (Serax)	
	Other Neurological Agents	Deutetrabenazine (Austedo) Dextromethorphan / Quinidine (Nuedexta) Flibanserin (Addyi) Valbenazine (Ingrezza)	Tetrabenazine (Xenazine)	
Rheumatology	Anti-Hyperuricemics and Anti-Gout Agents	Colchicine (Mitigare) Febuxostat (Uloric) Lesinurad (Zurampic)		
	Immunomodulators	Apremilast (Otezla) Leflunomide (Arava) Tofacitinib (Xeljanz)		
Transplantation	Immunosupressants	Tacrolimus (Prograf)		
Urologicals	5-Alpha Reductase Inhibitors for Benign Prostatic Hyperplasia	Dutasteride (Avodart) Finasteride (Proscar)		
	Alpha-Blockers for Benign Prostatic Hyperplasia	Alfuzosin (UroXatral) Doxazosin (Cardura) Silodosin (Rapaflo) Tamsulosin (Flomax) Terazosin (Hytrin)		
	Antispasmodics for Overactive Bladder	Darifenacin (Enablex) Fesoterodine (Toviaz) Mirabegron (Myrbetriq) Oxybutynin (Ditropan) Solifenacin (Vesicare) Tolterodine (Detrol) Trospium (Sanctura)		
	Phosphodiesterase Inhibitors for Erectile Dysfunction	Avanafil (Stendra) Sildenafil (Viagra) Tadalafil (Cialis) Vardenafil (Levitra)		

Dosing Guidance

Amitriptyline
Elavil

Possible Non-Response to Amitriptyline (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: consider an alternative drug, or prescribe amitriptyline at increased dose and monitor the plasma concentrations of amitriptyline and metabolites (there is insufficient data to calculate dose adjustment).

Amitriptyline
Elavil

Increased Sensitivity to Amitriptyline (CYP2C19: Rapid Metabolizer) — INFORMATIVE

Consider an alternative drug, or consider prescribing amitriptyline at standard dose and monitor the plasma concentrations of amitriptyline and nortriptyline to guide dose adjustments.

Atomoxetine
Strattera

Possible Non-Response to Atomoxetine (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: the patient may fail to achieve adequate plasma levels of atomoxetine if the drug is prescribed at standard recommended doses. Consider prescribing atomoxetine with careful titration and monitoring for reduced efficacy. There is insufficient data to calculate dose adjustment. Or consider an alternative medication.

Citalopram
Celexa

Insufficient Response to Citalopram (CYP2C19: Rapid Metabolizer) — ACTIONABLE

At standard label-recommended dosage, citalopram plasma concentrations levels are expected to be low which may result in a loss of efficacy. Consider an alternative medication. If citalopram is warranted, consider increasing the dose to a maximum of 150% and titrate based on the clinical response and tolerability.

Clomipramine
Anafranil

Possible Non-Response to Clomipramine (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: consider an alternative drug, or prescribe clomipramine at an increased dose and monitor the plasma concentrations of clomipramine and desmethylclomipramine.

Clomipramine
Anafranil

Increased Sensitivity to Clomipramine (CYP2C19: Rapid Metabolizer) — INFORMATIVE

Consider an alternative drug, or consider prescribing clomipramine at standard dose and monitor the plasma concentrations of clomipramine and desmethyl-clomipramine to guide dose adjustments.

Codeine
Codeine; Fioricet with Codeine

Possible Increased Response to Codeine (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer. Codeine is converted into its active metabolite morphine by CYP2D6. Since this patient may be a ultra-rapid metabolizer, greatly increased morphine levels may occur, and the patient may be at high risk of toxicity when taking codeine. The ultra-rapid conversion of codeine to morphine in breast feeding mothers can result in high and unsafe levels of morphine in the breast milk potentially causing life threatening respiratory depression in the breastfed infant. Avoid prescribing codeine, and consider an alternative opioid or a non-opioid analgesic such as a NSAID or a COX-2 inhibitor. Unless contraindicated, available alternative opioids not sensitive to CYP2D6 function include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.

Desipramine
Norpramin

Possible Non-Response to Desipramine (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: consider an alternative drug, or prescribe desipramine at an increased dosage and observe the patient for decreased efficacy. Adjust dosage in response to desipramine and metabolites plasma concentrations and clinical response.

Doxepin
Silenor

Possible Non-Response to Doxepin (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: consider an alternative drug, or increase doxepin dose by 100%. Adjust maintenance dose according to nordoxepin plasma concentrations.

Doxepin
Silenor

Increased Sensitivity to Doxepin (CYP2C19: Rapid Metabolizer) — INFORMATIVE

Consider an alternative drug, or consider prescribing doxepin at standard dose and monitor the plasma concentrations of doxepin and desmethyl-doxepin to guide dose adjustments.

Escitalopram
Lexapro

Insufficient Reponse to Escitalopram (CYP2C19: Rapid Metabolizer) — ACTIONABLE

At standard label-recommended dosage, escitalopram plasma concentrations levels are expected to be low which may result in a loss of efficacy. Consider an alternative medication. If escitalopram is warranted, consider increasing the dose to a maximum of 150% and titrate based on the clinical response and tolerability.

Flecainide
Tambocor

Altered Response to Flecainide (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: titrate carefully and consider adjusting dose in response to plasma concentration and ECG monitoring, OR consider an alternative drug. Examples of alternatives drugs not affected by CYP2D6 include: sotalol, disopyramide, quinidine, and amiodarone.

Haloperidol
Haldol

Possible Non-Response to Haloperidol (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: consider an alternative drug, or prescribe haloperidol at standard dose and adjust dosage to achieve a favorable clinical response. Be alert to decreased haloperidol plasma concentrations.

Imipramine
Tofranil

Possible Non-Response to Imipramine (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: consider an alternative drug, or consider increasing the imipramine dose and adjust the dosage in response to imipramine and desipramine plasma concentrations.

Imipramine
Tofranil

Increased Sensitivity to Imipramine (CYP2C19: Rapid Metabolizer) — INFORMATIVE

Consider an alternative drug, or consider prescribing imipramine at the standard dose and monitor the plasma concentrations of imipramine and desipramine to guide dose adjustments.

Metoprolol
Lopressor

Possible Non-Responder to Metoprolol (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: the patient may experience a decrease in the pharmacological effect when taking metoprolol at standard dosage. Heart Failure: Consider alternative beta-blockers such as bisoprolol or carvedilol, or prescribe metoprolol at a higher dose. Other indications: Consider alternative beta-blockers such as bisoprolol or atenolol, or prescribe metoprolol at a higher dose. If metoprolol is prescribed, titrate the dose to a maximum of 250% of the normal dose in response to efficacy and adverse events.

Nortriptyline
Pamelor

Possible Non-Response to Nortriptyline (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: consider an alternative drug, or prescribe nortriptyline at an increased dose and monitor the plasma concentration of nortriptyline and hydroxynortriptyline.

Ondansetron
Zofran, Zuplenz

Possible Non-Response to Ondansetron (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: a substantially decreased antiemetic effect has been reported in these patients when taking standard doses of this medication. Consider prescribing an alternative drug not metabolized by CYP2D6 such as granisetron.

Paroxetine

Paxil, Brisdelle

Possible Reduced Response to Paroxetine (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: there is a risk for decreased efficacy at standard dosage. If a standard dose is prescribed to a CYP2D6 ultra-rapid metabolizer, suboptimal plasma concentrations of the drug are likely. Consider an alternative medication.

Protriptyline

Vivactil

Possible Non-Response to Protriptyline (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: consider alternative drugs or prescribe protriptyline at increased dosage and observe the patient for decreased efficacy. Adjust dosage in response to protriptyline and metabolites plasma concentrations and clinical response.

Risperidone

Risperdal

Possible Non-Response to Risperidone (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: consider an alternative drug, or prescribe risperidone, be extra alert to insufficient response, and adjust dosage in response to clinical response and adverse events.

Tramadol

Ultram

Possible Increased Response to Tramadol (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, and is at high risk of toxicity when taking tramadol at standard dosing. Consider reducing tramadol dose by 30%. Careful monitoring for side effects (nausea, vomiting, constipation, respiratory depression, confusion, urinary retention) and weekly titration are recommended. In case of toxicity, consider alternative opioids other than codeine, or a non-opioid analgesic such as a NSAID or a COX-2 inhibitor. Unless contraindicated, available alternative opioids not sensitive to CYP2D6 function include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.

The accelerated conversion of tramadol to its active metabolite can result in high and unsafe levels of this metabolite in breast milk potentially causing life threatening respiratory depression in the breastfed infant. Use of tramadol should be avoided in breastfeeding mothers.

Trimipramine

Surmontil

Possible Non-Response to Trimipramine (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: consider an alternative drug, or consider prescribing trimipramine at an increased dose, then adjust dosage in response to trimipramine plasma concentrations.

Trimipramine

Surmontil

Increased Sensitivity to Trimipramine (CYP2C19: Rapid Metabolizer) — INFORMATIVE

Consider an alternative drug, or consider prescribing trimipramine at standard dose and monitor the plasma concentrations of trimipramine and desmethyl-trimipramine to guide dose adjustments.

Venlafaxine

Effexor

Possible Non-Response to Venlafaxine (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: consider an alternative drug, or increase the venlafaxine dose to a maximum of 150% of the normal dose and monitor venlafaxine and O-desmethylvenlafaxine plasma concentrations.

Voriconazole

Vfend

Non-Response to Voriconazole (CYP2C19: Rapid Metabolizer) — ACTIONABLE

Voriconazole plasma concentrations are expected to be low if a standard dose is used, increasing the risk of loss of response and effectiveness and subsequent disease progression. Consider an alternative medication that is not dependent on CYP2C19 metabolism, such as isavuconazole, liposomal amphotericin B or posaconazole.

Amoxapine

Amoxapine

Possible Non-Response to Amoxapine (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

Like other tricyclic and tetracyclic antidepressants, amoxapine is metabolized by CYP2D6. However, the overall contribution of this enzyme in the metabolism of this drug is not well documented. Based on the genotype result, this patient may be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: patients with increased CYP2D6 function may metabolize amoxapine more rapidly which can result in sub-therapeutic drug concentrations; these patients may require higher doses to achieve adequate plasma concentrations. There are no established dosing adjustments for patients with increased CYP2D6 function; therapy must be initiated cautiously and adjusted according to the patient's response.

Carisoprodol

Soma

Altered Sensitivity to Carisoprodol (CYP2C19: Rapid Metabolizer) — INFORMATIVE

There is insufficient data to allow calculation of dose adjustment. If carisoprodol is prescribed, it is recommended to use a lower dose, and to carefully monitor the patient for side effects.

Chlorpromazine

Thorazine

Possible Non-Response to Chlorpromazine (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

Chlorpromazine is metabolized by CYP2D6, CYP3A4 and flavin-containing monooxygenases. Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: subjects with increased CYP2D6 function will metabolize chlorpromazine more rapidly which can result in sub-therapeutic drug concentrations. Consider a standard dose and adjust dosage according to the patient's tolerability and response. Higher doses may be necessary to achieve efficacy.

Clonidine

Kapvay

Possible Altered Response to Clonidine (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers. Approximately 40-60% of an orally administered dose of clonidine is eliminated unchanged by the kidneys, with the remainder undergoing hepatic metabolism. CYP2D6 plays a major role in clonidine oxidative metabolism, followed by CYP3A and CYP1A2. **Preliminary studies that individuals with high CYP2D6 activity, have increased clonidine clearance and may require higher doses to reach target therapeutic plasma concentrations and respond to therapy.** There is insufficient data to calculate dose adjustments and careful titration is recommended until a favorable response is achieved in this patient. An alternative medication not metabolized by CYP2D6 can also be considered if the patient fails to respond to higher doses of clonidine.

Treatment with clonidine can cause dose related decreases in blood pressure and heart rate Measure heart rate and blood pressure prior to initiation of therapy, following dose increases, and periodically while on therapy. Titrate Clonidine slowly in patients with a history of hypotension, and those with underlying conditions that may be worsened by hypotension and bradycardia.

Clopidogrel

Plavix

Increased Response to Clopidogrel (CYP2C19: Rapid Metabolizer) — ACTIONABLE

Clopidogrel can be prescribed at standard label-recommended dosage. Individuals with the *17 allele may have an increased risk of bleeding while taking clopidogrel.

Clozapine

Clozaril

Non-Response to Clozapine (CYP1A2: Normal Metabolizer - Higher Inducibility) — INFORMATIVE

Smokers have a high risk for non-response at standard doses and may require higher doses. There is an association between high clozapine doses and the risk of seizures, and therefore careful monitoring is recommended during dosing adjustment. Smoking cessation will increase plasma drug levels, leading to adverse events. Therefore, therapeutic drug monitoring accompanied by dose reduction is recommended in patients who have quit smoking.

Dexlansoprazole

Dexilant, Kapidex

Insufficient Response to Dexlansoprazole (CYP2C19: Rapid Metabolizer) — INFORMATIVE

- Helicobacter pylori eradication: increase dose by 200% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase of 200%.

Diazepam

Valium

Possible Altered Sensitivity to Diazepam (CYP2C19: Rapid Metabolizer) — INFORMATIVE

CYP2C19 rapid and ultra-rapid metabolizers metabolize diazepam and nordiazepam more rapidly than normal metabolizers. However, there is insufficient data to allow calculation of dose adjustment when diazepam is prescribed. Monitor the patient's response and adjust the dose accordingly.

Dihydrocodeine

Synalgos-DC

Possible Altered Response to Dihydrocodeine (CYP2D6: Ultra-Rapid or Normal Metabolizer) **INFORMATIVE**

Increased conversion of dihydrocodeine to the more active metabolite dihydromorphine is expected in CYP2D6 ultra-rapid metabolizers. This may result in an exaggerated response. Adequate pain relief can be achieved by decreasing the dose in response to pain symptoms. Other opioids not metabolized by CYP2D6 (i.e., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone) may also be considered if signs of overdose (excessive sleepiness, confusion, or shallow breathing) are reported.

Dolasetron

Anzemet

Possible Altered Response to Dolasetron (CYP2D6: Ultra-Rapid or Normal Metabolizer) **INFORMATIVE**

The reduction of dolasetron to its active metabolite hydrodolasetron is mediated by a carbonyl reductase. Hydrodolasetron is further eliminated by multiple routes, including renal excretion and by glucuronidation or hydroxylation by CYP2D6. Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: compared to CYP2D6 normal metabolizers, CYP2D6 ultra-rapid metabolizers may have lower hydroxydolasetron plasma concentrations at standard dosing. However, the clinical significance of this change remains unclear. Dolasetron can be prescribed at standard label-recommended dosage and administration. Monitor the patient for possible decreased efficacy.

Donepezil

Aricept

Possible Altered Response to Donepezil (CYP2D6: Ultra-Rapid or Normal Metabolizer) **INFORMATIVE**

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: when compared to a normal metabolizer, a ultra-rapid metabolizers has a 24% increase in donepezil clearance. The clinical significance of this increase is not well documented. Consider using a standard dosing regimen and adjust dosage in response to clinical response and tolerability.

Esomeprazole

Nexium

Insufficient Response to Esomeprazole (CYP2C19: Rapid Metabolizer) **INFORMATIVE**

- Helicobacter pylori eradication: increase dose by 50-100% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase of 50-100%.

Fentanyl

Actiq

Altered Response to Fentanyl (OPRM1: Altered OPRM1 Function) **INFORMATIVE**

The patient carries one copy of the OPRM1 118A>G mutation. Acute postoperative and cancer pain: the patient's genotype has been shown to be associated with reduced analgesia at standard fentanyl doses. Therefore, the patient may require higher doses of this drug. Because fentanyl has a narrow therapeutic window, it is advised to carefully titrate this drug to a tolerable dose that provides adequate analgesia with minimal side effects.

Fluphenazine

Prolixin

Possible Non-response to Fluphenazine (CYP2D6: Ultra-Rapid or Normal Metabolizer) **INFORMATIVE**

Fluphenazine is metabolized by CYP2D6, CYP1A2 and other enzymes and based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: **patients with increased CYP2D6 function will metabolize fluphenazine more rapidly which can result in sub-therapeutic drug concentrations; these patients may require higher doses to achieve adequate plasma concentrations.** There are no established dosing adjustments for patients with increased CYP2D6 function therefore, therapy must be initiated cautiously with oral or parenteral fluphenazine hydrochloride. When the pharmacological effects and an appropriate dosage are apparent, an equivalent dose of fluphenazine decanoate (IM or SC) may be administered and subsequent dosage adjustments may be necessary.

Fluvoxamine

Luvox

Possible Reduced Response to Fluvoxamine (CYP2D6: Ultra-Rapid or Normal Metabolizer) **INFORMATIVE**

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: there is a risk for decreased efficacy at standard dosage. If a standard dose is prescribed to a CYP2D6 ultra-rapid metabolizer, suboptimal plasma concentrations of the drug are likely. There is insufficient data to calculate dose adjustments and careful titration is recommended until a favorable response is achieved. An alternative medication not metabolized by CYP2D6 can also be considered.

Hydrocodone

Vicodin

Altered Response to Hydrocodone (OPRM1: Altered OPRM1 Function) **INFORMATIVE**

Acute postoperative and cancer pain: the patient's genotype has been shown to be associated with reduced analgesia and increased opioid side effects at standard or high hydrocodone doses. If the patient fails to respond to increased hydrocodone doses, an alternative opioid may be considered.

Hydrocodone
Vicodin

Possible Altered Response to Hydrocodone (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer. Increased conversion of hydrocodone to the more active metabolite hydromorphone is expected in CYP2D6 ultra-rapid metabolizers. Usually, adequate pain relief without an increase in adverse events can be achieved by using standard or lower hydrocodone doses. Other opioids not metabolized by CYP2D6 (e.g., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone) may also be considered if excessive side effects are reported.

Lansoprazole
Prevacid

Insufficient Response to Lansoprazole (CYP2C19: Rapid Metabolizer) — INFORMATIVE

- Helicobacter pylori eradication: increase dose by 200% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase of 200%.

Lorazepam
Ativan

Possible Altered Response to Lorazepam (UGT2B15: Intermediate Metabolizer) — INFORMATIVE

Lorazepam clearance may be reduced in this patient. However, there is insufficient evidence whether this change results in a significant clinical effect. Consider monitoring the patient for increased sedation and adjust dosing accordingly.

Maprotiline
Ludiomil

Possible Non-response to Maprotiline (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

Like other tricyclic and tetracyclic antidepressants, maprotiline is metabolized by CYP2D6 as well as CYP1A2. Patients with increased CYP2D6 function may metabolize maprotiline more rapidly which can result in sub-therapeutic drug concentrations; these patients may require higher doses to achieve adequate plasma concentrations. There are no established dosing adjustments for patients with increased CYP2D6 function. Seizures have been associated with the use of maprotiline especially at high doses. Therefore, therapy must be initiated at a standard dose and gradually increased in small increments according to the patient's response.

Mexiletine
Mexitil

Altered Response to Mexiletine (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: because mexiletine plasma concentrations may be decreased, consider adjusting dose in response to mexiletine plasma concentration and ECG monitoring, until a favorable response in achieved.

Morphine
MS Contin

Altered Response to Morphine (OPRM1: Altered OPRM1 Function) — INFORMATIVE

The patient carries one copy of the OPRM1 118A>G mutation. Acute postoperative and cancer pain: the patient's genotype has been shown to be associated with possible reduced analgesia at standard morphine doses and decreased risk for nausea and vomiting during the first 24-hour postoperative period. Therefore, the patient may require higher doses of this drug. The dosing regimen needs to be individualized for each patient, taking into account the patient's prior analgesic treatment experience.

Morphine
MS Contin

Altered Response to Morphine (COMT: High/Normal COMT Activity) — INFORMATIVE

The patient does not carry the COMT Val158Met mutation. The patient may require higher doses of morphine for adequate pain control. The dosing regimen needs to be individualized for each patient, taking into account the patient's prior analgesic treatment experience.

Netupitant-Palonosetron
Akynzeo

Possible Altered Response to Netupitant-Palonosetron (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

Netupitant: Netupitant is extensively metabolized to three major metabolites (desmethyl, N-oxide and a hydroxy-methyl derivatives). Metabolism is mediated primarily by CYP3A4 and to a lesser extent by CYP2C9 and CYP2D6. No genetically guided drug selection or dosing recommendations are available for this drug. Netupitant can be prescribed at standard label-recommended dosage and administration.
Palonosetron: Palonosetron is eliminated by multiple routes including metabolism. While CYP2D6 and to a lesser extent, CYP3A4 and CYP1A2 are involved in its metabolism to two inactive metabolites. Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: compared to CYP2D6 normal metabolizers, CYP2D6 ultra-rapid metabolizers may have lower palonosetron plasma concentrations at standard dosing. However, the clinical significance of this change remains unclear. Palonosetron can be prescribed at standard label-recommended dosage and administration. Monitor the patient for possible decreased efficacy.

Olanzapine
Zyprexa

Non-Response to Olanzapine (CYP1A2: Normal Metabolizer - Higher Inducibility) — INFORMATIVE

There is little evidence regarding the impact of CYP1A2 genetic variants on olanzapine response. Smokers may be at risk for non-response at standard doses. Careful monitoring is recommended during dosing adjustment. Smoking cessation may increase plasma drug levels, leading to adverse events. Therefore, therapeutic drug monitoring accompanied by dose reduction may be needed in patients who have quit smoking.

Omeprazole
Prilosec

Insufficient Response to Omeprazole (CYP2C19: Rapid Metabolizer) — ACTIONABLE

- Helicobacter pylori eradication: increase dose by 100-200% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase of 100-200%.

Oxazepam
Serax

Possible Altered Response to Oxazepam (UGT2B15: Intermediate Metabolizer) — INFORMATIVE

Oxazepam clearance may be reduced in this patient. However, there is insufficient evidence whether this change results in a significant clinical effect. Consider monitoring the patient for increased sedation and adjust dosing accordingly.

Oxycodone
Percocet, Oxycontin

Possible Altered Response to Oxycodone (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer. Increased conversion of oxycodone to the more active metabolite oxymorphone is expected in CYP2D6 ultra-rapid metabolizers. Usually, adequate pain relief without an increase in adverse events can be achieved by using standard or lower oxycodone doses. Other opioids not metabolized by CYP2D6 (e.g., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone) may also be considered if excessive side effects are reported.

Palonosetron
Aloxi

Possible Altered Response to Palonosetron (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

Palonosetron is eliminated by multiple routes including metabolism. While CYP2D6 and to a lesser extent, CYP3A4 and CYP1A2 are involved in its metabolism to two inactive metabolites. Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: compared to CYP2D6 normal metabolizers, CYP2D6 ultra-rapid metabolizers may have lower palonosetron plasma concentrations at standard dosing. However, the clinical significance of this change remains unclear. Palonosetron can be prescribed at standard label-recommended dosage and administration. Monitor the patient for possible decreased efficacy.

Pantoprazole
Protonix

Insufficient Response to Pantoprazole (CYP2C19: Rapid Metabolizer) — ACTIONABLE

- Helicobacter pylori eradication: increase dose by 400% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase of 400%.

Perphenazine
Trilafon

Possible Non-Response to Perphenazine (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: subjects with increased CYP2D6 function will metabolize perphenazine more rapidly, which can result in sub-therapeutic drug concentrations. Consider a dose increase with close monitoring until a favorable response is achieved.

Pimozide
Orap

Possible Non-Response to Pimozide (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: there is insufficient data to calculate dose adjustment, and if pimozide is prescribed at standard dosing, monitor response and be alert to reduced efficacy. Standard starting dose: 1 to 2 mg/day (adult) or 0.05 mg/kg/day (children). Doses may be increased to a maximum of 10 mg/day or 0.2 mg/kg/day.

Propafenone
Rythmol

Altered Response to Propafenone (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers:titrate carefully and consider adjusting dose in response to plasma concentration and ECG monitoring, OR consider an alternative drug. Examples of alternatives drugs not affected by CYP2D6 include: sotalol, disopyramide, quinidine, and amiodarone.

Sertraline

Zoloft

Possible Reduced Response to Sertraline (CYP2C19: Rapid Metabolizer) — INFORMATIVE

Sertraline can be prescribed at standard label-recommended dosage and administration. If patient does not respond to recommended maintenance dosing, consider an alternative medication.

Tetrabenazine

Xenazine

Unknown Sensitivity to Tetrabenazine (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

For treating chorea associated with Huntington's disease: Individualization of dose with careful weekly titration is required. The first week's starting dose is 12.5 mg daily; second week, 25 mg (12.5 mg twice daily); then slowly titrate at weekly intervals by 12.5 mg to a tolerated dose. **The maximum daily dose in CYP2D6 ultra-rapid metabolizers is not defined. The maximum daily dose in normal metabolizers is 100 mg with a maximum single dose of 37.5 mg**. If serious adverse events occur, titration should be stopped and the dose of tetrabenazine should be reduced. If the adverse event(s) do not resolve, consider withdrawal of tetrabenazine.

Tizanidine

Zanaflex

Possible Non-Response to Tizanidine (CYP1A2: Normal Metabolizer - Higher Inducibility) — INFORMATIVE

There is little evidence regarding the impact of CYP1A2 genetic variants on tizanidine response. Smokers may be at risk for non-response and may require higher doses. There is an association between high tizanidine plasma concentrations and the risk of hypotension and excessive sedation. Therefore, careful monitoring is recommended during dosing adjustment. Smoking cessation may increase plasma drug levels, leading to excessive hypotension and sedation. Careful monitoring accompanied by dose reduction may be needed in patients who have quit smoking.

Test Details

Gene	Genotype	Phenotype	Clinical Consequences
CYP2C9	*1/*1	**Normal Metabolizer**	Consistent with a typical CYP2C9 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.
CYP2C19	*1/*17	**Rapid Metabolizer**	Consistent with a significant increase in CYP2C19 activity. Potential risk for side effects or loss of efficacy with drug substrates.
CYP3A5	*3/*3	**Poor Metabolizer**	Consistent with a poor CYP3A5 activity. This phenotype is the most common in the general population. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.
CYP3A4	*1/*1	**Normal Metabolizer**	Consistent with a typical CYP3A4 activity. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.
VKORC1	-1639G>A G/G	**Low Warfarin Sensitivity**	VKORC1 is the site of action of warfarin. The patient may require an increase in warfarin dose.
Apolipoprotein E	ε3/ε4	**Altered APOE function**	Not associated with type III hyperlipoproteinemia - Increased risk of cardiovascular disease
CYP2D6	*1/*4 XN	**Ultra-Rapid or Normal Metabolizer**	Consistent with typical or increased CYP2D6 activity. Potential risk for side effects or loss of efficacy with drug substrates.
CYP2B6	*1/*1	**Normal Metabolizer**	Consistent with a typical CYP2B6 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.
CYP1A2	*1A/*1F	**Normal Metabolizer - Higher Inducibility**	Consistent with a typical CYP1A2 activity in absence of inducing substances. Rapid Metabolism occurs in presence of inducers such as barbiturates, cruciferous vegetables, carbamazepine, rifampin and smoking.
SLCO1B1	521T>C T/T	**Normal Function**	Consistent with a typical SLCO1B1 transporter function. The patient's risk for statin-induced myopathy is not increased.
COMT	Val158Met G/G	**High/Normal COMT Activity**	Consistent with a normal catechol O-methyltransferase (COMT) function.
OPRM1	A118G A/G	**Altered OPRM1 Function**	Consistent with a reduced OPRM1 receptor signaling efficiency induced by exogenous opioids. This is associated with a possible reduced analgesia following standard opioid doses and a favorable response to naltrexone.
UGT2B15	*1/*2	**Intermediate Metabolizer**	Consistent with a moderately decreased UGT2B15 glucuronidation function. Potential risk for side effects with drug substrates.
MTHFR	1298A>C AA 677C>T CC	**No Increased Risk of Hyperhomocysteinemia**	With a normal MTHFR activity, this patient is unlikely to have elevated plasma levels of homocysteine, which is a known risk factor for cardiovascular diseases and thrombosis. Unless other risk factors are present, the patient is not expected to have an increased risk for venous thromboembolism (VTE).
MTHFR	677C>T CC	**Normal MTHFR Activity**	The patient does not carry the MTHFR C677T mutation (wild-type) and the patient's MTHFR activity is normal. This is not associated with an increased risk of hyperhomocysteinemia.
Factor II **Factor V Leiden**	20210G>A GG 1691G>A GG	**No Increased Risk of Thrombosis**	The patient's risk of thrombosis is not increased (average risk of clotting is about 1 in 1000 for anyone in a year). However, because this test cannot find all of the inherited reasons for abnormal clotting, other factors may affect this risk assessment.

Alleles Tested: Apolipoprotein E ε2, ε4, (ε3 is reference); **COMT** Val158Met; **CYP1A2** *1C, *1D, *1E, *1F, *1J, *1K, *1L, *1V, *1W; **CYP2B6** *7, *16, *5, *6, *9, *18, *22; **CYP2C19** *2, *3, *4, *4B, *5, *6, *7, *8, *9, *17; **CYP2C9** *2, *3, *4, *5, *6, *11; **CYP2D6** *2, *3, *4, *4M, *6, *7, *8, *9, *10, *11, *12, *14A, *14B, *15, *17, *29, *41, *5 (gene deletion), XN (gene duplication); **CYP3A4** *1B, *12, *17, *22; **CYP3A5** *2, *3, *3B, *3C, *6, *7; **Factor II** 20210G>A; **Factor V Leiden** 1691G>A; **MTHFR** 1298A>C, 677C>T; **OPRM1** A118G; **SLCO1B1** 521T>C; **UGT2B15** *2; **VKORC1** -1639G>A

Limitation: This test will not detect all the known alleles that result in altered or inactive tested genes. This test does not account for all individual variations in the individual tested. Absence of a detectable gene mutation does not rule out the possibility that a patient has different phenotypes due to the presence of an undetected polymorphism or due to other factors such as drug-drug interactions, comorbidities and lifestyle habits.

Methodology: Array based assays detect listed alleles, including all common and most rare variants with known clinical significance at analytical sensitivity and specificity >99%.

Disclaimer: The information presented on this report is provided as general educational health information. The Content is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Only a physician, pharmacist or other healthcare professional should advise a patient on the use of the medications prescribed. Mako Medical Laboratories developed this test and its performance characteristics. This test has not been cleared or approved by the U.S. Food and Drug Administration. The pharmacogenetic report is one of multiple pieces of information that clinicians should consider in guiding their therapeutic choice for each patient. It remains the responsibility of the health-care provider to determine the best course of treatment for a patient. Adherence to dose guidelines does not necessarily assure a successful medical outcome.

The pharmacogenetic assay involves non-FDA approved interpretational software and genotype-phenotype associations performed by Translational Software. A qualified designee within Mako Medical Laboratories uses Translational Software to generate and subsequently review the report.

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Translational Software
12410 SE 32nd Street, Suite 250
Bellevue, WA 98040
www.translationalsoftware.com | (206) 777-4603

Patient Information Card

This is a summary genetic report for your patient to share with other healthcare providers. The card can be cut out along the dashed line and carried with the patient.

REPORT DETAILS

Patient: Gene Omics2
DOB: 1/1/1935
ACC #: P1777777

Pharmacogenetic Test Summary

CYP2C19	*1/*17	Rapid Metabolizer
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For a complete report contact Mako Medical Laboratories, LLC
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