ProMedicDNA

Periodontitis Sensor

Jane Doe
DEMO_DS

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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

Periodontitis Sensor

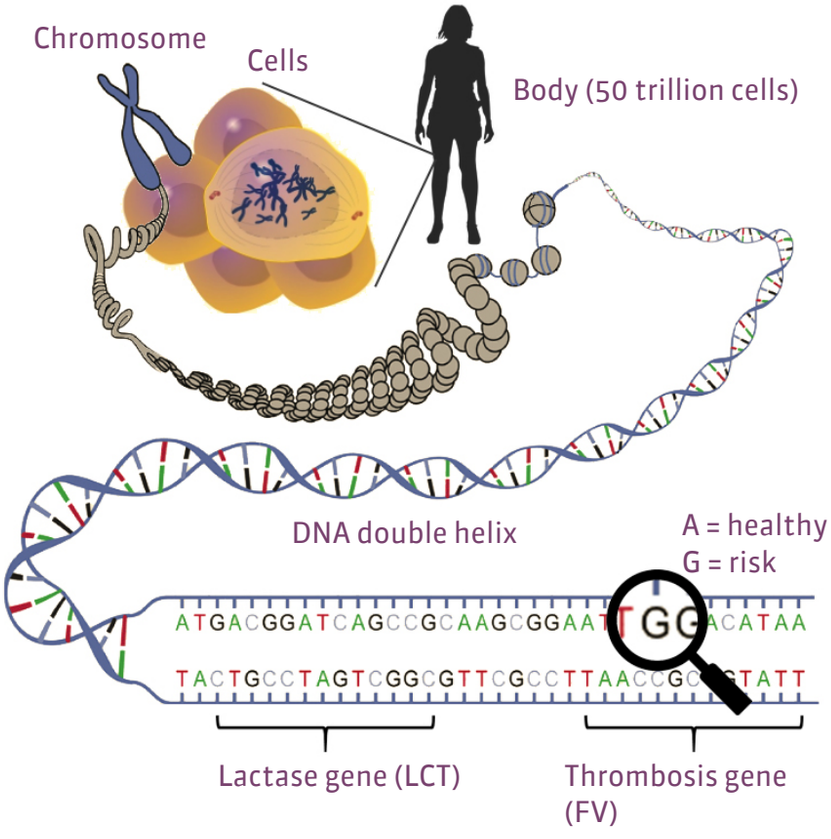
Personal analysis results for:
Jane Doe | Date of birth: 01/01/1990

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.

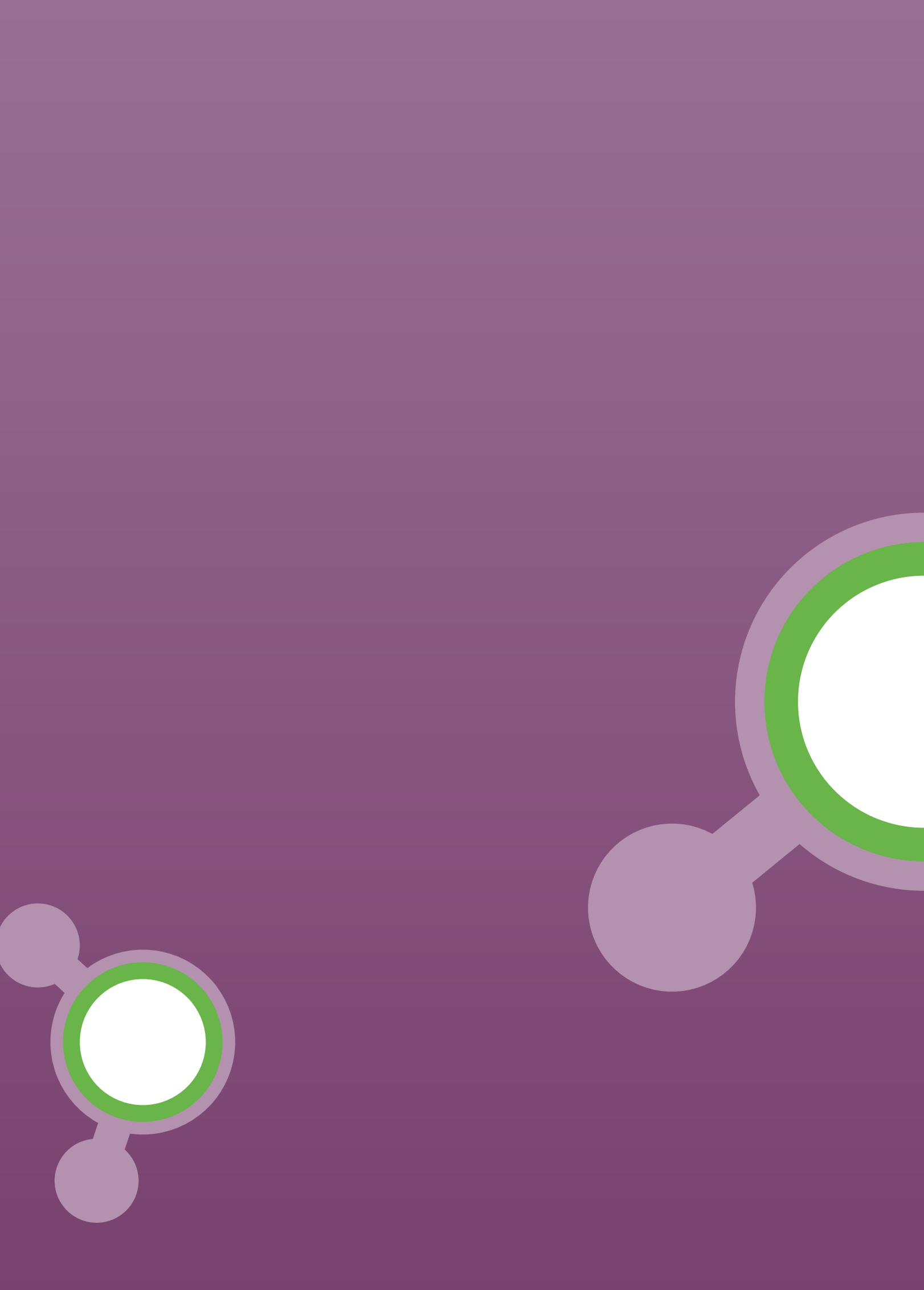
External influences can affect individual genes and disrupt their function, but the majority of our defective genes are inherited from our parents. Each embryo receives half of its genes from the father and half from the mother, resulting in a new human being with some characteristics of each parent.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

Periodontitis Sensor



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Periodontitis Sensor

Prevent periodontal disease and select the proper implant type

Periodontitis

Inflammatory periodontitis disease affects the gums and the jawbone. Periodontitis disease and tooth decay are the two major oral diseases. More than half of the population between ages 35 and 44 suffers from tooth decay, and about 20% of the population has severe tooth decay. Most cases result from poor oral hygiene. Tooth decay is caused primarily by high consumption of refined sugar but good oral hygiene helps us prevent tooth decay so that more people have their own teeth at an older age. Since the age of the teeth plays an important role in developing periodontitis, this disease is more common in older people. 40% of the population older than 65 suffer from a severe form of the disease.

Plaque is constantly forming in the mouth from a combination of food particles, saliva and bacteria. If this plaque is not removed regularly with brushing and dental care, bacteria breaks the sugar contained in food into acids that attack tooth enamel and cause cavities. Over time, additional material accumulates, which makes the condition worse. In addition to destroying tooth enamel, plaque and tartar penetrate the gums causing the immune system to fight the resulting inflammation. This causes gingivitis, which is the persistent inflammation of the gums. Normally, the immune system can prevent bacteria from spreading further. However, in people with weakened immune systems or other complicating factors, the bacteria are able to spread, infecting part of the jawbone that anchors the teeth. In response, the immune system produces enzymes and chemical mediators to fight the bacterial infection but this also attacks and gradually destroys the oral tissues. This powerful immune reaction causes inflammation in the entire jawbone, which causes the tooth to gradually loosen until it falls out. Often, the whole jaw is affected because the tooth only loosens after the disease has progressed significantly. Periodontitis is caused by a combination of many factors but poor oral hygiene and certain genetic traits play a crucial role. Since most of the damage is caused by an immune response, genetic traits that make the response too aggressive can lead to severe periodontitis. However, the immune system responds only when bacteria penetrate into the tissue. This means that people carrying these genetic traits need to take special care of their teeth by avoiding several risk factors:

- Poor oral hygiene with dental plaque and tartar buildup
- Tobacco use, since smoking increases the risk by 4 to 6 times
- Contracting periodontal disease from other infected people (especially within the family)
- Tooth decay (cavities)
- Mouth breathing
- Teeth Grinding
- Poor diet
- Piercings in the mouth, lips, frenulum or tongue
- Diabetes, especially uncontrolled or poorly controlled
- Pregnancy, hormonal changes loosen connective tissue which makes it easier for bacteria to penetrate into the gums
- Weakened immune system, such as after chemotherapy, organ transplant or HIV

If the disease is detected early, it can usually be treated very effectively. However, the patient must maintain good oral hygiene in

order to prevent a recurrence since people who have previously suffered from periodontal disease are at an increased risk of relapse. If it is not diagnosed and treated in time, periodontal disease usually leads to tooth loss, which causes aesthetic and functional problems. This genetic analysis will inform you if have an increased risk, so that you can take preventive measures and get regular dental checkups to prevent the disease.

Titanium implant loss due to genetic variations:

Titanium is a popular material for dental implants because it causes no allergic reactions and bonds firmly with the surrounding bone within 3-6 months. The success of implant varies from person to person but some people can keep an inserted implant for several decades, while others lose the implant after 4 months. This is difference is caused by the varying inflammatory responses to titanium, which is triggered by four different genetic polymorphisms.

For people with the optimal genetic profile, the implant failure rate is approximately 3%. However, the risk of implant failure can be as high as 60% for some people, depending on the number of unfavourable genetic variations. People with an unfavorable genetic profile, which is determined by the genetic analysis, have the opportunity to choose the most appropriate implant, and thus prevent its premature loss.

Relevant genes for periodontitis

Several genetic variations have been identified, which taken individually slightly increase or decrease the risk of periodontitis. Taken together, they have a significant impact on the risk probability. The analysis of relevant genetic variations came to the following conclusion:

Genetic traits			
SYMBOL	**rs NCBI**	**POLYMORPH**	**GENOTYPE**
IL1RN	rs419598	C>T	C/T
IL6	rs1800795	G>C	G/C
IL1A	rs1800587	C>T	C/C
IL 1 Beta	rs1143634	C>T	C/T
TNFa	rs1800629	G>A	A/A

Probability of a titanium implant loss:

SYMBOL	rs NCBI	POLYMORPH	GENOTYPE
IL1RN	rs419598	C>T	C/T
IL1A	rs1800587	C>T	C/C
IL 1 Beta	rs1143634	C>T	C/T
TNFa	rs1800629	G>A	A/A

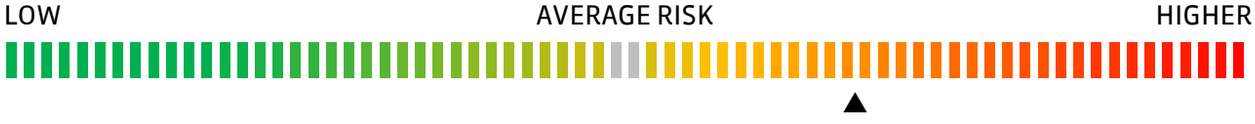
LEGEND: rsNCBI = description of examined genetic variation, POLYMORPHISM = form of the genetic variation, GENOTYPE = personal analysis result

Summary of effects

Several genes have an effect on the aggressiveness of the immune system. Some of these genes may increase the likelihood that an infected jawbone is destroyed by an overactive immune response so that the teeth eventually become loose and fall out. Other genes control how the immune system reacts to titanium implants. If these genes are defective your immune system may reject the titanium implant and you could lose the implant within four weeks.

- Your risk of developing periodontal disease is approximately 3.3 -times increased
- Increased risk of titanium implant loss (OR:4.2)

Risk for periodontitis



Probability of a titanium implant loss

Prevention

Based on your genetic profile, you have an increased risk of developing periodontitis. Preventative measures are very important for you so that you can continue to maintain healthy teeth and gums.

The best way to prevent periodontal disease is to brush your teeth consistently and have regular dental checkups. Disease prevention consists essentially of regular and thorough dental care and medical supervision.

The following points are important for you:

- Brush your teeth in the morning, after every meal and especially in the evening
- Replace your toothbrush regularly
- Use floss or an interdental brush to clean between your teeth.
- Clean the tongue
- Have your teeth cleaned by a dental hygienist every 3 to 6 months.
- Do not eat sugar more than once a day and brush thoroughly immediately afterwards
- Visit the dentist more frequently if you are pregnant, diabetic, or immunodeficient.

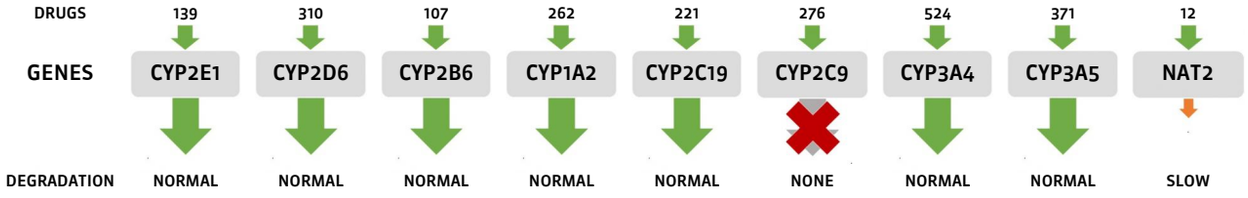
Also avoid, if possible, the following risk factors:

- Poor or improper oral hygiene with dental plaque and tartar
- Tobacco use, since smoking increases the risk 4 to 6-fold
- Contracting periodontal disease from other infected people (especially within the family)
- Tooth decay
- Mouth breathing
- Teeth grinding
- Poor diet
- Piercings in the mouth, lips, frenulum or tongue
- Diabetes, especially uncontrolled or when the blood sugar is poorly controlled
- During pregnancy, hormonal changes loosen the connective tissue and bacteria can easily penetrate into the gums
- A compromised immune system, such as after chemotherapy, organ transplant or HIV

Titanium implant loss due to genetic variations::

Since you have three genetic variations which increase the aggressiveness of your immune system, you have a significantly higher chance of rejecting an implant. You can decide, together with your dentist, if titanium is the appropriate implant material or whether you should choose alternatives such as ceramic implants, zirconium oxide implants, coated titanium implants or removable dentures or bridges.

Drug compatibility



Effect on relevant medication

	Effect	Breakdown	Dose
Amoxicillin	✓	✓	✓
Codeine	✓	✓	✓
Lidocain	✓	✓	✓
Tetracycline	✓	✓	✓

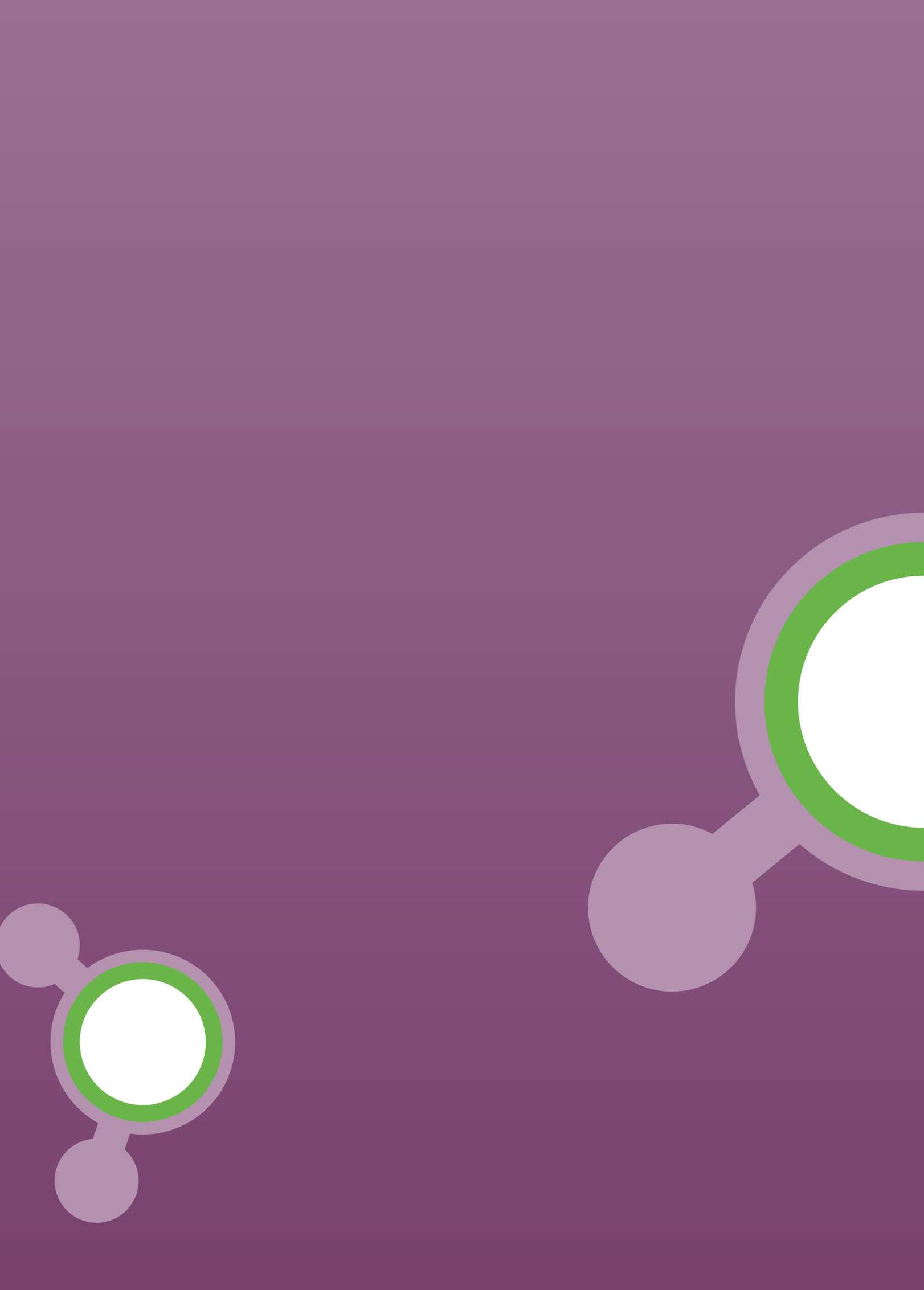
	Effect	Breakdown	Dose
Carbamide	✓	✓	✓
Doxycycline	✓	↑	↑
Metronidazole	✓	✓	✓
Triclofos	✓	✓	✓

	Effect	Breakdown	Dose
Chlorhexidine	✓	✓	✓
Ibuprofen	✓	✗	✗
Minocycline	✓	✓	✓

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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This chapter shows the science behind the test.

Periodontitis Sensor

IL1RN - interleukin 1 receptor antagonist (rs419598)

The interleukin 1 receptor antagonist (IL1RN) is involved in the regulation of immune and inflammatory responses. The rs419598 polymorphism can enhance the inflammatory activity, which leads to an increased risk of periodontitis. In addition, it was shown that carriers of the C-allele have an increased risk of titanium implant loss.

RES	Genotype	POP	Possible results
	T/T	67%	Increased risk of periodontitis (OR: 3.44) No increased risk of titanium implant loss
X	T/C	28%	Increased risk of periodontitis (OR: 3.44) Increased risk of titanium implant loss
	C/C	5%	No increased risk for periodontitis Increased risk of titanium implant loss

References

Braosi et al. Analysis of IL1 gene polymorphisms and transcript levels in periodontal and chronic kidney disease. Cytokine. 2012 Oct,60(1):76-82.

Trevilatto et al. Association of IL1 gene polymorphisms with chronic periodontitis in Brazilians. Arch Oral Biol. 2011 Jan,56(1):54-62.

Baradaran-Rahimi et al. Association of interleukin-1 receptor antagonist gene polymorphisms with generalized aggressive periodontitis in an Iranian population. J Periodontol. 2010 Sep,81(9):1342-6.

Komatsu et al. Association of interleukin-1 receptor antagonist +2018 gene polymorphism with Japanese chronic periodontitis patients using a novel genotyping method. Int J Immunogenet. 2008 Apr,35(2):165-70.

Jacobi-Gresser et al. Genetic and immunological markers predict titanium implant failure: a retrospective study. Int J Oral Maxillofac Surg. 2013 Apr,42(4):537-43.

Laine et al., IL-1RN gene polymorphism is associated with peri-implantitis. Clin Oral Implants Res. 2006 Aug, 17(4):380-5.

IL-6 - interleukin 6 (rs1800795)

Interleukin-6 is (IL-6) one of the pro-inflammatory cytokines and it is an essential part of the immune response to inflammatory processes. The polymorphism rs1800795, located in the promoter region of the gene, alters the expression of the cytokine. Carriers of the C- allele produce less IL-6.

RES	Genotype	POP	Possible results
	G/G	77%	No increased risk for periodontitis
X	G/C	19%	No increased risk for periodontitis
	C/C	5%	Increased risk of periodontitis (OR: 1.89)

References

Nibali et al. Association between periodontitis and common variants in the promoter of the interleukin-6 gene. Cytokine. 2009 Jan,45(1):50-4.

de Sá et al. Association of CD14, IL1B, IL6, IL10 and TNFA functional gene polymorphisms with symptomatic dental abscesses. Int Endod J. 2007 Jul,40(7):563-72.

Babel et al. Analysis of tumor necrosis factor-alpha, transforming growth factor-beta, interleukin-10, IL-6, and interferon-gamma gene polymorphisms in patients with chronic periodontitis. J Periodontol. 2006 Dec,77(12):1978-83.

IL1A - interleukin 1 alpha (rs1800587)

The interleukin-1 gene cluster on chromosome 2 contains the genes for IL1A and IL1B. In the presence of these polymorphisms (rs1800587 and rs1143634) the T-allele increases the IL-1 synthesis, leading to an increase of the inflammatory capacity.

RES	Genotype	POP	Possible results
	T/T	54%	Increased risk of periodontitis (OR: 1.73) Increased risk of titanium implant loss
	T/C	10%	Increased risk of periodontitis (OR: 1.31) Increased risk of titanium implant loss
X	C/C	36%	No increased risk for periodontitis No increased risk of titanium implant loss

References

Jacobi-Gresser et al. Genetic and immunological markers predict titanium implant failure: a retrospective study. Int J Oral Maxillofac Surg. 2013 Apr,42(4):537-43.

Nikolopoulos et al. Cytokine gene polymorphisms in periodontal disease: a meta analysis of 53 studies including 4178 cases and 4590 controls. J Clin Periodontol 2008

Jansson et al., Clinical consequences of IL-1 genotype on early implant failures in patients under periodontal maintenance. Clin Implant Dent Relat Res. 2005, 7(1)51-9.

Feloutzis et al., IL-1 gene polymorphism and smoking as risk factors for peri-implant bone loss in a wellmaintained population. Clin Oral Implants Res. 2003, 14(1)10-7.

IL1B - interleukin 1 beta (rs1143634)

The interleukin-1 gene cluster on chromosome 2 contains the genes for IL1A and IL1B. In the presence of these polymorphisms (rs1800587 and rs1143634) the T-allele increases the IL-1 synthesis, leading to an increase of the inflammatory capacity.

RES	Genotype	POP	Possible results
	T/T	2%	Increased risk of periodontitis (OR: 4.89) Increased risk of titanium implant loss
X	T/C	22%	Increased risk of periodontitis (OR: 2.85) Increased risk of titanium implant loss
	C/C	76%	No increased risk for periodontitis No increased risk of titanium implant loss

References

Gore et al. Interleukin-1beta+3953 allele 2: association with disease status in adult periodontitis. J Clin Periodontol. 1998 Oct,25(10):781-5.

Galbraith et al. Polymorphic cytokine genotypes as markers of disease severity in adult periodontitis. J Clin Periodontol. 1999 Nov,26(11):705-9.

Jacobi-Gresser et al. Genetic and immunological markers predict titanium implant failure: a retrospective study. Int J Oral Maxillofac Surg. 2013 Apr,42(4):537-43.

Jansson et al., Clinical consequences of IL-1 genotype on early implant failures in patients under periodontal maintenance. Clin Implant Dent Relat Res. 2005 7(1):51-9.

Feloutzis et al., IL-1 gene polymorphism and smoking as risk factors for peri-implant bone loss in a wellmaintained population. Clin Oral Implants Res. 2003, 14(1):10-7.

TNF-α - tumor necrosis factor a (TNF superfamily, member 2) (rs1800629)

The tumour necrosis factor (TNF or TNF-α) is a cytokine in the human immune system that regulates the activity of immune cells. TNF regulates apoptosis, cell proliferation, cell differentiation and the secretion of various cytokines. The polymorphism rs1800629 leads to a highly increased TNFa expression, and thus to an increased inflammatory capacity.

RES	Genotype	POP	Possible results
	G/G	83%	No increased risk of titanium implant loss
	G/A	17%	Increased risk of titanium implant loss
X	A/A	1%	Increased risk of titanium implant loss

References

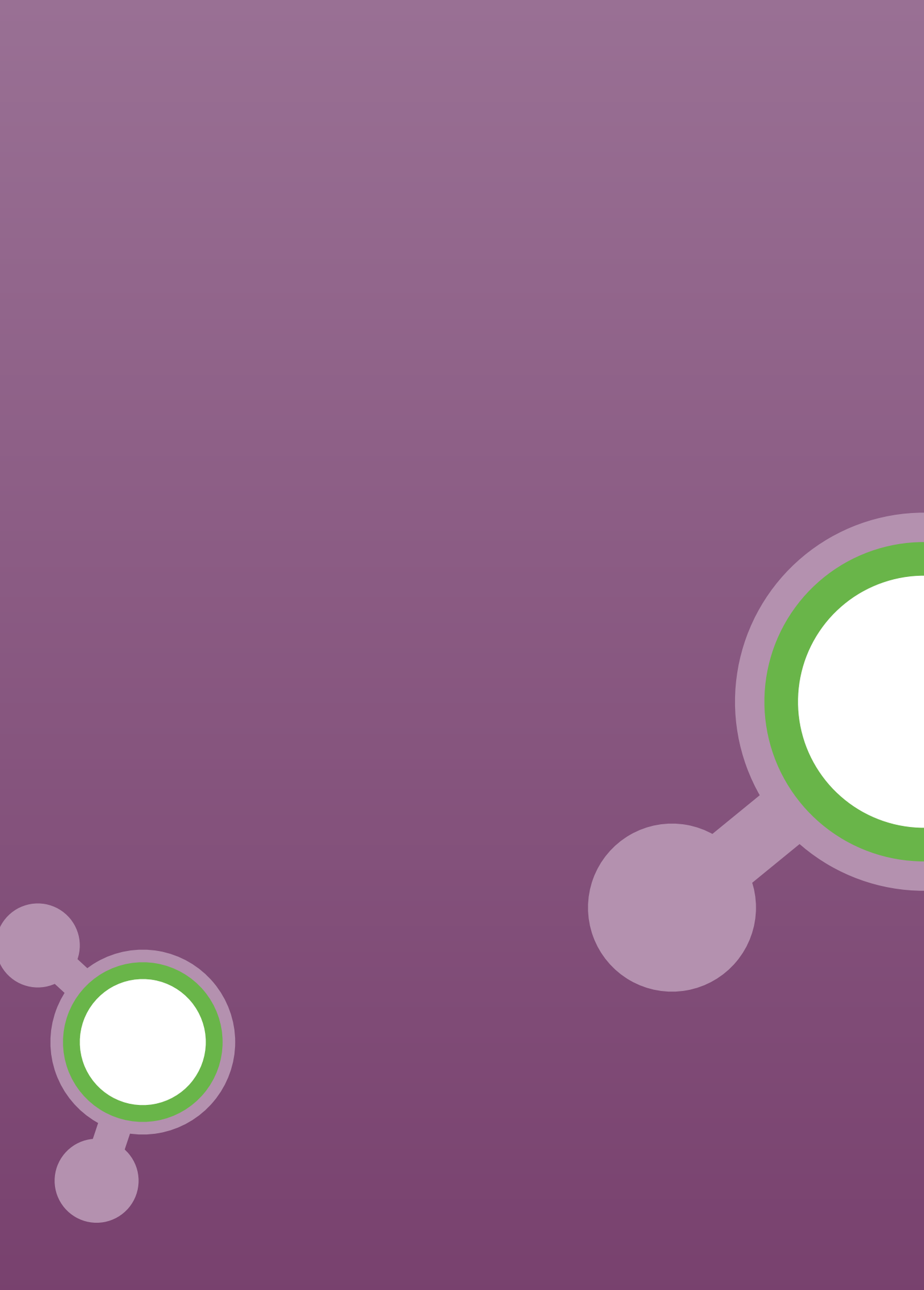
Jacobi-Gresser et al. Genetic and immunological markers predict titanium implant failure: a retrospective study. Int J Oral Maxillofac Surg. 2013 Apr,42(4):537-43.

Xue-Mei Wei et al. Tumor necrosis factor-α G-308A (rs1800629) polymorphism and aggressive periodontitis susceptibility: A meta-analysis of 16 case-control studies. Sci Rep. 2016, 6: 19099.

Dereka X et al. A systematic review on the association between genetic predisposition and dental implant biological complications. Clinical Oral Implants Research, 23(7), 775–788.

Nikolopoulos G et al. Cytokine gene polymorphisms in periodontal disease: a meta-analysis of 53 studies including 4178 cases and 4590 controls. Journal of Clinical Periodontology, 35(9), 754–767.

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.



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ADDITIONAL INFORMATION

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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
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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
M6PER

Current version
V538

Ordering company
ProGenom GmbH
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Laboratory Director

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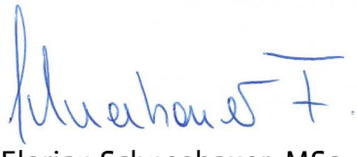
Laboratory Manager



Florian Schneebauer, MSc.

NOTES: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