ProMedicDNA

Bone Health 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

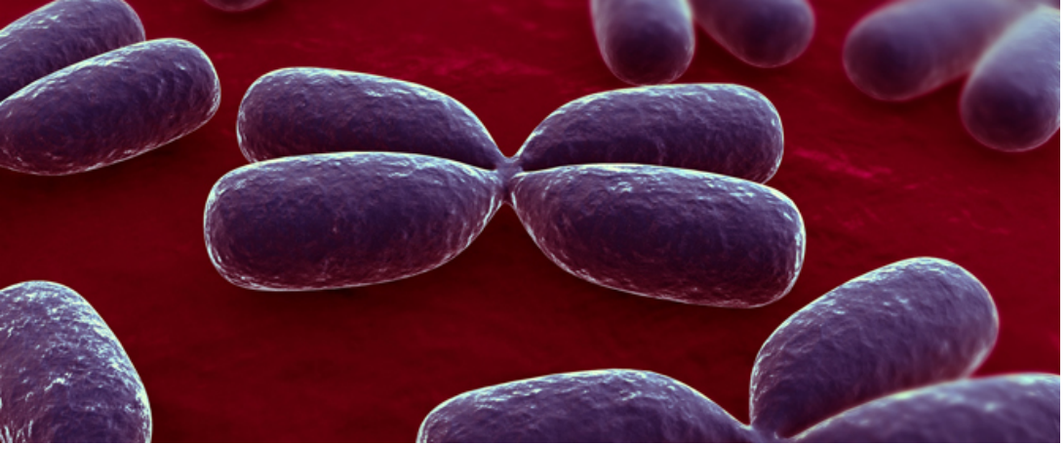
Florian Schneebauer, MSc.
Laboratory Manager

Bone Health Sensor

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

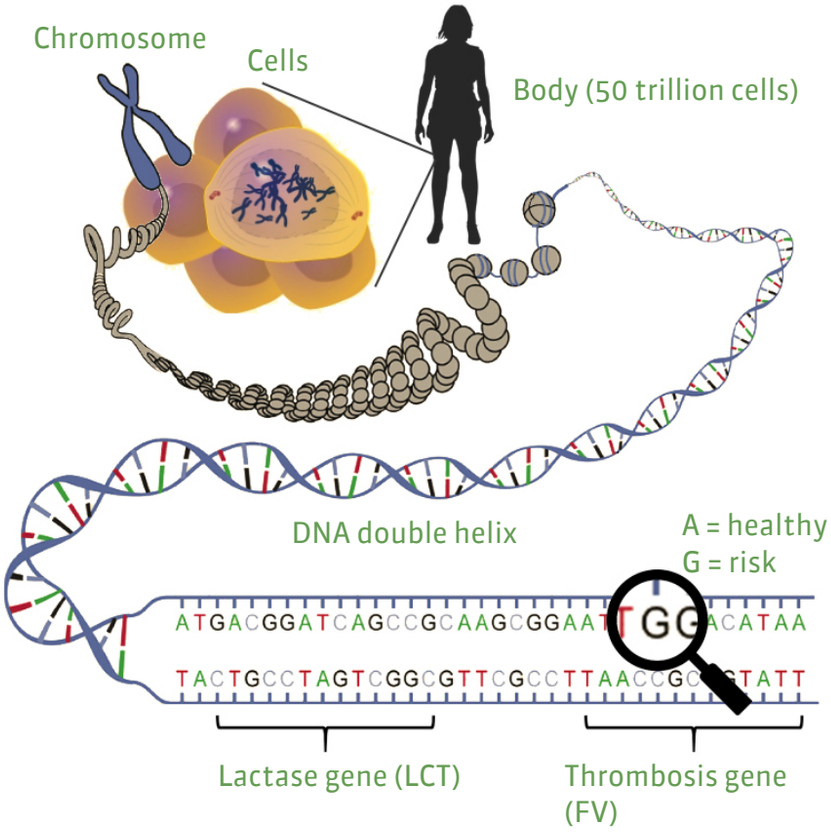
Order number:
DEMO_DS

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.

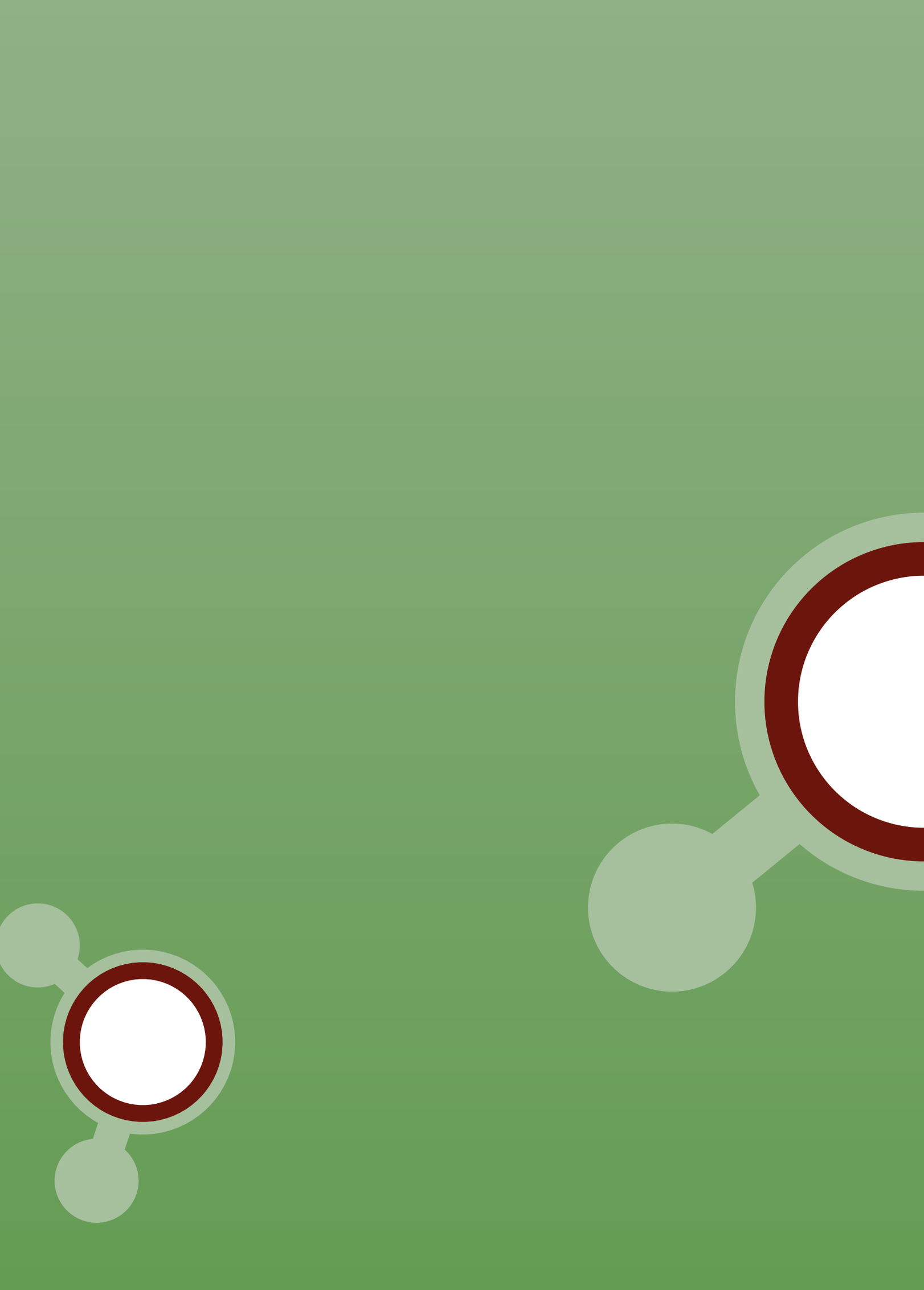
External influences can affect individual genes and disrupt their function, but the majority of our defective genes are inherited from our parents. Each embryo receives half of its genes from the father and half from the mother, resulting in a new human being with some characteristics of each parent. 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.

Bone Health Sensor



PHARMACO GENETICS
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ONCOLOGY
Not ordered

CARDIOVASCULAR SYSTEM
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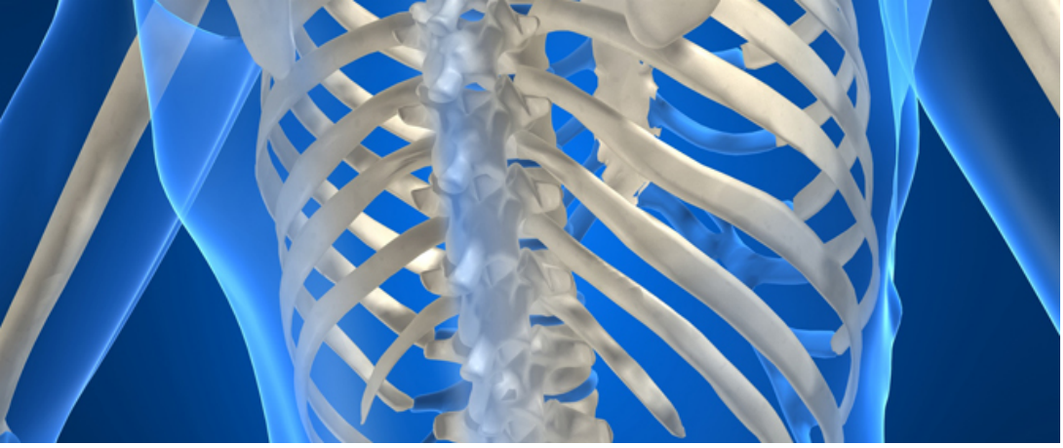
OTHERS
Not ordered

SCIENCE

ADDITIONAL INFORMATION

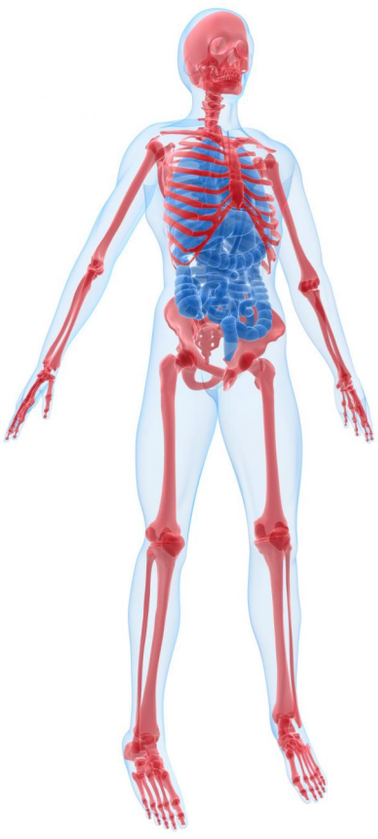
Bone Health Sensor

Stopping bone density loss and improving treatment



Osteoporosis

Osteoporosis is a disease that affects the bones. It causes bones to lose mass and strength, and makes them more fragile and easier to fracture. Even in normal development, bones become more likely to fracture with age. Bones reach maximum strength at about the age of 30 and then bone mass decreases progressively thereafter. However, some genetic traits lead to reduced bone strength, which increases the risk of osteoporosis and bone fractures- especially of the hips, forearms and vertebra. This risk grows with age.



Most fractures involve the hips, forearms and vertebrae. In normal development these bones grow throughout childhood and reach peak strength at about age 30. After that time, bone mass gradually decreases, leading to somewhat more brittle bones. However, some traits in the genes that are responsible for bone formation can cause your bones to become unusually fragile over time. As you age, this leads to increased bone loss and fractures. About 80% of osteoporosis cases occur in post-menopausal women, mainly because the body no longer produces the bone-protective hormone oestrogen. The disease is very common: 1 in 3 women over the age of 50 is diagnosed with osteoporosis. As oestrogen, the female sex hormone, plays a significant role for women in the formation of bone, women who have had lower estrogen levels throughout their life (e.g. due to a late start of menstruation or premature menopause) are particularly at risk.

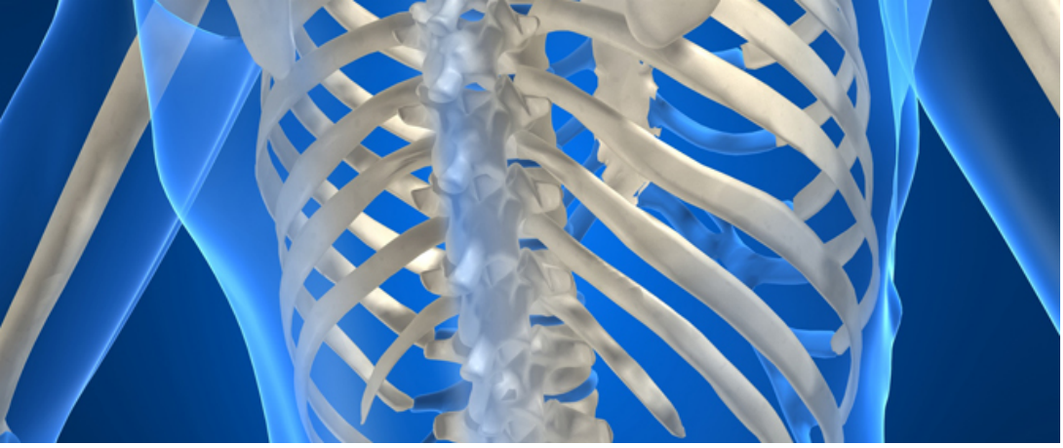
Osteoporosis is a common disease for men over the age of 70. Although women are more often affected by osteoporosis, this disease affects both sexes, and its development is accelerated by certain risk factors such as poor diet and unhealthy lifestyle. In addition to calcium, there are numerous other micronutrients (such as minerals, amino acids and vitamins) which are important in maintaining healthy bones. Bones have the ability to store calcium but these reserves can be depleted with nutritional deficiencies. Calcium is also crucial for other important processes in the body. Vitamin D plays an important role in the absorption of calcium from food.

In the elderly, the conversion to the active form of vitamin D is poor; in addition, the vitamin D from food is low due to poor

nutrition. Therefore, vitamin D deficiency is a widespread problem, but one that can be easily solved.

The incipient phases of the disease are sometimes not associated with any recognizable symptoms, and the diagnosis is made only when the first bone fractures occur. Prior to this point, the bone density is already compromised, and the bones may be fractured even in mild injuries, e.g. when bending or lifting a heavy bag.

If the disease is diagnosed at an advanced stage, treatment is based on preventing falls and increasing bone density as much as possible. This is achieved through a diet rich in calcium and vitamin D, adequate exercise and medication that promotes bone metabolism. The best defense against osteoporosis is prevention. The earlier the disease is diagnosed, the quicker you can take action to stop bone deterioration. Preventing bone loss is always easier than recovering lost bone. That is exactly what makes this gene test so valuable for preventative health care: you learn what your personal risk of disease is and can often completely prevent the disease from developing and follow a prevention program tailored to your individual needs.



Genes relevant in the context of osteoporosis

So far, scientists have identified several genes and polymorphisms which can increase the general risk of osteoporosis. An analysis can determine all relevant polymorphisms, the risk of illness, as well as other pertinent genetic properties. The following genes have an impact on the preservation of bone density:

Genetic traits

SYMBOL	rs NCBI	POLYMORPH	GENOTYPE
Col1A1	rs1800012	G/T Pos. 1546 (S/s)	T/T
VDR	rs1544410	G/A IVS7 Pos.+283	A/A
ESR1	rs2234693	-397T>C	C/T
LCT	rs4988235	T>C	T/T

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

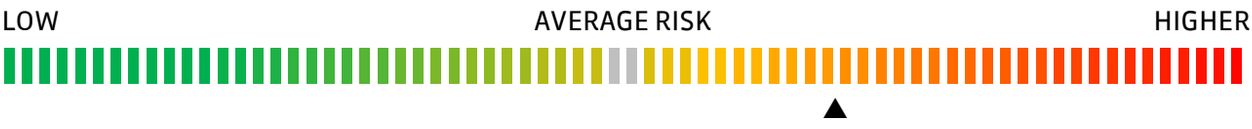
Summary of effects

In the case of osteoporosis, there are polymorphisms that protect against and those that promote its development. Polymorphisms that negatively impact calcium absorption also have an influence on bone density.

Here is a summary of the effects that the genetic variations have on your health:

- Your risk of osteoporosis is 1.8 times increased
- Etidronate therapy is particularly effective
- Clodronate therapy is particularly effective
- Raloxifene therapy is particularly effective
- Your daily calcium uptake is average

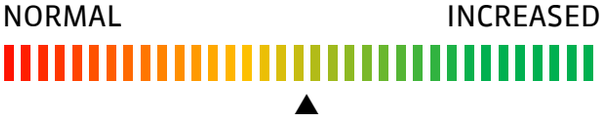
Risk of osteoporosis



Effectiveness of HRT in osteoporosis prevention

Effectiveness of alendronate therapy

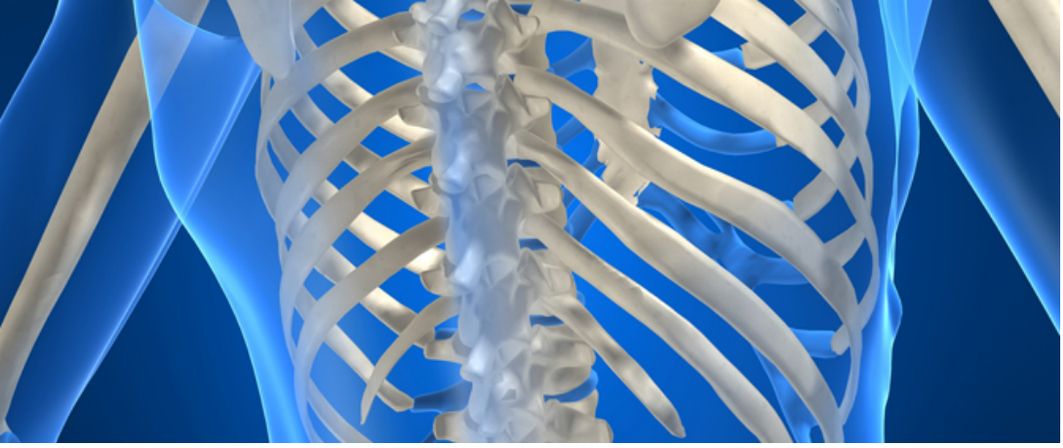
Effectiveness of etidronate therapy



Effectiveness of clodronate therapy

Effectiveness of raloxifene therapy

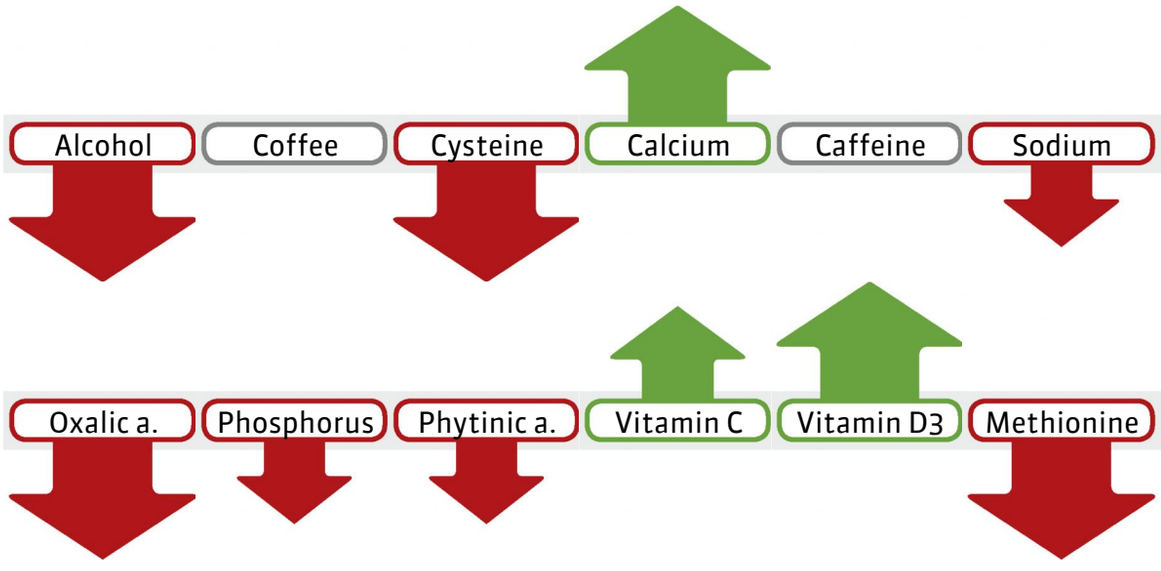
Your typical calcium absorption



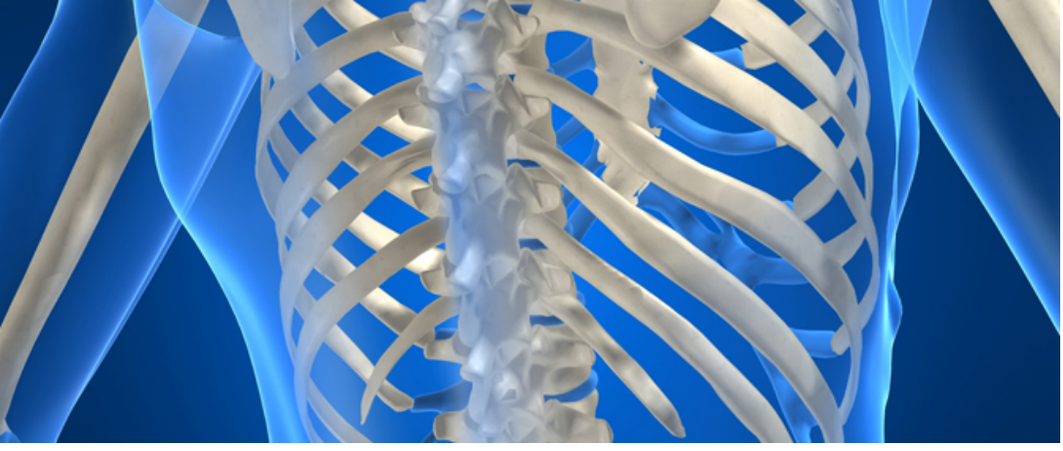
Nutritional Genes - Bones

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:



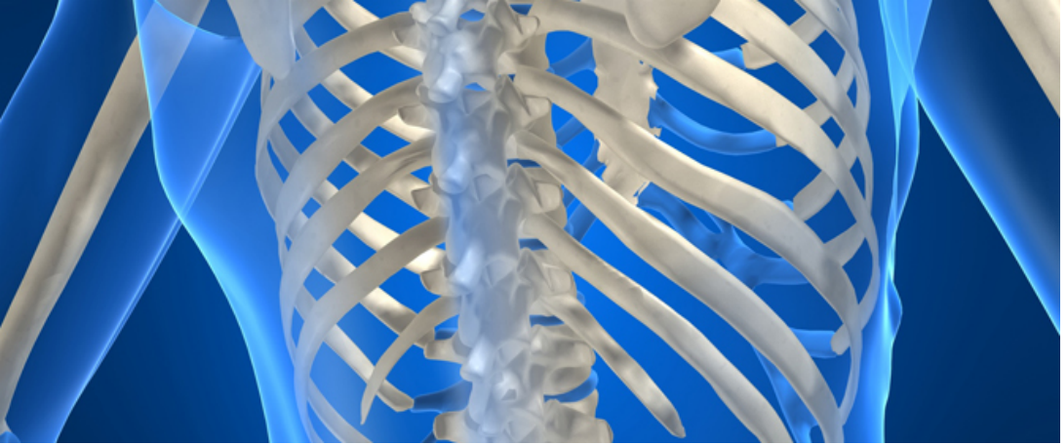
Legend: GREEN ARROWS > this nutrient or substance is classed as healthy for your genetic profile. Try to increase the intake of this substance. RED ARROWS > this substance is classed as unhealthy for your genetic profile. Try to reduce your intake of the substance. NO ARROWS > There is no effect of the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



Prevention

You have a moderate genetic predisposition for osteoporosis. It is important for you to take preventative measures in order to keep your bones as strong as possible. It is difficult to restore lost bone mass therefore it is better to prevent bone loss in the first place. The following precautions will help you keep your bones strong:

- Make sure you consume enough calcium. Calcium is the raw material necessary for bone regeneration, and it is vital to ensure you are getting sufficient. Dairy products, calcium supplements and some drugs for osteoporosis contain calcium.
- Ensure that you have enough vitamin D. Your body produces this vitamin in the sunlight, so you should spend a safe amount of time outdoors. However, vitamin D is also contained in food products such as fish, smaller quantities in milk, as well as in some nutritional supplements (fish oils).
- You should eat only limited amounts of foods that are high in phosphates, such as sausages, chocolate and meat. Phosphates extract calcium from bone material and weaken bones.
- Any form of exercise, such as jogging or walking, will strengthen your bones by forcing them to develop.
- Several diseases, including hormonal disorders, gastrointestinal, liver, kidney and joint diseases, can cause osteoporosis. These diseases should be treated to reduce symptoms.
- Alcohol and nicotine weaken bones, along with many other negative health effects. Giving up alcohol and cigarettes will reduce your osteoporosis risk.
- Get regular bone density scans from your doctor to track changes in bone density.
- If you have advanced osteoporosis, medication can slow or even stop the progression of the disease. Talk to your doctor about your options for drug therapy.
- Numerous drugs can interfere with bone formation and so people at risk for osteoporosis should consult their doctor before taking any medication. Drugs known to inhibit bone growth are: cortisone, anti-epileptics, oral anticoagulants and heparin, aromatase inhibitors (AI) for breast cancer, androgen deprivation therapy for prostate cancer, calcineurin inhibitors such as those for immunosuppression after organ transplantation, and gastric acid inhibitors.
- Certain foods can also lead to bone mineral density loss and should be avoided if possible. Try to reduce food types that are rich in table salt, phytinic acid, the amino acids cysteine and methionine, and oxalic acid. The excessive consumption of caffeine also leads to a gradual decrease in bone mineral density.



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
Alendronic Acid	✓	✓	✓
Codeine	✓	✓	✓
Fentanyl	✓	↑	↑
Ibuprofen	✓	✗	✗
Lidocain	✓	✓	✓
Oxycodone	✓	↑	✓
Raloxifene	✓	✓	✓
Strontium Ranelate	✓	✓	✓
Zoledronic Acid	✓	✓	✓

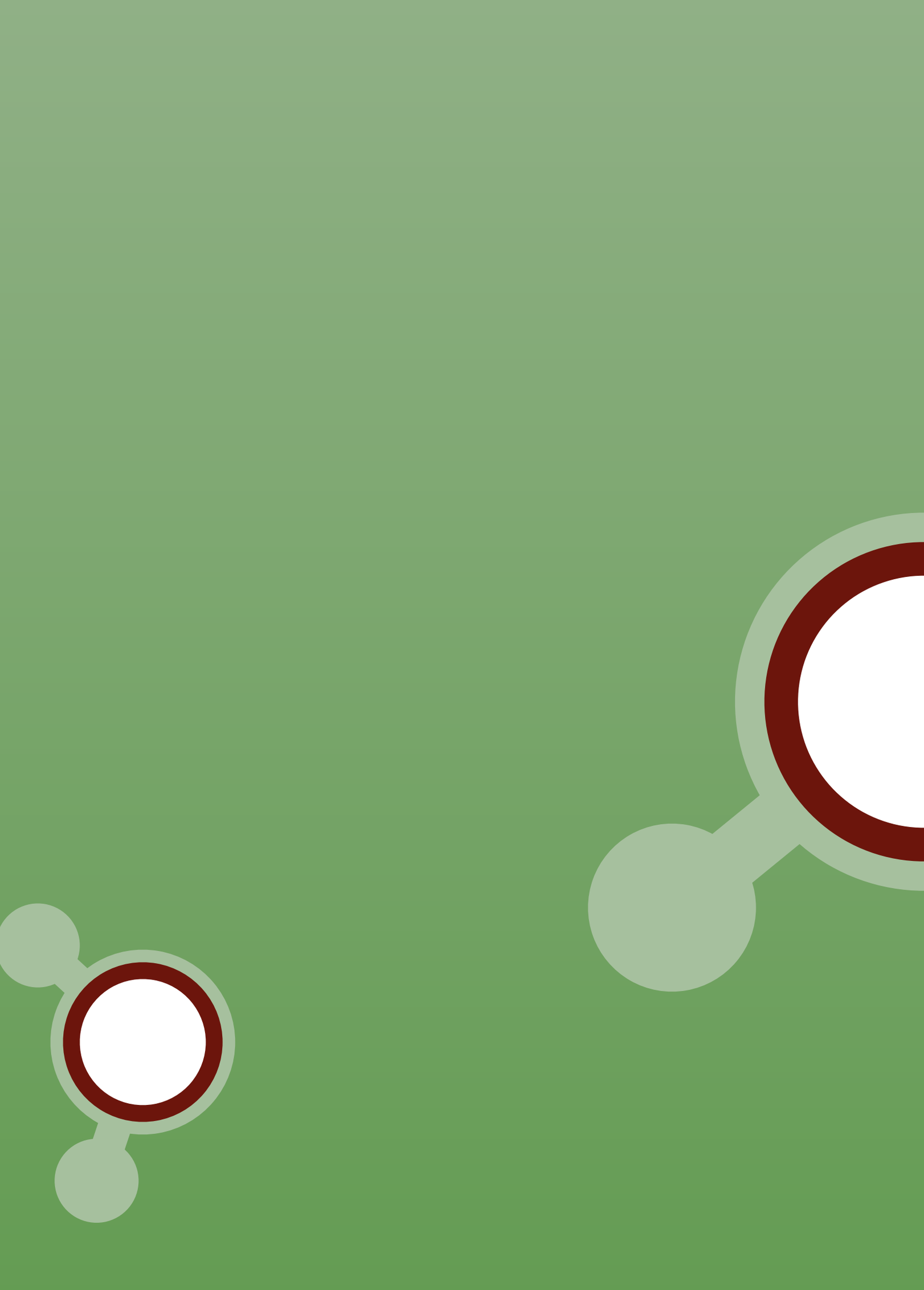
	Effect	Breakdown	Dose
Alfentanil	✓	↑	↑
Enflurane	✓	✓	✓
Halothane	✓	✓	✓
Isoflurane	✓	✓	✓
Methadone	✓	↑	↑
Paracetamol	✓	✓	✓
Ropivacaine	✓	✓	✓
Teriparatide	✓	✓	✓
Zolmitriptan	✓	✓	✓

	Effect	Breakdown	Dose
Buprenorphine	✓	↑	↑
Etidronic Acid	✓	✓	✓
Hydrocodone	✓	✓	✓
Levacetylmethadol	✓	↑	↑
Methoxyflurane	✓	✓	✓
Phenacetin	✓	✓	✓
Sevoflurane	✓	✓	✓
Tramadol	✓	↑	✓

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.



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OTHERS
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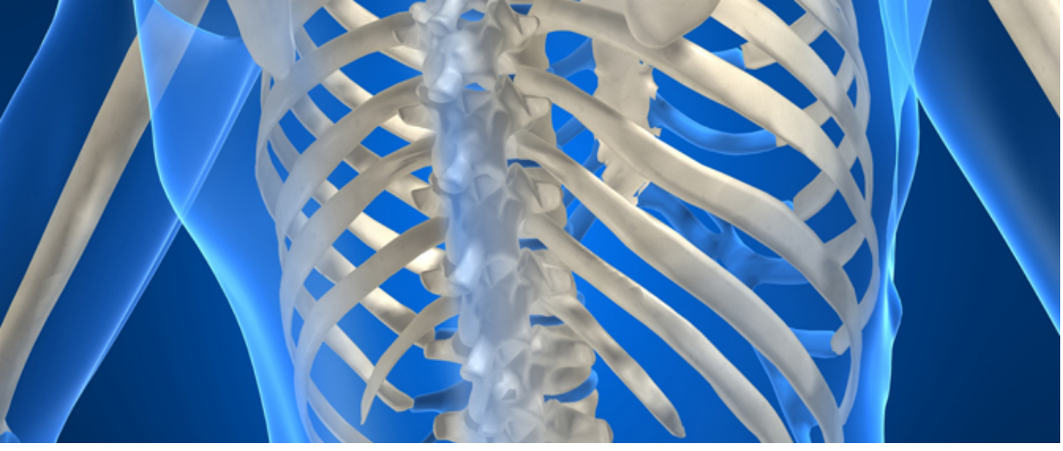
SCIENCE

ADDITIONAL INFORMATION

SCIENCE

This chapter shows the science behind the test.



Bone Health Sensor

Col1A1 - Collagen, type I, alpha 1 (rs1800012)

The protein encoded by the COL1A1 gene (collagen type I, alpha 1) is the main protein component of the bone matrix. Defects in the COL1A1 structure lead to changes in the bone matrix.

RES	Genotype	POP	Possible results
	G/G	83%	No increased risk of osteoporosis Etidronate is particularly effective
	G/T	15%	Increased risk of osteoporosis (OR: 1.26)
X	T/T	2%	Increased risk of osteoporosis (OR: 1.78)

References

Mann V et a. Meta-analysis of COL1A1 Sp1 polymorphism in relation to bone mineral density and osteoporotic fracture. Bone. 2003 Jun,32(6):711-7.

Jin et al. Polymorphisms in the 5' flank of COL1A1 gene and osteoporosis: meta-analysis of published studies. Osteoporos Int. 2011 Mar,22(3):911-21.

Qureshi et al. COLIA1 Sp1 polymorphism predicts response of femoral neck bone density to cyclical etidronate therapy. Calcif Tissue Int. 2002 Mar,70(3):158-63. Epub 2002 Feb 19.

VDR - Vitamin D (1,25- dihydroxyvitamin D3) receptor (rs1544410)

The vitamin D receptor protein (VDR) is the most important regulator of calcium and bone metabolism. Vitamin D also controls a large number of important functions, such as calcium absorption, bone growth and the production of hormones. A defect in this gene leads to a change in bone density, amongst other things.

RES	Genotype	POP	Possible results
	G/G	52%	Increased protection against osteoporosis (OR: 0.61) Alendronate is particularly effective HRT is particularly effective as a preventative measure
	A/G	37%	No increased protection against osteoporosis Etidronate is particularly effective Clodronate is particularly effective
X	A/A	11%	No increased protection against osteoporosis Etidronate is particularly effective Clodronate is particularly effective Raloxifene is particularly effective

References

Palomba et al. BsmI vitamin D receptor genotypes influence the efficacy of antiresorptive treatments in postmenopausal osteoporotic women. A 1-year multicenter, randomized and controlled trial. Osteoporos Int. 2005 Aug,16(8):943-52. Epub 2005 Mar 1.

Jia et al. Vitamin D receptor BsmI polymorphism and osteoporosis risk: a meta-analysis from 26 studies. Genet Test Mol Biomarkers. 2013 Jan,17(1):30-4.

Palomba et al. Raloxifene administration in post-menopausal women with osteoporosis: effect of different BsmI vitamin D receptor genotypes. Hum Reprod. 2003 Jan,18(1):192-8.

Marc J et al. VDR genotype and response to etidronate therapy in late postmenopausal women. Osteoporos Int. 1999,10(4):303-6.

Creatsa M et al. The effect of vitamin D receptor BsmI genotype on the response to osteoporosis treatment in postmenopausal women: a pilot study. J Obstet Gynaecol Res. 2011 Oct,37(10):1415-22.

Mossetti G et al. Vitamin D receptor gene polymorphisms predict acquired resistance to clodronate treatment in patients with Paget's disease of bone. Calcif Tissue Int. 2008 Dec,83(6):414-24.

ESR1 - Estrogen receptor 1 (rs2234693)

Oestrogens have a positive effect on the human skeleton through regulation of bone metabolism, control of the optimal bone mass and limitation of bone loss. Defects in this gene can impact negatively on these effects.

RES	Genotype	POP	Possible results
	C/C	20%	No increased risk for osteoporosis HRT is particularly effective
X	C/T	49%	Increased risk of osteoporosis (OR: 2)
	T/T	31%	Increased risk of osteoporosis (OR: 4)

References

Gennari L et al. Estrogen receptor gene polymorphisms and the genetics of osteoporosis: a HuGE review. Am J Epidemiol. 2005 Feb 15,161(4):307-20.

van Meurs JB et al. Association of 5' estrogen receptor alpha gene polymorphisms with bone mineral density, vertebral bone area and fracture risk. Hum Mol Genet. 2003 Jul 15,12(14):1745-54.

Herrington DM et al. Estrogen-receptor polymorphisms and effects of estrogen replacement on high-density lipoprotein cholesterol in women with coronary disease. N Engl J Med. 2002 Mar 28,346(13):967-74.

Herrington DM et al. Common estrogen receptor polymorphism augments effects of hormone replacement therapy on E-selectin but not C-reactive protein. Circulation. 2002 Apr 23,105(16):1879-82.

LCT - lactase (rs4988235)

The LCT gene encodes for the protein lactase, an enzyme in the small intestine that splits the milk sugar (lactose) so that it can be absorbed. If the LCT gene is defective, the lactose consumed can either be absorbed insufficiently, or not at all. This is known as lactose intolerance. The avoidance of dairy products usually leads to a reduced absorption of calcium.

RES	Genotype	POP	Possible results
X	T/T	76%	Normal calcium intake from nutrition
	T/C	8%	Normal calcium intake from nutrition
	C/C	16%	Reduced calcium intake from nutrition

References

Koek et al. The T-13910C polymorphism in the lactase phlorizin hydrolase gene is associated with differences in serum calcium levels and calcium intake.

Bácsi Ket al. LCT 13910 C/T polymorphism, serum calcium, and bone mineral density in postmenopausal women. Osteoporosis International, 20(4), 639–645.

Tolonen S et al. Cardiovascular Risk in Young Finns Study Group. (2011). Lactase Gene C/T-13910 Polymorphism, Calcium Intake, and pQCT Bone Traits in Finnish Adults. Calcified Tissue International, 88(2), 153–161.

Laaksonen MM et al. Genetic lactase non-persistence, consumption of milk products and intakes of milk nutrients in Finns from childhood to young adulthood. Br J Nutr. 2009 Jul,102(1):8-17.

Almon R et al. Lactase non-persistence as a determinant of milk avoidance and calcium intake in children and adolescents. J Nutr Sci. 2013 Jul 24,2:e26.

Kuchay RA et al. Effect of C/T -13910 cis-acting regulatory variant on expression and activity of lactase in Indian children and its implication for early genetic screening of adult-type hypolactasia. Clin Chim Acta. 2011 Oct 9,412(21-22):1924-30.

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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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

qualityaustria
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

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Product codes
M4BON

Current version
V538

Ordering company
ProGenom GmbH
Riedstrasse 1
6343 Rotkreuz
SWITZERLAND

Analyzing company
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Laboratory Director

Dr. Daniel Wallerstorfer Bsc.

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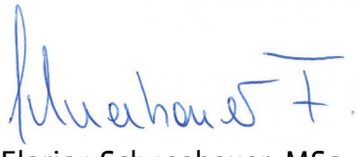

Florian Schneebauer, MSc.

NOTES:


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ProMedicDNA

Bone Health Sensor

Jane Doe
DEMO_DS

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ProGenom
www.progenom.com