ProMedicDNA

Hypertension Sensor

Jane Doe
DEMO_DS

ProGenom
www.progenom.com

COVER LETTER

Dear Ms. Doe,

Your sample for the analysis arrived on in the laboratory and was evaluated according to the highest laboratory quality standards. The results were evaluated and released by two independent geneticists and molecular biologists. After obtaining the results, your personal report was compiled. We hereby convey the results to you in the format of your choice.

We would like to thank you for your trust and hope that you are satisfied with our service. We are always open to questions and suggestions. Please do not hesitate to contact us. We value your feedback. This is the only way we can continuously improve our services.

We hope the analysis meets your expectations.

Kind regards,

Dr. Daniel Wallerstorfer BSc.
Laboratory Director

Florian Schneebauer, MSc.
Laboratory Manager

Hypertension Sensor

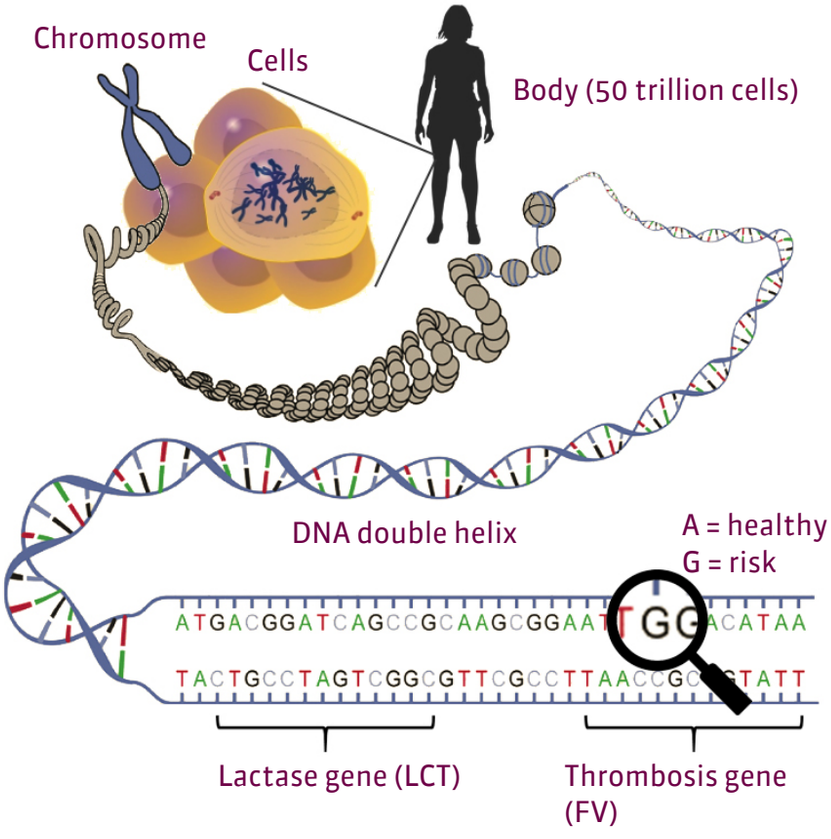
Personal analysis results for:
Jane Doe | Date of birth: 01/01/1990

Order number:
DEMO_DS

This report contains personal medical information that is highly confidential. Data protection must be ensured.

How genes influence our health

The human body consists of about 50 trillion individual cells. Most of these cells have a nucleus, which contains 46 chromosomes. A chromosome consists of a very closely wound thread, the DNA "double helix."



DNA, the genetic code, is the blueprint of the human body. This genetic code consists of approximately 3.1 billion molecules, which are each represented by a letter. About 1% of this code makes up the genes. Each gene is an instruction for the body, usually with a single function. For example, some genes tell the body how to colour the iris and differences in these genes produce different eye colors. Every function of the body is controlled by one or more genes, including the way we break down food or medication.

Our genes are not completely error-free. The genes of each person are altered slightly by environmental effects. Most of these changes have no effect but a small number have a harmful effect. An even tinier number can produce a beneficial effect. Parents pass these changes, including defects, to their children. Thus most of our genetic defects are inherited from our parents.

In addition, our genes evolved to help us live in a completely different world, and some of our genetic traits can interact with our modern environment to create negative effects on the body. For example, the genetic predisposition to store dietary fat quickly and lose it slowly is beneficial for people who go through times when food is scarce: they have a better chance of surviving because their bodies use fat efficiently and store it for later. However, in the modern world, this trait is harmful because it programs the body to gain weight quickly and lose weight

slowly. Genes increase our risk of heart attacks, trigger asthma and allergies, cause lactose intolerance, and many other disorders.

Genetic traits can affect our health. While some genetic defects cause disease in all cases, most genetic traits just increase our risk of developing a disease. For example, a person may have genes that increase their risk for diabetes. However, not everyone at risk for diabetes actually develops the disease. Furthermore, even people with a high risk of diabetes can lower their risk with the right diet and exercise plan. Other genetic traits only cause illness when they are triggered by a specific environmental feature. For example, lactose intolerance is a genetic condition that causes a person who drinks milk to have digestive issues. A lactose-intolerant person who never drinks milk will not have any symptoms.

Thanks to the latest technologies, it is now possible to test specific genes to determine if you have genetic traits that are linked to various diseases. Based on the results of the analysis, we can develop a prevention program that significantly reduces your personal disease risk and helps you stay healthy.

A healthy lifestyle will decrease your risk of many diseases whether or not you have specific information about your genetic traits. However, we provide you with additional information that may point out other changes to your lifestyle that are not part of the standard medical advice. There are many examples, but one of the traits we test for is a gene that increases your body's ability to absorb iron. If you have this trait, you must not take iron supplements as the iron would accumulate and cause a life-threatening disease called haemochromatosis.

Experts estimate that every person carries about 2,000 genetic defects, which may affect their health, and in some cases, cause illnesses. A variety of factors can cause changes in our genes (also called mutations). In a few cases, these mutations can benefit us. However, the vast majority either have no effect or have a negative impact on our health. The best-known cause of mutations is radioactivity. Radioactive rays and particles actually impact the DNA in our cells and physically alter our genes. They mostly go unnoticed or cause deadly diseases, such as cancer, or congenital abnormality in newborns. Mutations are also caused by substances in burned food. The substances enter the cells and damage our genes, which can lead to colon cancer, among other forms of cancer. UV radiation from the sun can also damage our genes and cause diseases, such as skin cancer.

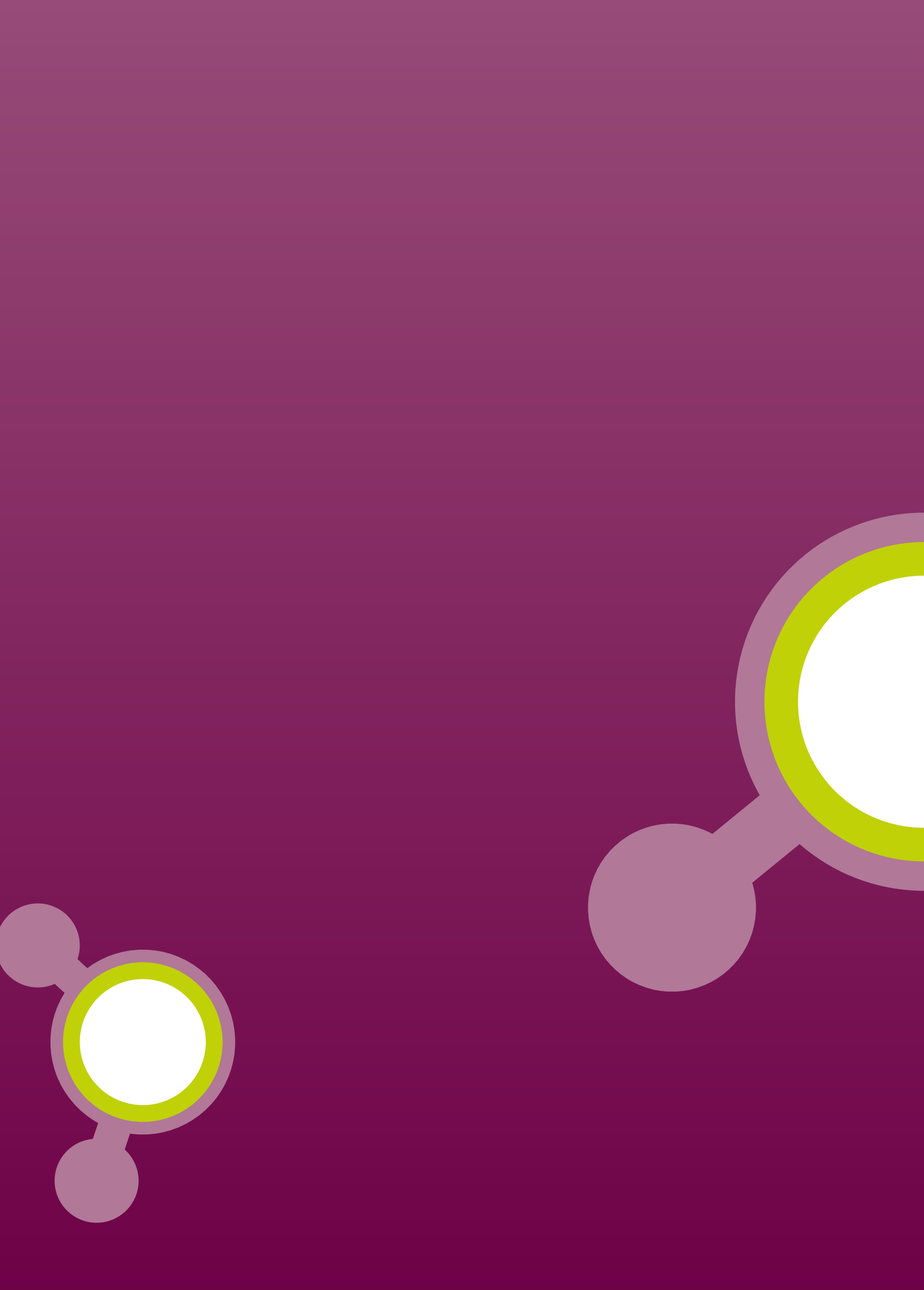
External influences can affect individual genes and disrupt their function, but the majority of our defective genes are inherited from our parents. Each embryo receives half of its genes from the father and half from the mother, resulting in a new human being with some characteristics of each parent. Whether a genetic defect is passed on, is determined randomly, and it may be that some of the children carry the defective gene and others do not.

Each person is the unique product of generations of accumulation and combination of different genetic traits. Some of those traits have negative effects on our health. With the latest technology, it is now finally possible to examine genes and determine personal health risks and strengths. In many cases, taking advantage of this knowledge, and following some precautionary measures, the diseases may be prevented. This is the next step in preventive medicine and a new generation of health care.

Action index

Discuss risks marked in orange or red with your doctor. All other results do not require any further attention assuming there are no current medical conditions.

Hypertension Sensor



PHARMACO GENETICS
Not ordered

ONCOLOGY
Not ordered

CARDIOVASCULAR SYSTEM

NEUROLOGY
Not ordered

METABOLISM
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MOVEMENT
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OPHTHALMOLOGY
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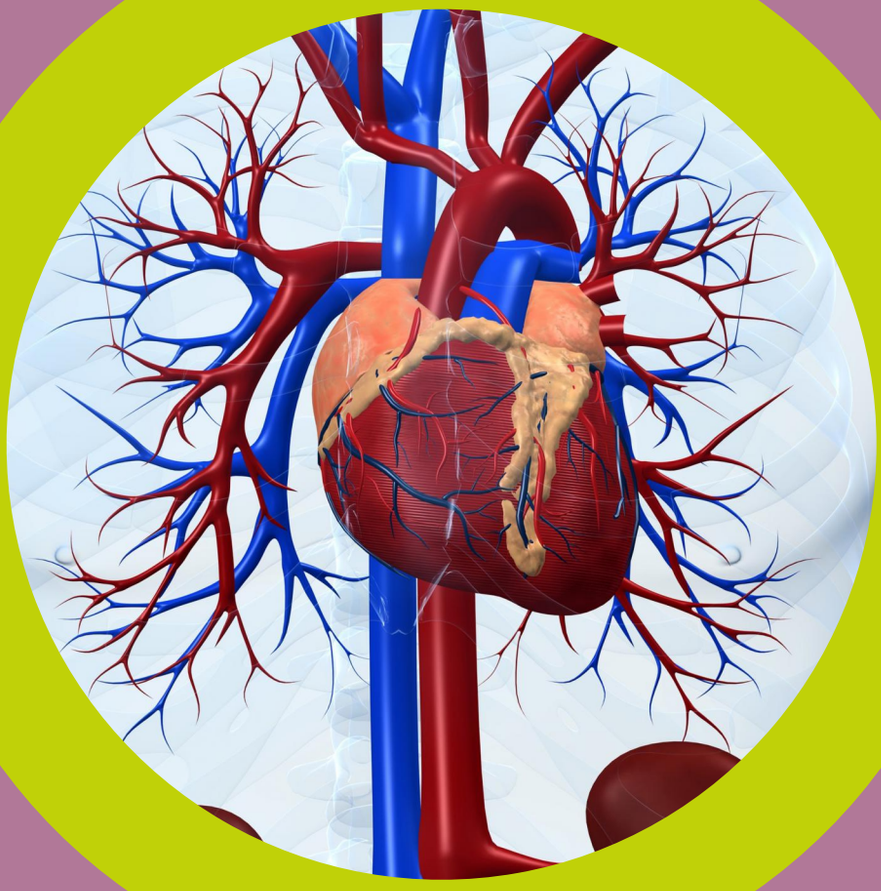
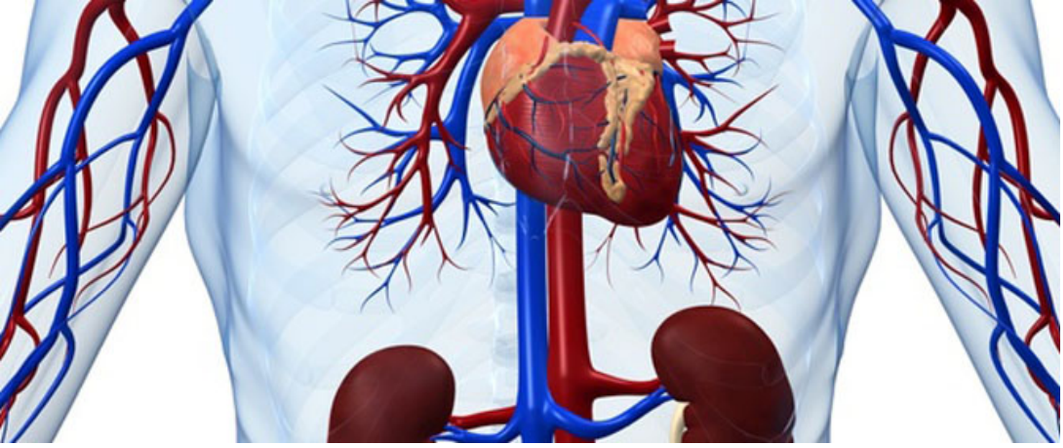
SCIENCE

ADDITIONAL INFORMATION



Hypertension Sensor

Effective prevention and treatment of hypertension



Hypertension

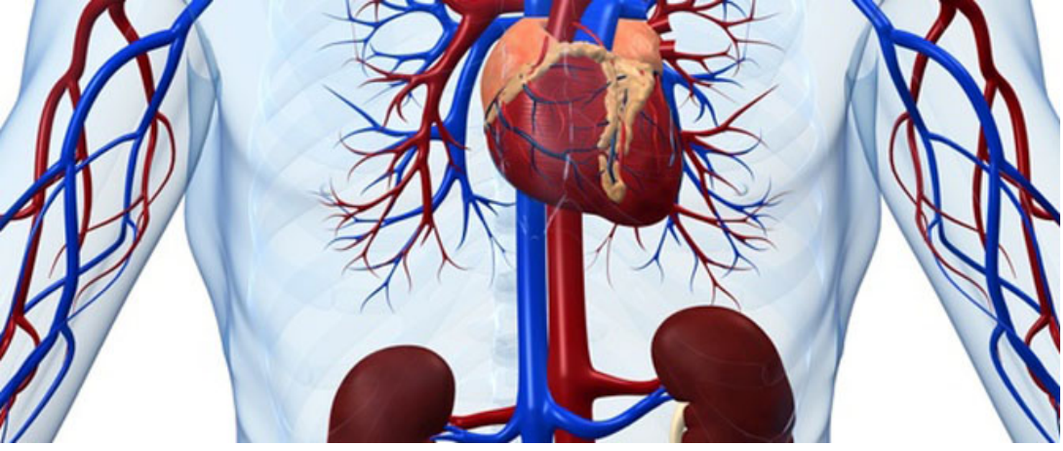
Hypertension is a condition in which the blood pressure of the vascular system is chronically elevated. A chronic systolic blood pressure higher than 140mmHg or a diastolic blood pressure greater than 90 mmHg (both measured after 10 minutes of sitting) are considered high blood pressure. This measurement method is the current standard because the blood pressure often decreases after sitting down, and increases when physical activities are performed.

This disease is very common and it is estimated that 29% of the total population suffers from it. Blood pressure tends to increase with age. High blood pressure is particularly dangerous because it is not always noticeable. Some of the symptoms are: morning headache, dizziness, nausea, nosebleeds, fatigue or insomnia. Often, the disease progresses without symptoms, and it is only identified by the consequential damages, which is why it is also known as the "silent killer".

Hypertension is a major risk factor in the development of atherosclerosis (a hardening of the arteries), especially if other risk factors such as excessive weight, diabetes, or elevated cholesterol/triglyceride levels are present. The resulting cardiovascular diseases, like coronary heart disease (CHD), heart attack, heart failure, kidney failure, stroke and vascular disease cause about 45% of deaths in men and 50% of deaths in women.

Apart from the increased risk of atherosclerosis, a chronically high blood pressure also causes damage to the heart muscle. The muscles become thicker and stiffer so that the heart cannot easily relax in diastole (relaxation phase) and draw in the blood. This causes a poor filling of the heart, and the appearance of heart failure symptoms. If left untreated, high blood pressure can damage the retina causing blindness, or damage the kidneys where kidney function is seriously reduced. Today, treatments exist to lower high blood pressure and alleviate the side effects. These modern drugs increase life expectancy and also improve the quality of life tremendously.

Several genes are responsible for blood pressure regulation. Each one can carry a trait that increases the risk of developing high blood pressure. A person who is aware of their personal risk can take preventative measures to lower blood pressure and also consult a doctor about their risk factors and condition. These steps can usually prevent the severe and often fatal diseases that are caused by long-term high blood pressure.



Relevant genes for hypertension

Several genetic variations have been identified that can significantly increase the risk of hypertension. An analysis of these polymorphisms can determine the risk of developing hypertension and how to reduce it with specific preventive measures. The genetic analyses also help in identifying the most effective therapy for lowering blood pressure. The following genes have an impact on your blood pressure:

Genetic traits

SYMBOL	rs NCBI	POLYMORPH	GENOTYPE
AGT	rs699	T>C	T/T
ADRB1	rs1801253	G>C	G/C
GNB3	rs5443	C>T	C/T
MTHFR	rs1801133	C>T	C/C

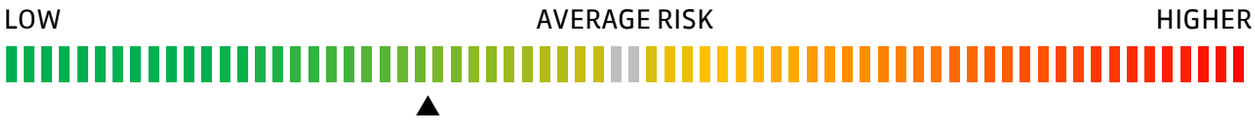
LEGEND: rsNCBI = description of examined genetic variation, POLYMORPHISM = form of the genetic variation, GENOTYPE = personal analysis result

Summary of effects

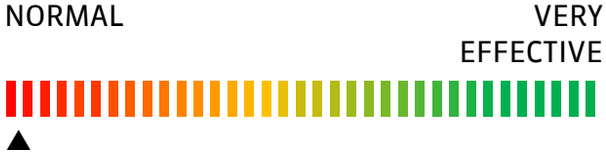
The analysed genes have an influence on your risk of hypertension, which can be also measured in the conventional way. Therefore, the benefit of this analysis is primarily to identify high blood pressure through regular examinations, properly treat it through lifestyle changes, and if necessary, use the most effective drug therapy. Here you can see a summary of the impact your genetic variations have on your health:

- You have no increased risk for elevated blood pressure.
- A reduced dietary salt intake is effective on average to reduce the risk of hypertension
- Taking vitamin B2 has no effect for your blood pressure

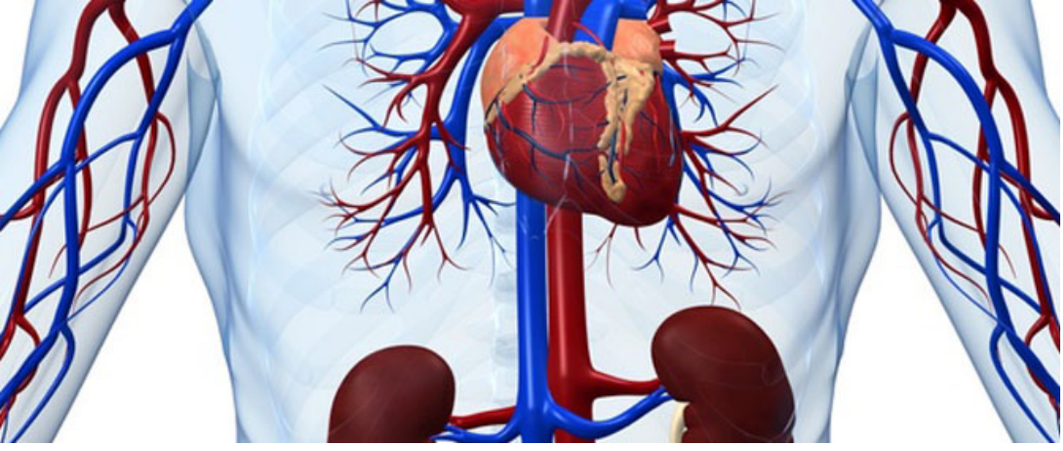
Your risk of hypertension



Lower blood pressure due to reduced salt consumption



Lower blood pressure by taking vitamin B2

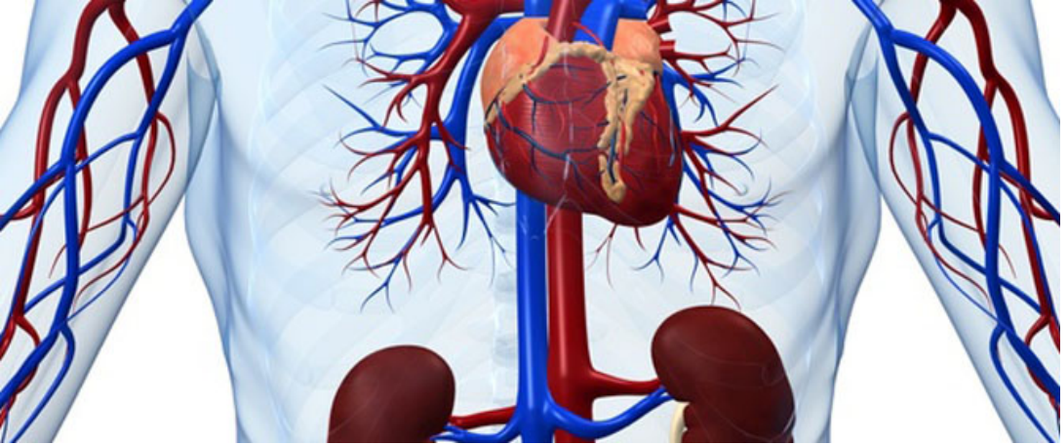


Nutritional Genes - Blood pressure

Your nutrition is very important. Based on your genes and their associated strengths and weaknesses you should increase or decrease certain foods and nutrients. These recommendations are calculated based on your genetic profile.

Your personalized recommendations based on this section:

Legend: GREEN ARROWS > this nutrient or substance is classed as healthy for your genetic profile. Try to increase the intake of this substance. RED ARROWS > this substance is classed as unhealthy for your genetic profile. Try to reduce your intake of the substance. NO ARROWS > There is no effect of the nutrient on the genetics of this section. PLEASE NOTE! This interpretation only considers your genetic profile of this section.



Prevention

Based on your genetic profile, you have no increased risk of high blood pressure. Therefore, you do not have to follow any specific preventive measures, but only the general guidelines of a healthy lifestyle. However, some people develop high blood pressure even without genetic defects due to their own unhealthy lifestyle. If you suffer from high blood pressure, despite your genetic profile, you can take the following precautionary measures.

Prevention

In addition to genetic factors, environment and lifestyle also play a crucial role in the development of high blood pressure. Therefore, it is important for you to understand the risk factors and to modify your lifestyle to avoid these risk factors.

Giving up smoking is one of the most important ways to lower blood pressure. People who quit smoking in middle age have a similar life expectancy as those who have never smoked. Smoking also affects the effectiveness of blood pressure medication.

After the age of 40, limit the amount of alcohol you consume because alcohol has a direct impact on blood pressure, and moderate or heavy drinking increases the risk of stroke. Light alcohol consumption of 250mL of red wine a day may lower your blood pressure by 2-4mmHg.

Obesity is an important risk factor and also increases your blood pressure. Therefore, reducing your weight will have a major impact and also lower your blood pressure. Losing 10kg of weight will lower your blood pressure by 5-20mmHg. Keep your BMI (Body Mass Index) under 25 to reduce your risk.

Regular physical activity such as swimming, running or walking, even at low intensity, lowers blood pressure by 4-9mmHg. You can reduce blood pressure by getting 30 minutes of exercise several times a week. However, intensive exercise is not recommended.

Salt consumption is also an important risk factor for high blood pressure. You should limit sodium intake to 2500mg or less. This is expected to reduce blood pressure by 8mmHg. Due to a special genetic variation, a decrease in daily salt intake can be particularly effective.

A healthy diet, with a large amount of fruit and vegetables, and low in saturated fats can reduce blood pressure by 8-14mmHg.

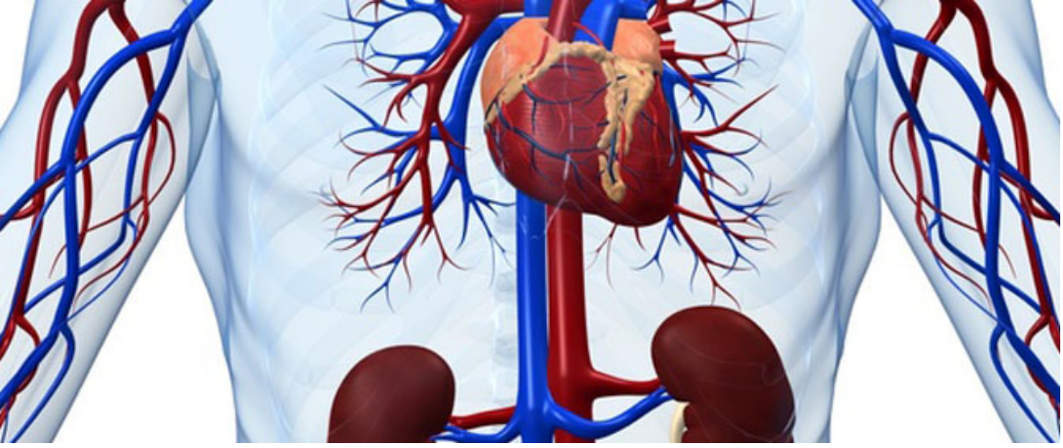
Medical care and treatment

Monitor your blood pressure to see how effective your lifestyle changes are. Ask your doctor to measure your blood pressure regularly or measure it yourself. Use the following guidelines to

determine how often to check:

Blood pressure	Systolic	Diastolic
Optimal blood pressure	under 120	under 80
Normal blood pressure	120-129	80-84
High-normal blood pressure	130-139	85-89
Mild hypertension (stage 1)	140-159	90-99
Moderate hypertension (stage 2)	160-179	100-109
Severe hypertension (stage 3)	under 180	above 110
Isolated systolic hypertension	above 140	under 90

If your blood pressure is normal, check it every week and try to keep it within the normal range by following the measures described above.
If your blood pressure is too high, take steps to lower it. If those measures do not lower your blood pressure to normal levels, talk to your doctor about possible medications to lower blood pressure. The choices are ACE inhibitors, AT1 antagonists, beta blockers, diuretics and calcium antagonists.



Drug compatibility

DRUGS	139	310	107	262	221	276	524	371	12
GENES	CYP2E1	CYP2D6	CYP2B6	CYP1A2	CYP2C19	CYP2C9	CYP3A4	CYP3A5	NAT2
DEGRADATION	NORMAL	NORMAL	NORMAL	NORMAL	NORMAL	NONE	NORMAL	NORMAL	SLOW

Effect on relevant medication

	Effect	Breakdown	Dose
Acebutolol	✓	✓	✓
Amlodipine	✓	↑	↑
Bisoprolol	✓	↑	↑
Candesartan	✓	↓	↓
Clevidipine	✓	✓	✓
Doxazosin	✓	✓	✓
Eprosartan	✓	✓	✓
Furosemide	✓	✓	✓
Hydrochlorothiazide	✓	✓	✓
Lercanidipine	✓	↑	↑
Metolazone	✓	✓	✓
Nadolol	✓	✓	✓
Nifedipine	✓	↑	↑
Olmesartan Medoxomil	✓	✓	✓
Prazosin	✓	✓	✓
Ramipril	✓	✓	✓
Telmisartan	✓	✓	✓
Triamterene	✓	✓	✓

	Effect	Breakdown	Dose
Aliskiren	✓	↑	↑
Atenolol	✓	✓	✓
Bosentan	✓	↓	↓
Captopril	✓	✓	✓
Clonidine	✓	✓	✓
Enalapril	✓	✓	✓
Felodipine	✓	↑	↑
Guanfacine	✓	✓	✓
Irbesartan	✓	✗	✗
Lisinopril	✓	✓	✓
Metoprolol	✓	✓	✓
Nebivolol	✓	✓	✓
Nisoldipine	✓	↑	↑
Perindopril	✓	✓	✓
Propranolol	✓	✓	✓
Reserpine	✓	✓	✓
Terazosin	✓	✓	✓
Valsartan	✓	✗	✗

	Effect	Breakdown	Dose
Amiloride	✓	✓	✓
Benazepril	✓	✓	✓
Bumetanide	✓	✓	✓
Carvedilol	✓	✗	✗
Diltiazem	✓	↑	↑
Eplerenone	✓	↑	↑
Fosinopril	✓	✓	✓
Hydralazine	✓	✓	✓
Labetalol	✓	✓	✓
Losartan	✗	↓	✗
Minoxidil	✓	✓	✓
Nicardipine	✓	↑	↑
Nitrendipine	✓	↑	↑
Pindolol	✓	✓	✓
Quinapril	✓	✓	✓
Spironolactone	✓	✓	✓
Toremifene	✓	↑	↑
Verapamil	✓	↑	↑

Please note: The right choice and dose of medication is always the responsibility of the doctor. Never make your own decision on whether to stop taking a medication or changing its dose!

Legend:

Effect: Normal. Degredation: Normal. Recommendation: Normal dosage.

Effect: Normal. Degradation: Slower. Recommendation: Reduce the dosage.

Effect: Normal. Degradation: None. Recommendation: Alternative drug.

Effect: Lower. Degradation: Normal. Recommendation: Normal dosage.

Effect: Lower. Breakdown: Lower. Recommendation: Reduce the dosage.

Effect: Stronger. Degradation: Stronger. Recommendation: Normal dosage.

PHARMACO GENETICS
Not ordered

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ODONTOLOGY
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OTHERS
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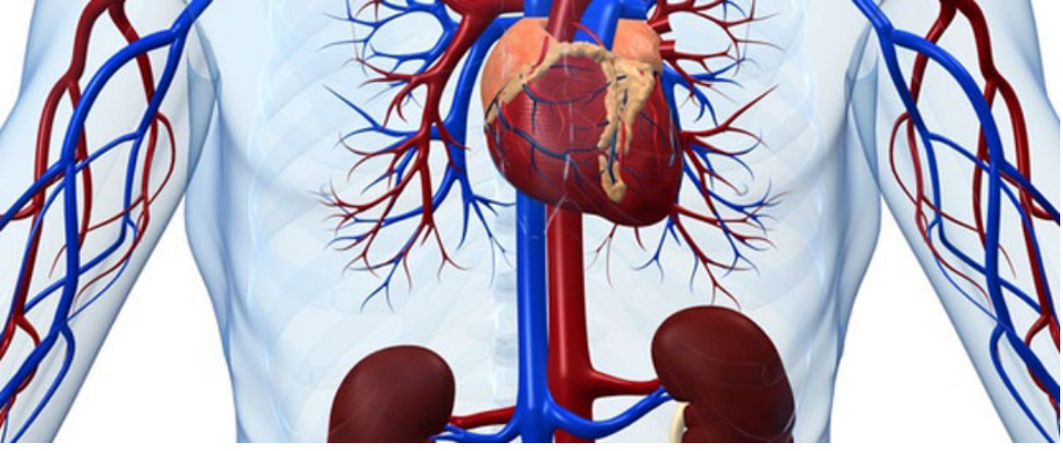
SCIENCE

ADDITIONAL INFORMATION

SCIENCE

This chapter shows the science behind the test.



Hypertension Sensor

AGT - Angiotensinogen (serpin peptidase inhibitor, clade A, member 8) (rs699)

The polymorphism rs699 in the angiotensinogen gene (AGT) leads to an increased concentration of angiotensinogen in the blood serum, and thus to a predisposition to high blood pressure.

RES	Genotype	POP	Possible results
X	T/T	54%	No predisposition to high blood pressure/hypertension A reduced salt intake is effective on average for the prevention of hypertension / hypertension
	T/C	34%	Predisposition to high blood pressure/hypertension (OR: 1.2) A reduced salt intake is particularly effective for the prevention of hypertension / hypertension
	C/C	13%	Predisposition to high blood pressure/hypertension (OR: 1.4) A reduced salt intake is particularly effective for the prevention of hypertension / hypertension

References

Nakajima et al.Nucleotide Diversity and Haplotype Structure of the Human Angiotensinogen Gene in Two Populations. Am J Hum Genet. Jan 2002, 70(1): 108–123.

Jeunemaitre et al. Molecular basis of human hypertension: role of angiotensinogen. Cell. 1992 Oct 2,71(1):169-80.

Corvol et al. Molecular Genetics of Human Hypertension: Role of Angiotensinogen. Endocrine Reviews 18(5): 662–677.

Hunt SC et al. Angiotensinogen genotype, sodium reduction, weight loss, and prevention of hypertension: trials of hypertension prevention, phase II. Hypertension. 1998 Sep,32(3):393-401.

Norat T et al. Blood pressure and interactions between the angiotensin polymorphism AGT M235T and sodium intake: a cross-sectional population study. Am J Clin Nutr. 2008 Aug,88(2):392-7.

Svetkey LP et al. Angiotensinogen genotype and blood pressure response in the Dietary Approaches to Stop Hypertension (DASH) study. J Hypertens 2001

MTHFR - Methylenetetrahydrofolate reductase (NAD(P)H) (rs1801133)

The methylenetetrahydrofolate reductase (MTHFR) is involved in many metabolic pathways in the human body. In homocysteine metabolism, it is responsible for the degradation of homocysteine to methionine. The rs1801133 polymorphism leads to a reduced enzymatic activity of methylenetetrahydrofolate reductase, and thus to an increased homocysteine level.

RES	Genotype	POP	Possible results
X	C/C	59%	Vitamin B2 does not lower the blood pressure
	C/T	33%	Vitamin B2 does not lower the blood pressure
	T/T	8%	Vitamin B2 does lower the blood pressure

References

McNulty et al. Riboflavin, MTHFR genotype and blood pressure: A personalized approach to prevention and treatment of hypertension. Mol Aspects Med. 2017 Feb,53:2-9

McAuley et al. Riboflavin status, MTHFR genotype and blood pressure: current evidence and implications for personalised nutrition. Proc Nutr Soc. 2016 Aug,75(3):405-14

Wilson et al. Blood pressure in treated hypertensive individuals with the MTHFR 677TT genotype is responsive to intervention with riboflavin: findings of a targeted randomized trial. Hypertension. 2013 Jun,61(6):1302-8.

Ward et al. B-vitamins, methylenetetrahydrofolate reductase (MTHFR) and hypertension. Int J Vitam Nutr Res. 2011 Jul,81(4):240-4

ADRB1 - Adrenoceptor beta 1 (rs1801253)

The β1-adrenoceptor protein encoded by the gene ADRB1 is the main adrenergic receptor of the human heart. It is mainly responsible for the effect of the adrenaline and the target structure of the beta-blockers.

RES	Genotype	POP	Possible results
	G/G	10%	No predisposition to high blood pressure/hypertension
X	G/C	40%	No predisposition to high blood pressure/hypertension
	C/C	50%	Predisposition to high blood pressure/hypertension (OR: 1.9)

References

Johnson et al. Association of hypertension drug target genes with blood pressure and hypertension in 86,588 individuals. Hypertension. 2011 May,57(5):903-10.

Peng Y et al. Polymorphisms of the beta1-adrenergic receptor gene are associated with essential hypertension in Chinese. Clin Chem Lab Med. 2009,47(10):1227-31.

Gjesing AP et al. Studies of associations between the Arg389Gly polymorphism of the beta1-adrenergic receptor gene (ADRB1) and hypertension and obesity in 7677 Danish white subjects. Diabet Med. 2007 Apr,24(4):392-7. Epub 2007 Feb 28.

GNB3 - Guanine nucleotide binding protein (G protein), beta polypeptide 3 (rs5443)

G-proteins are signal transduction proteins, bonded to the inside of the cell membrane receptors, and involved in a variety of signaling pathways. The polymorphism rs5443 is associated with both high blood pressure and a predisposition to excessive weight.

RES	Genotype	POP	Possible results
	C/C	30%	No predisposition to high blood pressure/hypertension
X	C/T	41%	Predisposition to high blood pressure/hypertension (OR: 6.1)
	T/T	29%	Predisposition to high blood pressure/hypertension (OR: 6.1)

References

Siffert W. G-protein beta3 subunit 825T allele and hypertension. Curr Hypertens Rep. 2003 Feb,5(1):47-53.

El Din Hemimi NS et al. Prediction of the Risk for Essential Hypertension among Carriers of C825T Genetic Polymorphism of G Protein β3 (GNB3) Gene. Biomark Insights. 2016 May 17,11:69-75.

Cabadak H et al. The role of G protein β3 subunit polymorphisms C825T, C1429T, and G5177A in Turkish subjects with essential hypertension. Clin Exp Hypertens. 2011,33(3):202-8.

LEGEND: RES = your personal analysis result (marked with an X), GENOTYPE = different variations of the gene (called alleles),
POP = percent of the general population that have this genetic result,
POSSIBLE RESULTS = influence of the genetic variation.

PHARMACO GENETICS
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ODONTOLOGY
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OTHERS
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SCIENCE

ADDITIONAL INFORMATION

ADDITIONAL INFORMATION

In this chapter you will receive useful information

Certifications

Our laboratory is one of the most modern and automated laboratories in Europe and has numerous certifications and quality assurance systems that meet, and even exceed, international standards. The various areas of business are certified separately to the highest standards.

Laboratory diagnostics, manufacturing & sales

Quality management system in accordance with ISO 9001:2015

qualityaustria
SYSTEM CERTIFIED
ISO 9001:2015 No.14365/0

Licensed for medical genetics

Approved by the Federal Ministry of Health, Austria

BUNDESMINISTERIUM FÜR GESUNDHEIT

Cosmetic/genetic diagnostics and cosmetics manufacturing

Good manufacturing practice (GMP) in accordance with ISO 22716:2007

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SYSTEM CERTIFIED
EN ISO 22716:2007 No.00010/0

Food supplement manufacturing

Management system for food safety in accordance with ISO 22000:2018

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SYSTEM CERTIFIED
ISO 22000:2018 No.00521/0

Customer Service

Questions or comments about our service?

Our customer service team is happy to help with any enquiries or problems. You can contact us in the following ways:

- Phone +41 (0) 41 525 100.1
- office.ch@progenom.com

Our team is looking forward to your call. Customer satisfaction is our first priority. If you are not fully satisfied with our service, please let us know. We will do our best to help find a satisfactory solution to your problem.

Contact | Impressum
ProGenom GmbH
Riedstrasse 1
6343 Rotkreuz
SWITZERLAND

Technical details

Order number
DEMO_DS

Date of birth
01/01/1990

Established analysis methods
qRT-PCR, DNA sequencing, fragment length analysis, CNV assay, GC-MS, Immunocap ISAC, Cytolisa

Report generated
19/03/2021 16:32:59

Product codes
M1HYP

Current version
V538

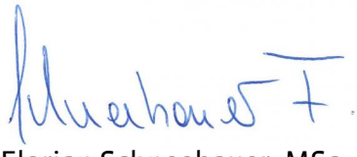
Ordering company
ProGenom GmbH
Riedstrasse 1
6343 Rotkreuz
SWITZERLAND

Analyzing company
DNA Plus - Zentrum für Humangenetik
Georg Wrede Strasse 13
83395 Freilassing
Deutschland

Laboratory Director

Dr. Daniel Wallerstorfer Bsc.

Laboratory Manager



Florian Schneebauer, MSc.

NOTES: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