ProBabyDNA

Pregnancy Sensor

Maria Musterfrau

DEMO_ML

ProGenom
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COVER LETTER

Dear Ms. Musterfrau,

Your sample for the analysis arrived on 25/11/2020 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

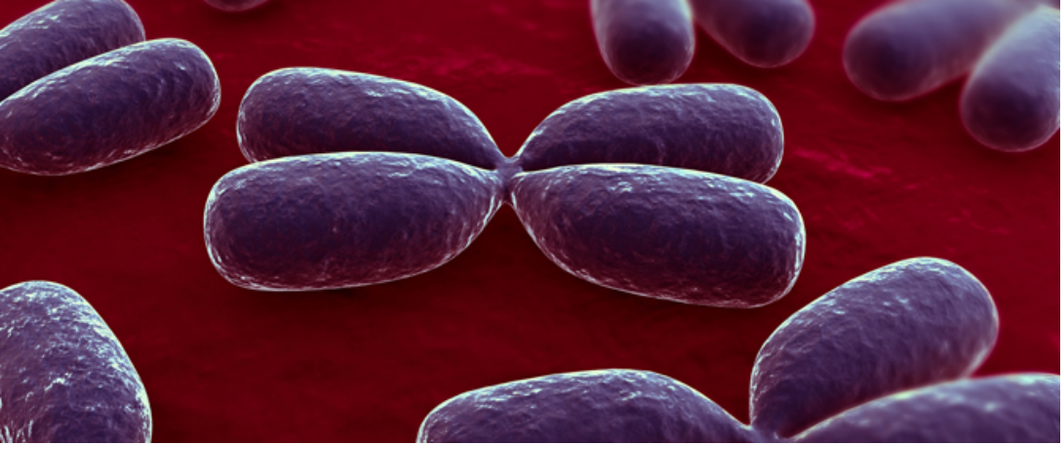
Florian Schneebauer, MSc.
Laboratory Manager

Pregnancy Sensor

Personal analysis results for:
Maria Musterfrau | Date of birth: 01/01/1990

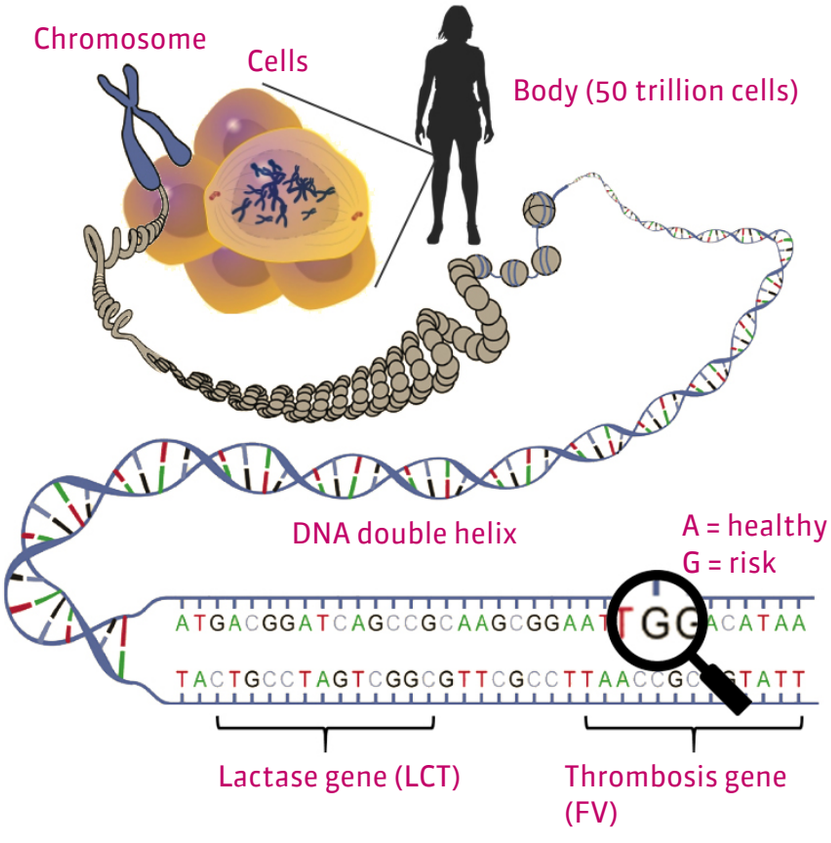
Order number:
DEMO_ML

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.

PREGNANCY

Risk assessment and prevention during pregnancy

Pregnancy

When the question of starting a family and the wish for children emerge one of the happiest phases in the shared life of most couples begins. While some couples have these thoughts from early on, others need a bit more time until they decide to have offspring. Unfortunately, a great percentage of pregnancies end in abortion. Scientists assume that genetic factors are responsible for 50% of pregnancies ending in a miscarriage; of very early (unnoticed) miscarriages even 80% are suspected. Genetic factors also have an influence on pregnancy illnesses, so called gestosis (e.g. preeclampsia) and prenatal development disruptions.

Gestosis is the umbrella term for illnesses that only occur during pregnancy and only affect the mother. Previously they were known as "pregnancy poisoning", however, that is an outdated and incorrect term. It is differentiated between early gestosis (regurgitation, increased salivation) in the first three months and late gestosis (eclampsia, HELLP syndrome, superimposed preeclampsia) during the last third of the pregnancy. The different disease patterns can manifest themselves through various symptoms of which the 3 most common (oedemata, proteinuria and high blood pressure) have become known under the term EPH gestosis or preeclampsia. The exact causes of preeclampsia are to date not know. It is assumed that aside genetic factors also a healthy diet plays a significant role. For the early detection of a gestosis a thorough and strict preventative health examination of pregnant women is essential.

Miscarriage (Abortion)

During the first weeks of the pregnancy the risk of a miscarriage (spontaneous abortion) is especially high. 80% of the miscarriages occur in this time and are described as early miscarriages. During the first 12 weeks the zygote settles in and the placenta develops. These processes are extremely complex and can often be disturbed. When the pregnancy is more advanced the danger of a miscarriage decreases as well. In the 15th week of pregnancy the risk of a miscarriage is already under 3%. The reasons of a miscarriage vary. Often genetic factors, as trisomy (a chromosome or a part of a chromosome exists thrice instead of twice) are the cause. Further causes can be infections, hormonal disturbances, chronic illnesses, ovarian insufficiency or a malformation of the uterus. Science is already aware of genetic constellations which dramatically increase the risk of a miscarriage. If you are the carrier of such a constellation you should perform a miscarriage prevention to minimize the risk.

Fetal dystrophy

Fetal or prenatal dystrophies are various prenatal development disturbances (e.g. low birth weight). Worldwide the most common causes of this retardation of growth are malnutrition, different diseases, consumption of tobacco and genetic mutations.

Especially the smoking of tobacco during the pregnancy can risk the unborn child. It has been proven that the consumption of only a few cigarettes a day can dramatically reduce the birth weight of the child. This effect can even be reinforced through the combination with different detoxification genes, which are

responsible for the production of important detoxification enzymes.

Thrombosis in pregnancy

Further studies have shown that the thrombosis risk of a pregnant woman is 4 to 10 times higher than that of a not pregnant woman. This risk increases in the months after the delivery to about 10 to 20 times. Also, the young age (15-19 years) in which most cases occur is striking. On the average every twentieth European woman is already without a pregnancy genetically prone to thrombosis and her thrombosis risk lies about 8 to 80 times higher than that of the average population. When a genetically defect person is pregnant these two risk factors collide and a dangerous constellation of a gen defect and a risk situation arises which increases the thrombosis risk to about 60 times and can lead to life-threatening health conditions. It is estimated that thrombosis is responsible for about a third of the deaths that occur during pregnancy and about 30-60% of the women, who developed thrombosis were also genetically defect. Therefore, it is already accepted in the medical field that genetically defect women are medically treated during the entire pregnancy to prevent cases of thrombosis.

Gestational diabetes

Pregnancy diabetes (or gestational diabetes) is a form of sugar disease which can develop during pregnancy and disappears again immediately after birth. Overall, pregnancy diabetes is one of the most common diseases occurring during pregnancy and can be detected in approximately 4% of all pregnant women. Normally, there are no symptoms with gestational diabetes, which is why it can usually only be determined by means of a test. This glucose tolerance test is one of the mandatory tests during pregnancy in many countries around the world. The disease can usually be treated very successfully by a diet change.

Folic acid and folate during pregnancy

Folic acid and folate belong to the group of water-soluble B vitamins and play an important role in cell division, growth and development. For this reason, folic acid is particularly important before and during pregnancy. If expectant mothers do not ensure an adequately supply of folate, the development of the embryo can be disrupted and the central nervous system be damaged.

Since the body can not produce folate itself, it is dependent on sufficient food intake. Since there is a strong increase in need during pregnancy, folic acid supplements are usually recommended.

However, for folic acid to be utilized by the body, it must first be converted to its active form (5-methyltetrahydrofolate). Scientific studies have shown that a very common genetic variation results in a limitation of this conversion (up to 75% decrease). Therefore, about every other woman can not convert folic acid into its active form optimally.

If such genetic variation is present, these individuals require higher amounts of folic acid or can also directly take the active form 5-MTHF in the form of a dietary supplement.

RESULT

Here you can learn all about relevant genes and their effects on you

Relevant genes for the pregnancy

To date science has identified several genes and polymorphisms which can increase the risk of an abortion and/or pregnancy associated diseases. By analyzing all relevant polymorphisms the risk can be assessed more easily. The following genes can have an impact on the pregnancy:

Genetic traits

SYMBOL	rs NCBI	POLYMORPH	GENOTYPE
AGT	rs699	T>C	T/T
MTHFR	rs1801133	C>T	C/C
MTHFR	rs1801131	A>C	A/C
Factor-V	rs6025	G>A	G/G
Factor-II	rs1799963	G>A	G/G
GSTT1	Null allele	del=Null allele	DEL
GSTM1	Null allele	T=Null allele	INS
CYP1A1	rs4646903	T>C	T/T
MTHFR	rs1801131	A>C	A/C
TCF7L2	rs7903146	VS3C>T	C/C

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

Summary of effects

Here you can see a summary of the influence your genetic variations have on your health:

- Your risk of a preeclampsia is not increased
- Your risk of developing venous thrombosis is not increased
- You do not have an increased risk of developing a fetal dystrophy
- You do not have an increased risk of having a miscarriage during pregnancy
- You do not have an elevated risk of gestational diabetes
- Your body is able to convert enough folic acid into its active form

Risk of a preeclampsia

NORMAL INCREASED

Risk of a fetal dystrophy

NORMAL INCREASED

Risk of a thrombosis during pregnancy

NORMAL INCREASED

Risk of a habitual miscarriage

NORMAL INCREASED

Your risk of gestational diabetes

NORMAL INCREASED

Conversion of folic acid into its active form

NORMAL REDUCED

Recommended folate supplement during pregnancy

FOLIC ACID 5-MTHF

Prevention

Based on your genetic profile you are not having an increased risk of developing a preeclampsia. As preeclampsia can also occur without a genetic defect you should pay attention to the following:

- Regularly attend the medical examination during your pregnancy
- Go to all the preventive medical checkups
- Have your blood pressure and urine values examined
- Avoid stress
- Keep an eye open for symptoms of a preeclampsia (e.g. high blood pressure, swollen limbs, dizziness, headaches, drowsiness, impaired vision, nausea)
- Obesity increases the risk of a preeclampsia
- Pay attention to a healthy and balanced diet

Based on your genetic profile you have no increased risk of a venous thrombosis. As the thrombosis risk is dramatically increased during the pregnancy (even without genetic defects) it is recommendable you take some precautionary measures to prevent the development of the disease as best as you can:

- Pay attention to sufficient exercise
- Keep a balanced and healthy diet
- Compression stockings can relieve the veins and support the backflow of the blood to the heart
- Avoid sitting for too long, e.g. have enough breaks during long car drives
- Varicose veins in the legs increase the risk
- Abandon by all means alcohol and cigarettes completely
- When having a very high risk blood-thinning medication (heparin) can be used under medical surveillance

Your genetic risk of an induced abortion (miscarriage) is not increased. Therefore, there are no special precautionary measures necessary for you. There are, however, factors that can increase the risk of a miscarriage even when you're not genetically defect - these should be therefore avoided. Please not following points:

- Attend the pregnancy medical examination regularly in order to e.g. detect infections early on and treat them
- Self-tests from the pharmacy can be helpful to recognize a possible vaginal infection
- Keep your histology in mind (e.g. diabetes) and discuss it with your doctor
- Pay attention to a healthy, balanced and nutrition-rich diet
- Drink at least 2.5 liters a day
- Do not diet during the pregnancy
- Forgo by all means alcohol and cigarettes during the pregnancy completely
- Keep an eye on a high caffeine consumption. Drink a maximum of 2 cups of coffee a day

- Avoid stress and take care of your spirit
- Don't forget sufficient exercise (walks, swimming, yoga etc.)

Your genetic risk of developing gestational diabetes is not increased. However, since a pregnancy diabetes can occur without genetic pre-stress, a sugar test (oral glucose tolerance test) is recommended between the 24th and 27th week of pregnancy. If the condition is diagnosed, it can usually be very easily treated with a diet change. In addition, these factors favor the development of gestational diabetes:

- Overweight (obesity)
- Age of mother over 30 years
- Cases of diabetes mellitus in the close family
- An already born child with a birth weight of over 4500 g
- Repeated miscarriages
- A gestational diabetes in a previous pregnancy
- Excessive weight gain during pregnancy
- Disturbed glucose tolerance before pregnancy
- Certain diseases and/or drugs which have a negative effect on the insulin household

Your risk of a fetal dystrophy is not increased. According to your provided information you are a non-smoker and therefore no other precautionary measures are recommended other than the pregnancy health examination.

Due to your genetics, your body is capable of converting enough folic acid into its active form (5-MTHF). Folic acid supplements are therefore sufficient to meet the increased need for folate during pregnancy. Please discuss use of any dietary supplements with your doctor prior to taking them during pregnancy.

SCIENCE

This chapter shows the science behind the test.

FemSensor Pregnancy

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

Angiotensinogen and his metabolits Angiotensin (AT) I, II, III and IV play a key role as potent vasopressores and regulators of the electrolyt- and fluidhomeostasis. A polymorph mutation of this gene (Met235Thr) is associated with the development of essential hypertension and elevated risk levels for developing preeclampsia in pregnancy.

RES	Genotype	POP	Possible results
X	T/T	37%	No increased risk of a preeclampsia No increased risk of a hypertension caused by pregnancy
	T/C	43%	Increased risk of a preeclampsia Increased risk of a hypertension caused by pregnancy
	C/C	20%	Increased risk of a preeclampsia Increased risk of a hypertension caused by pregnancy

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Factor-II - Coagulation factor II (thrombin) (rs1799963)

The G>A Pos. +20210 polymorphism of the prothrombin (F2) gene, a Vitamine dependent clotting factor, leads to a increased prothrombin activity in the plasma. Prothrombin is the preamplifier of the active clotting enzyme thrombin which has a key position in the regulation of clotting. The F2 G20210A mutation increased the Thrombose risk drastically. The polymorphism is furthermore associated with an increased abortion risk.

RES	Genotype	POP	Possible results
	A/A	1%	Increased risk of a thrombosis caused by pregnancy Increased risk of a habitual miscarriage
	A/G	3%	Increased risk of a thrombosis caused by pregnancy Increased risk of a habitual miscarriage
X	G/G	96%	No increased risk of a thrombosis caused by pregnancy No increased risk of a habitual miscarriage

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Factor-V - Coagulation factor V (proaccelerin, labile factor) (rs6025)

The F5 Leiden mutation is the most common reason for developing APC resistence. About 50% of the women, who develop pregnancy induced thrombosis, carry this polymorphism. Women, who take ethinylestradiol containing oral contraceptives and carry the heterozygote form of the factor 5 Leiden mutation have a 30 to 50% elevated risk of developing thrombosis. Morover, the incidence of thrombosis in women, who take HRT and carry heterozygote F5 mutation is about 1.5/100/year. Furthermore, this polymorphism is associated with preeclampsia, recurrent misscariage and subfertility.

RES	Genotype	POP	Possible results
	A/A	1%	Increased risk of a thrombosis caused by pregnancy Increased risk of a habitual miscarriage
	A/G	3%	Increased risk of a thrombosis caused by pregnancy Increased risk of a habitual miscarriage
X	G/G	96%	No increased risk of a thrombosis caused by pregnancy No increased risk of a habitual miscarriage

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

The Ala>Val Codon 222 polymorphism of the methylenetetrahydrofolacid reductase gene (MTHFR) has also been associated with pregnancy complications. Methylenetetrahydrofolacid is a key enzyme for the reduction of homocysteine to methionine. This polymorphism leads to increased thermolability of the enzyme, therefore reduced enzyme activity, increased homozytsteine and decreased methionine and folic acid levels. Homozygous carriers of this polymorphism also have serologically proven hyperhomocysteinemia and therefore an increased risk of illnesses which are akin to hyperhomocysteine (infarction, heart or vascular diseases).

RES	Genotype	POP	Possible results
X	C/C	59%	No increased risk of a preeclampsia No increased of a miscarriage No increased risk of thrombosis (venous) Folic acid can be converted into its active form
	C/T	33%	Increased risk of a preeclampsia Increased risk of a miscarriage No increased risk of thrombosis (venous) Folic acid can only be converted into its active form to a limited extent
	T/T	8%	Increased risk of a preeclampsia Increased risk of a miscarriage Increased risk of thrombosis (venous) (OR: 3) Folic acid can only be converted into its active form to a limited extent

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MTHFR - Methylenetetrahydrofolate reductase (NAD(P)H) (rs1801131)

Methylenetrahydrofolic Acid Reductase is a key enzyme in the breakdown of homocysteine to methionine. Polymorphisms of the MTHFR gene can affect both the production and activity of the MTHFR enzyme. This can lead to increased homocysteine levels.

RES	Genotype	POP	Possible results
	A/A	47%	Folic acid can be converted into its active form
X	A/C	44%	Folic acid can be converted into its active form
	C/C	9%	Folic acid can only be converted into its active form to a limited extent

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GSTT1 - glutathione s-transferase theta 1 (null allele)

Gluthatione-S-Transferases (GST) are enzymes that detoxify many different exogene and endogene substances. In the human liver the represent 4% of the dissoluble proteins and catalyze the agglomeration of glutathione to a number of potentially toxic xenobiotics A deletion polymorphism in the Glutathione-S-Transferase Theta 1 (GSTT1) gene has special effects and leads to a reduced enzymatic activity and that the environmental toxins and the tobacco smoke is more difficult to break down. The so-called zero genotypes miss a functioning GSTT1 protein. This polymorphism is especially important to the prevention of pregnancy complications.

RES	Genotype	POP	Possible results
	A/A	36%	No increased risk
	A/DEL	42%	Increased risk of a low birth weight due to tobacco consumption during the pregnancy
X	DEL/DEL	22%	Increased risk of a low birth weight due to tobacco consumption during the pregnancy

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GSTM1 - glutathione s-transferase mu1 (null allele)

The glutathione s-transferases are found in the liver and in lymphocytes. They are involved in the detoxification of endogenous and exogenous substances. A defective GSTM1 gene reduces the enzymatic activity of the protein, which leads to a limited cellular detoxification.

RES	Genotype	POP	Possible results
X	C/C	10%	No increased risk
	C/DEL	38%	Increased risk of a low birth weight due to tobacco consumption during the pregnancy
	DEL/DEL	52%	Increased risk of a low birth weight due to tobacco consumption during the pregnancy

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CYP1A1 - Cytochrome P450, family 1, subfamily A, polypeptide 1 (rs4646903)

Cytochrome P450 1A1 (CYP1A1), an important phase I detoxification enzyme, catalyzes next to other reactions also the activation of pro-carcinoges. To this pro-carcinoges also the group of polycyclic, aromatic hydrocarbons (PAH) in the tobacco smoke count. A well-documented polymorphism (T>C Pos. -3801) in the CYP1A1 gene is associated with an increased enzyme activity.

RES	Genotype	POP	Possible results
X	T/T	62%	No increased risk
	T/C	37%	Increased risk of a low birth weight due to tobacco consumption during the pregnancy
	C/C	1%	Increased risk of a low birth weight due to tobacco consumption during the pregnancy

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TCF7L2 - Transcription factor 7-like 2 (T-cell specific, HMG-box) (rs7903146)

TCF7L2 (transcription factor 7-like 2) is a transcription factor which affects many different genes. The polymorphism rs7903146 is considered the most important genetic risk factor for type 2 diabetes.

RES	Genotype	POP	Possible results
X	C/C	55%	No increased risk of gestational diabetes
	C/T	35%	Increased risk of gestational diabetes
	T/T	10%	Increased risk of gestational diabetes

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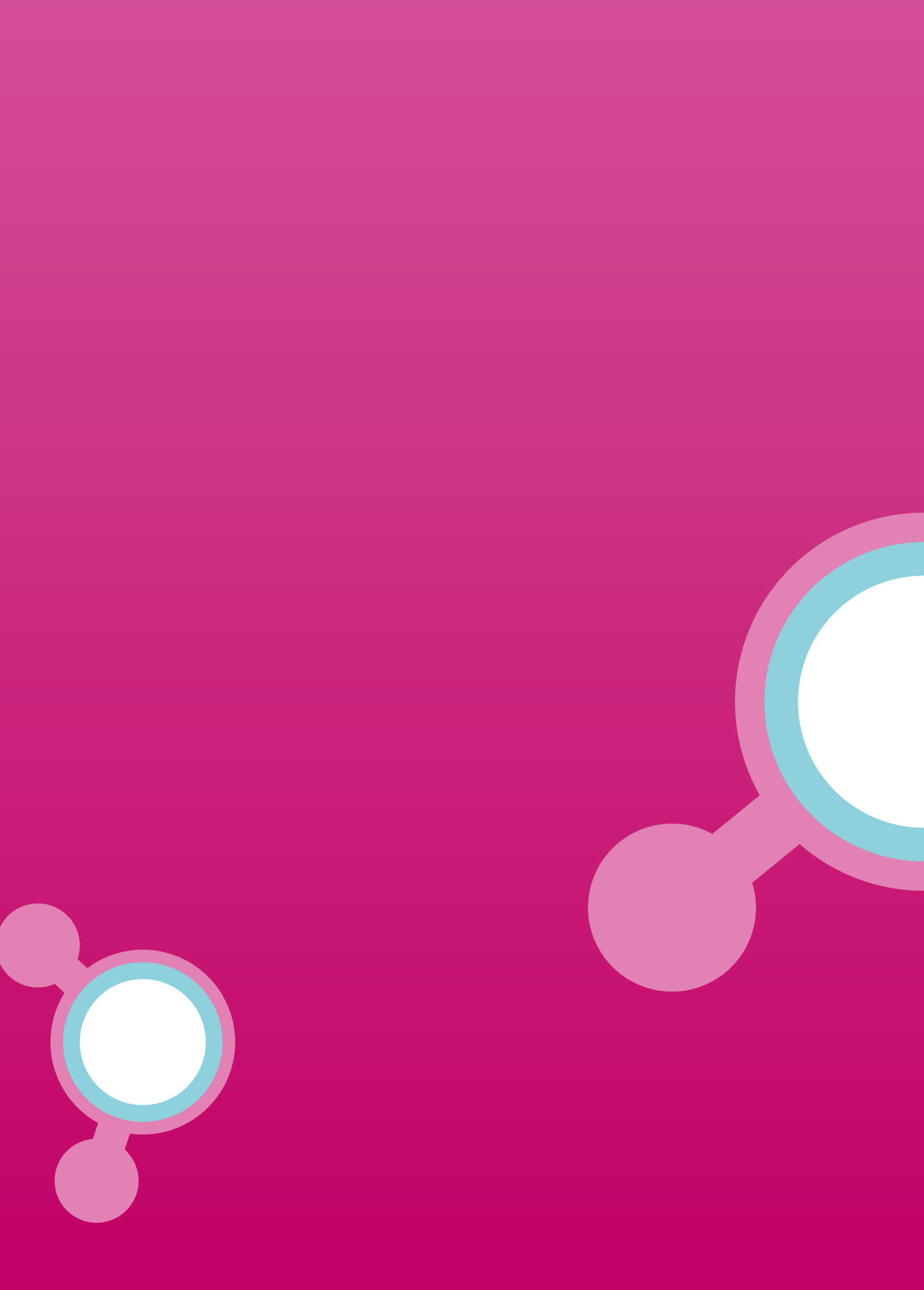

ADDITIONAL INFORMATION

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
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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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Technical details

Order number
DEMO_ML

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
B1BAB, B2MIL, B4PRE

Current version
V538

Ordering company
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ProBabyDNA

Pregnancy Sensor

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