CeGaT

Disease Prevention Panel

Understand genetic risk factors.
Plan individual health care.

Disease Prevention Panel

Every human being is unique and genetically different from others. This is reflected in appearance, special talents, and personality, but also in the genetic predisposition to various diseases, such as tumors or cardiovascular diseases. If you know your genetic risk factors, you can actively contribute to preventing or delaying a disease's onset or alleviating its symptoms.

Genetic risk factors play an important role in many diseases that frequently occur in our society. However, an individual genetic predisposition to a disease is not necessarily an inevitable fate. Environmental factors such as lifestyle, diet, and exercise may also influence whether a genetic disease breaks out or the affected person remains healthy.

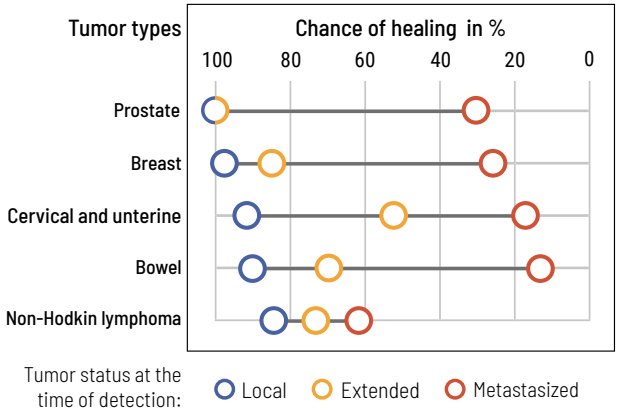
The genetic screening results are, therefore, a guide to health-conscious living. They enable recommendations such as participation in early detection programs for diseases, an adjustment of lifestyle or medication, e.g., to prevent thrombosis on long-distance flights. Therefore, early identification of genetic risk factors and taking preventive measures are important for health promotion.

Disease Prevention Panel

Early Detection of Tumor Diseases Increases Survival Rate Drastically

For tumor diseases, the following applies: The earlier a tumor is detected, the better the prognosis. The figure illustrates this principle using 5 different tumor entities. If the tumor is diagnosed during the early stages (local), the chances of surviving for 5 years or longer is 80 % to 100 %. Survival rates significantly decrease if the tumor is detected after it has metastasized.

CeGaT's screening panel checks whether you are at increased risk for tumor disease and should therefore take intensified early detection measures.



Quelle: SEER | Economist.com | 2016

Pharmacogenetics - Individual Medication Selection and Dosage

Not every person processes drugs the same way. What one individual benefits from can be ineffective or harmful to others. The CeGaT Disease Prevention Panel detects whether active ingredients are broken down particularly fast or very slowly. Based on this information, the physician can select the best medication and administer it in the correct dosage. This also applies to future therapies.

Genetic Diagnostics at the Highest Level

Full gene sequencing based on NGS – not restricted to hotspots

Comprehensive medical report incl. individual recommendations

Reports created manually by our doctors and scientists compared to only automatically generated reports

99,87 % sensitivity for the detection of heterozygous single nucleotide variants

Sequencing in Germany with the highest quality

Reliable advice and support throughout all steps of the examination

Data protection is guaranteed at all times

Patient samples are processed by CeGaT according to accredited procedures

Anna, 32 years

Lifestyle: Conscious diet, normal sleep patterns, regular exercise

Result: Increased tumor risk due to variant in *BRCA1* gene

Consequence: Semi-annual examination, close supervision

Oliver, 45 years

Lifestyle: Active in sports, high travel activity

Result: Factor V Leiden mutation

Consequence: Sensitization to thrombosis, preventive measures in case of immobilization, e.g., during long-haul flights or surgeries

Modules

Tumor Diseases

Disease-causing changes in the genome of individual cells play a decisive role in cancer development. These genetic changes can be triggered by external factors, such as exposure to radiation and smoking. However, disease onset can also be caused by inborn alterations in the genotype, most of which are inherited. In the 'tumor diseases' module of our Disease Prevention Panel, 51 genes are analyzed that are associated with an increased susceptibility to tumor diseases. For example, we investigate genes that are particularly relevant to digestive tract tumors (various forms of colorectal cancer, stomach cancer, and pancreatic cancer), breast cancer, ovarian cancer, skin cancer, thyroid tumors, endocrine tumors, and more.

If our Disease Prevention Panel reveals an increased risk for a specific type of cancer, appropriate action will be advised. In the event of disease onset, relevant treatment can be provided in a timely manner.

Cardiovascular Diseases

Cardiovascular diseases are the number one cause of death globally. The chance of developing heart disease increases with age, and in addition, certain genetic factors also increase the risk. Disease-causing changes in the genome can functionally disrupt the heart muscle structure (e.g., in cardiac myopathies). They can also impair the function of ion channels in the heart, which are important for transmitting electrical signals. This can cause cardiac arrhythmia. Pathogenic changes in further genes included on the Disease Prevention Panel can cause a disturbance in the structure of vessels. This can lead to pathological dilation, splitting of the vessel wall layers, or even rupture of vessels. Identifying these pathogenic changes will ensure that appropriate measures can be taken.

The 'cardiovascular diseases' module of our Disease Prevention Panel analyzes 55 genes that are involved in cardiovascular function. Pathogenic changes in these genes may give the treating physician an indication of whether closer monitoring is needed, or lifestyle adjustment, or therapy, are necessary.

Thrombosis and Coagulation Disorders

Genetic factors can disrupt blood clotting (coagulation). This can cause blood to clot within a vessel (thrombosis), eventually blocking the vessel entirely and possibly causing a stroke. Hereditary forms of thrombosis strongly increase the risk of leg vein thrombosis, stroke, pulmonary embolism, and miscarriage. Another manifestation of abnormal coagulation is a heamophilia (easy and prolonged bleeding). Due to a genetic defect, the function of blood clotting factors can be impaired. In haemophilic individuals, blood takes much longer to clot, or does not clot at all. Even minor injuries or interventions can cause extensive bleeding in joints and tissues, leading to severe blood loss.

The 'thrombosis and coagulation disorders' module of the CeGaT Disease Prevention Panel analyzes 28 genes associated with coagulation disorders. If genetic risk factors for coagulation disorders are identified, an attending physician will take appropriate precautions.

Iron and Copper Storage Disorders

These hereditary diseases are characterized by the accumulation of iron or copper in the body. In individuals with iron and copper storage disorders, the balance between uptake and elimination of iron or copper is disturbed. As a result, excessive amounts can accumulate in organs and tissues, causing damage and discomfort. Our genetic analysis can reveal a predisposition to iron and copper storage disorders even before the onset of symptoms.

In the 'iron and copper storage disorders' module of our Disease Prevention Panel, 8 genes involved in copper and iron metabolism are analyzed. Disease-causing changes in these genes will be identified, and appropriate measures can be taken to prevent disease-related damage.

Hypercholesterolaemia

Familial hypercholesterolaemia is a hereditary disturbance of lipid metabolism. In 85 % - 90 % of cases, this is caused by a mutation in the low-density lipoprotein (LDL) receptor (docking site for LDL on cells) gene, which increases blood lipid LDL cholesterol by 2 to 10 times the normal value. This increases the amount of LDL deposited in blood vessels (vascular calcification), which increases the risk of a heart attack.

Familial hypercholesterolaemia is thought to occur in 1:500 individuals, but only 15 % of cases are actually diagnosed. In young individuals, it is usually only diagnosed after a heart attack. Other diagnostic factors include:

- Frequent familial heart attacks
- Xanthomas (nodular fat deposits in the skin)
- Strongly elevated LDL cholesterol levels in the blood

In the 'hypercholesterolaemia' module of the CeGaT Disease Prevention Panel, 4 disease-relevant genes are analyzed, including genes that encode the LDL receptor and proteins that affect LDL receptor function. Early diagnosis means LDL cholesterol can be reduced by early interventions and lifestyle changes that reduce vascular deposits, thereby lowering the risk of a heart attack.

One form of therapy, in that case, could be the administration of lipid-lowering drugs (e.g., statins). In this context, the CeGaT ‚Pharmacogenetics' module offers the possibility to investigate genetic variants that influence the effect of e.g., statins. With this knowledge, the physician can individually adjust the drug dose.

Glaucoma

Glaucoma is one of the most typical causes of blindness worldwide. Glaucomas often develop with age and without a specific reason. Degeneration of retinal cells during the course of the disease irreversibly damages the visual field.

Risk factors for glaucoma include higher inner eye pressure, ethnic origin, diabetes, chronic eye infections, or cardiovascular diseases. Around 5 % of glaucomas are caused by inherited genetic changes that can induce disease onset from 35 years of age. In the 'glaucoma' module of our Disease Prevention Panel, 2 genes are tested that are known to cause glaucoma.

If the test reveals an elevated risk of glaucoma, further monitoring is recommended to ensure that appropriate treatments are initiated as soon as they are necessary. The earlier glaucoma is detected, the better the prognosis and the sooner the appropriate therapy can be initiated to slow down or even stop disease progression.

Malignant Hyperthermia (Anaesthesia Intolerance)

Malignant hyperthermia is characterized by a life-threatening response to anaesthesia. In the presence of certain genetic risk factors, anaesthetics or muscle relaxants disrupt calcium metabolism in the muscle. This disruption causes muscles to cramp, become rigid, and increase blood pressure and body temperature. If these symptoms are not treated quickly, the patient will die from metabolic and organ failure.

This inherited disease is usually recognized for the first time when anaesthetics or muscle relaxants cause a life-threatening situation. However, a well-tolerated response to anaesthesia does not exclude a predisposition to malignant hyperthermia because patients can undergo an average of three narcoses before disease onset.

The 'malignant hyperthermia' module of CeGaT's Disease Prevention Panel tests 2 genes that are responsible for more than 70 % of malignant hyperthermia cases. Diagnosing a predisposition to malignant hyperthermia before a surgical intervention means that the individual can be anaesthetized in a way that will not trigger an unfavorable reaction.

Pharmacogenetics

Pharmacogenetics illustrates how genetic changes can affect the influence of drugs. Genetic changes in the proteins responsible for absorption, distribution, metabolism, and excretion of drugs can have a huge impact on their effectiveness and compatibility.

Some drugs have different effects on different people, e.g., antidepressants, analgesics, neuroleptics, chemotherapeutics, AIDS medication, thrombosis medication, anaesthetics, beta-blockers, and statins. A specific enzyme's reduced or missing activity may increase the drug level and cause unwanted side effects. On the other hand, a medication that is activated by metabolism may not work if an enzyme is inactive. Enhanced enzyme activity can also affect the response to medication, e.g., by degrading the active ingredients.

The 'pharmacogenetics' module of our Disease Prevention Panel analyzes known variations in 22 genes that are involved in the metabolism of pharmaceuticals. If gene variants are found, the physician can customize the therapy to avoid serious side effects and treatment failure.

Familial Diabetes

Diabetes mellitus (diabetes) describes a group of diseases associated with elevated blood glucose levels. Genetics plays a central role in the development of familial diabetes mellitus. The 'Maturity-Onset Diabetes of the Young' (MODY) analyzed here is a hereditary disease that can be diagnosed partly in adolescence and partly in adulthood and is often associated without concomitant obesity. During the course of the disease, microvascular complications, such as kidney, eye, and nerve damage, etc. may occur. The presence of familial genetic diabetes should also be considered in the context of gestational diabetes. Depending on the form of the disease, a possible necessary therapy may consist of a lifestyle adjustment such as dietary changes or drug therapy, if required.

In the 'familial diabetes' module, 5 genes are analyzed that are associated with an increased risk of developing familial diabetes mellitus. If these are identified at an early stage, appropriate preventive measures can be initiated.

From Sample to Report

Genetic counseling by qualified specialists and **blood or saliva collection** for analysis

Sequencing all genes of the Disease Prevention Panel using **next-generation sequencing**

Analysis and interpretation of the sequencing data

Preparation of a **comprehensive** and **easy-to-understand medical report** with an interpretation of the findings and recommendations

Final **specialist discussion** of the findings and **recommendations** of the detailed medical report

Gene List

The individual modules of CeGaT's Disease Prevention Panel contain genes that have been scientifically confirmed as risk genes and pose a risk of disease that can be reduced by timely detection or adequate prevention. The compilation of genes is based on the recommendations of the American College of Medical Genetics and Genomics (ACMG) and has been supplemented by our specialists with other known risk genes.

Tumor Diseases

(Module 01, 51 Genes)

APC, ATM, AXIN2, BAP1, BARD1, BMPR1A, BRCA1, BRCA2, BRIP1, CDC73, CDH1, CDKN2A, CHEK2, DICER1, EPCAM, FH, FLCN, KIT, MEN1, MET, MLH1, MSH2, MSH6, NF1, NF2, PALB2, PDGFRA, PMS2, POLD1, POLE, PTCH1, PTEN, RAD51C, RAD51D, RB1, RET, SDHA, SDHAF2, SDHB, SDHC, SDHD, SMAD4, SMARCA4, SMARCB1, STK11, TMEM127, TP53, TSC1, TSC2, VHL, WT1

Cardiovascular Diseases

(Module 02, 55 Genes)

ACTA2, ACTC1, ACVRL1, ALPK3, BAG3, BMPR2, CALM1, CALM2, CALM3, CASQ2, COL3A1, DES, DSC2, DSG2, DSP, EMD, ENG, FBN1, FHL1, FLNC, GDF2, JUP, KCNH2, KCNK3, KCNQ1, LAMP2, LMNA, LOX, MYBPC3, MYH11, MYH7, MYL2, MYL3, MYLK, PKP2, PLN, PRKAG2, PRKG1, RBM20, RYR2, SCN5A, SMAD3, SMAD9, TBX4, TECRL, TGFB2, TGFBR1, TGFBR2, TMEM43, TNNC1, TNNI3, TNNT2, TPM1, TTN, TTR

Thrombosis and Coagulation Disorders

(Module 03, 28 Genes)

ADAMTS13, F10, F11, F12, F13A1, F13B, F2, F5, F7, F8 (intronic inversions not covered), *F9, GFI1B, GP1BA, GP1BB, GP6, GP9, HRG, ITGA2B, ITGB3, LMAN1, MCFD2, NBEAL2, PROC, PROS1, SERPINC1, SERPIND1, SERPINF2, VWF*

Iron and Copper Storage Disorders

(Module 04, 8 Genes)

ATP7B, CP, GLRX5, HAMP, HFE, HJV, SLC40A1, TFR2

Hypercholesterolaemia

(Module 05, 4 Genes)

APOB, LDLR, LDLRAP1, PCSK9

Glaucoma

(Module 06, 2 Genes)

CYP1B1, MYOC

Malignant Hyperthermia

(Module 07, 2 Genes)

CACNA1S, RYR1

Pharmacogenetics*

(Module 08, 22 Genes)

ABCG2, CACNA1S, CYP2B6, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, CYP4F2, DPYD, G6PD, HLA-A, HLA-B, IFNL3, MT-RNR1, NUDT15, POR, RYR1, SLCO1B1, TPMT, UGT1A1, VKORC1

Familial Diabetes

(Module 09, 5 Genes)

GCK, HNF1A, HNF1B, HNF4A, PDX1

* Relevant variants according to CPIC (Clinical Pharmacogenetics Implementation Consortium) and DPWG (Dutch Pharmacogenetics Working Group)

Quality Made in Germany

- Comprehensive and easy-to-understand medical report with an interpretation of the findings and recommendations
- Prepared by an interdisciplinary team of scientists and medical doctors specialized in human genetics
- In-house optimized design based on the latest clinical research
- Excellent price-performance-quality ratio

Sample Requirements and Order Form

Sample Requirements

Our standard sample requirements are 1-2 ml EDTA blood. We also accept a variety of different materials, such as DBS cards, buccal swabs, saliva, or isolated DNA.

Order Form

1 Patient details

Name, date of birth, sample material, ...

2 Declaration of consent

The declaration of consent should be read carefully, and the relevant items should be marked with a cross. The form is then signed by the patient and the ordering physician.

3 Referring physician information

The name and details of the qualified physician are indicated here.

4 Family history/pre-existing conditions

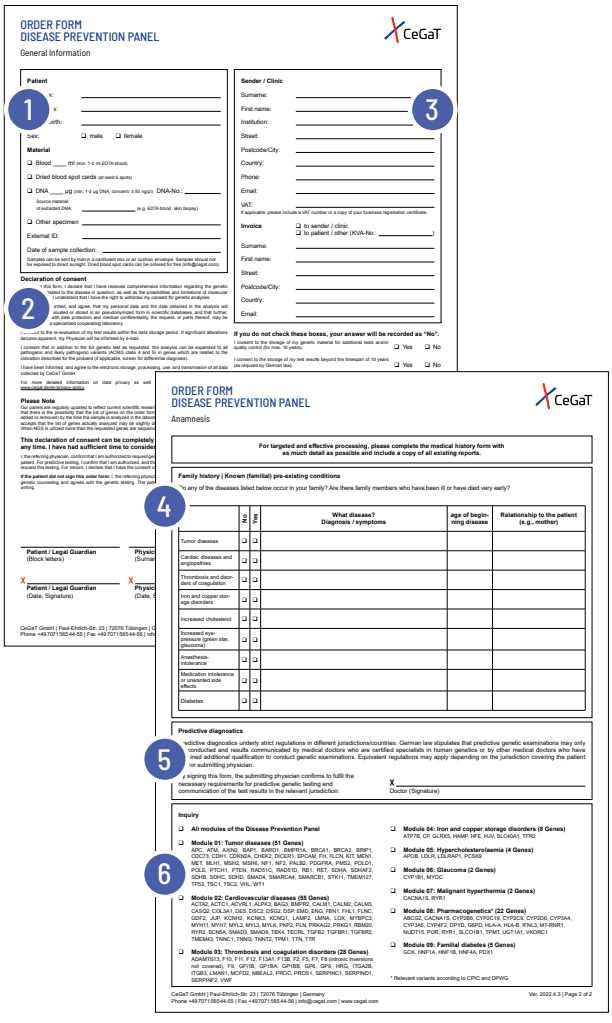
To accurately interpret the results, we need to know of any pre-existing conditions that the patient or their relatives suffer from.

5 Signature of physician

In addition to (2), the submitting physician confirms that the patient received the necessary genetic counseling.

6 Inquiry

The patient decides whether all or just some modules of the Disease Prevention Panel will be carried out. The medical report only comprises the selected modules.


ORDER FORM
DISEASE PREVENTION PANEL
General Information
CeGaT
1
2
3
Patient
Sender / Clinic
Material
Declaration of consent
Please Note
Patient / Legal Guardian (Block letters)
Patient / Legal Guardian (Date, Signature)
ORDER FORM
DISEASE PREVENTION PANEL
Anamnesis
CeGaT
For targeted and effective processing, please complete the medical history form with as much detail as possible and include a copy of all existing reports.
4
Family history | Known (familial) pre-existing conditions
Are any of the diseases listed below occur in your family? Are there family members who have been ill or have died very early?
No
Yes
What disease? Diagnosis / symptoms
age of beginning disease
Relationship to the patient (e.g., mother)
Tumor diseases
Cardiac diseases and angiopathies
Thrombosis and disorders of coagulation
Iron and copper storage disorders
Increased cholesterol
Increased eye-pressure (green star, glaucoma)
Anesthesia-intolerance
Medication intolerance or unwanted side effects
Diabetes
5
Predictive diagnostics
Doctor (Signature)
6
Inquiry
All modules of the Disease Prevention Panel
Module 01: Tumor diseases (51 Genes)
Module 02: Cardiovascular diseases (55 Genes)
Module 03: Thrombosis and coagulation disorders (28 Genes)
Module 04: Iron and copper storage disorders (8 Genes)
Module 05: Hypercholesterolaemia (4 Genes)
Module 06: Glaucoma (2 Genes)
Module 07: Malignant hyperthermia (2 Genes)
Module 08: Pharmacogenetics* (22 Genes)
Module 09: Familial diabetes (5 Genes)
* Relevant variants according to CPIC and DPWG

Do You Need Help?

We are on hand to answer questions and give advice.

Phone: +49 7071 56544-238

Email: prevention@cegat.com

Medical Report

The medical report summarizes the results of the investigation. It is structured as follows:

1 Patient information

The header contains the supplied patient information:

- Name, date of birth, sex, patient ID
- Sample receipt date, sample material, report date

2 Summary of results

The first page of the report contains a table summarizing the results from all analyzed modules of the Disease Prevention Panel. The table shows at a glance which genetic changes were identified.

3 Results

All genetic variants that indicate a disease risk are listed in this section. The type of inheritance, population frequency, and pathogenicity of each variant are also listed in the table. Additionally, the identified risk genes are discussed. The following information is provided:

- The function of the healthy gene
- Diseases that can be triggered by changes in each detected gene

In addition, we evaluate the effects and severity of the disease-causing variants

4 Genetic relevance of the results

This section explains the inheritance pattern of the genetic changes and the probability that family members will be affected.

5 Recommendation

Here you will find specific recommendations for the patient. Examples are:

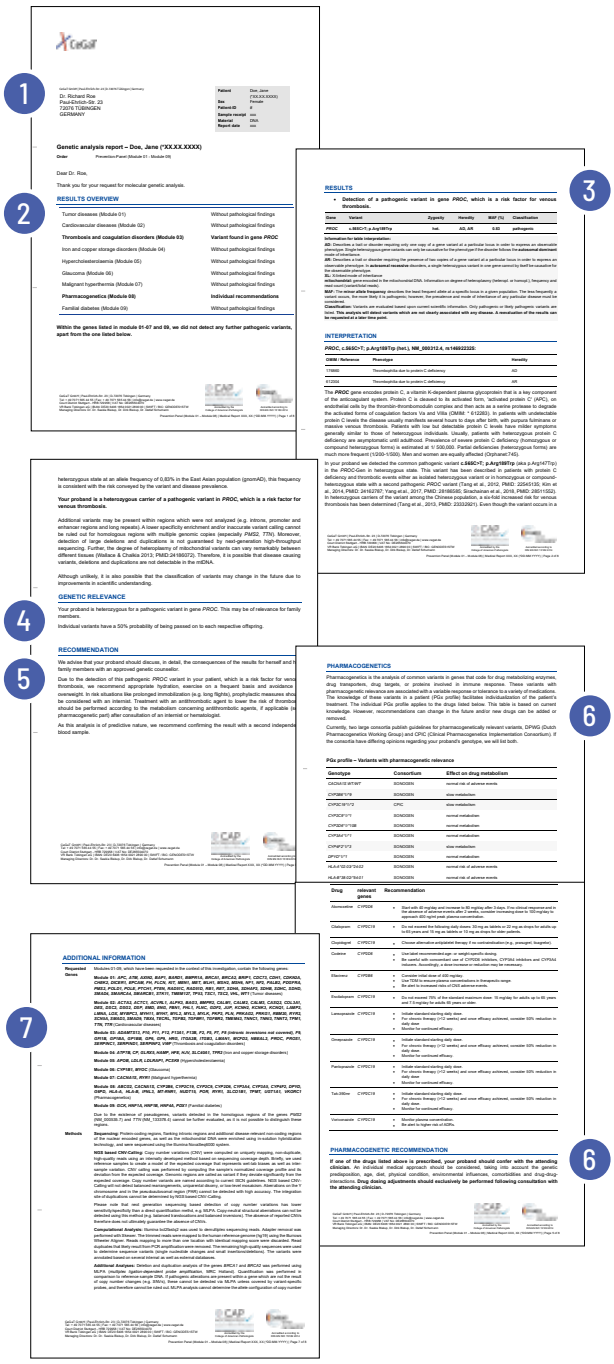
- Consultation with a specialized physician and targeted clinical examinations
- Adjusted screening
- Lifestyle adaptation

6 Pharmacogenetics and pharmacogenetic recommendations

This section describes the pharmacogenetic profile of the patient. It explains how active ingredients are processed in the body and the potential negative effects. Listed are the effects of the pharmacogenetic profile on drug metabolism, the active ingredients involved, and detailed dosing recommendations. Drug dosing adjustments should be exclusively performed following consultation with the treating physician.

7 Additional information

Technical information is provided at the end of the report. This includes the list of investigated genes and the methods used for analysis.



About Us

CeGaT is a global provider of genetic analyses for a wide range of medical, research, and pharmaceutical applications.

Founded in 2009 in Tübingen, Germany, the company combines state-of-the-art sequencing technology with medical expertise – with the aim of identifying the genetic causes of diseases and supporting patient care.

For researchers and pharmaceutical companies, CeGaT offers a broad portfolio of sequencing services and tumor analyses. CeGaT generates the data basis for clinical studies and medical innovations and drives science forward with its own insights.

The owner-managed company stands for independence, comprehensive personal customer service, and outstanding quality. CeGaT's laboratory is accredited according to CAP/CLIA, DIN EN ISO 15189, DIN EN ISO/IEC 17025, and thus meets the highest international standards.

DAkkS Deutsche Akkreditierungsstelle D-ML-13206-01-00

Accredited by DAkkS according to DIN EN ISO 15189:2014

CAP ACCREDITED
COLLEGE of AMERICAN PATHOLOGISTS

CLIA CERTIFIED ID: 99D2130225

Are You Interested?

We Look Forward to Hearing from You.

Contact us via email at **prevention@cegat.com** or call us at **+49 7071 565 44-238**. We will be glad to send you further information about our preventive care offer.

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