İNTERGEN | Genetics and Rare Diseases Diagnosis Center

Health for **Human,**
Science for **Health!**

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İntergen International Services Information Booklet

İNTERGEN Genetics and Rare Diseases Diagnosis Center

What Services Does İntergen Provide?

1- Clinical Consultation

- Patients with undiagnosed conditions
- Patients requiring confirmation of diagnosis
- Patients who have received an incorrect diagnosis
- Patients experiencing side effects during medical treatment
- Patients who have not responded to treatment or have relapsed after treatment
- All chronic diseases
- Rheumatological diseases
- Infertility (inability to have children)
- Pregnancy-related problems
- Epilepsy (seizures)
- Diabetes
- Obesity
- Immune system disorders
- Identification of individuals with a history of or risk for severe COVID-19
- Chronic pain
- Familial cancer
- Chronic anemia

2- Pregnancy Losses – High-Risk Pregnancies

- Stillbirth
- Recurrent pregnancy loss
- History of birth with anomalies

3- Prenatal Diagnosis

- Ultrasound anomalies – Genetic testing and counseling
- Positive family history
- Positive screening test – first trimester/quadruple screening/NIPT

4- NIPT (Non-Invasive Prenatal Testing)

- Aneuploidy (presence of extra or missing chromosomes)
- Microdeletion/microduplication
- Risk of uniparental disomy

5- Preimplantation Genetic Testing (PGT)

All families planning in vitro fertilization (IVF) should consult a genetic specialist before starting procedures.

6- Long-Read Whole Genome Sequencing (LRS)

The most advanced technology in the world for genomic studies in undiagnosed diseases.

7- Whole Exome Sequencing (WES)

8- Whole Genome Sequencing (WGS)

9- Cancer Genetic Testing

All cancer patients should consult a genetic specialist for treatment planning, family screening, and evaluation of additional risks.

- Cancer diagnosis and subtype determination
- Cancer drug selection tests – Pharmacogenetics
- Cancer monitoring – Minimal residual disease
- Familial cancer history

10- Personalized Medicine

- Definitive diagnosis – Detailed differential diagnosis
- Subtyping of diseases
- Multifactorial disease analysis
- Adverse effect risk assessment
- Pharmacogenetic analysis – Drug selection and dose adjustment

11- Preventive Medicine

- Screening tests
- Cancer risk analysis
- Pharmacogenetic analysis
- Accident and trauma risk analysis
- Pre-pregnancy and pre-marital risk assessment
- Colorectal Cancer Screening
- Liver Cancer Screening

12- Newborn Risk Analysis

- High-risk newborn – Urgent analysis
- Apparently healthy newborn – Risk analysis

13- Pre-Marital and Pre-Pregnancy Screening Tests

- Risk assessment for consanguineous marriages
- Risk assessment for non-consanguineous couples
- Screening for common diseases

14- Infertility

15- Pharmacogenetics

16- HLA Testing

- Organ and tissue transplantation
- HLA-based diagnostic tests (celiac disease, HLA B5, B27, B51, and others)

17- Histopathological Tests and Immunohistochemistry

- Conventional pathological examinations
- Smear
- Immunohistochemical analyses
- Consultation
- Cancer tests (PD-L1, etc.)

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Which Test When Is It Recommended?

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Whole Exome Sequencing (WES)

Whole Exome Sequencing (WES) is a next-generation sequencing (NGS) technique widely used both globally and in our country, which involves sequencing the protein-coding regions of the genome (exons). Exome sequencing includes all DNA segments responsible for protein production in humans. Although the human exome represents less than 2% of the entire genome, it contains approximately 85% of the variants associated with known human diseases.
Exome sequencing is performed to detect variants present in exons. It is a technique used to determine the sequence of DNA in an individual's genetic code and to identify genetic disorders.

What Does Whole Exome Sequencing (WES) Provide?
Preventive Medicine: It allows the assessment of risks for diseases that may develop later in life or emerge under stressful conditions such as trauma. In some cases, diseases can be prevented before they occur. In other cases, this information may guide the correct treatment approach or help prevent adverse drug reactions. (e.g., familial cancers, bleeding disorders)
Carrier Screening: Pre-marital and pre-pregnancy screening enables the identification of genetic conditions carried by couples, significantly reducing the risk of having an affected child.
It is considered one of the gold standards of expanded newborn screening and is being discussed for implementation in all newborns.
Cancer Research: The lifetime risk of cancer is approximately 40%, with slight differences between males and females. About 10% of these cases are familial. This means that approximately 4% of the population has familial cancer (0.40 × 0.1). The rate is higher in individuals with a positive family history. Therefore, while it is essential to investigate individuals with a family history of cancer, it is also reasonable to evaluate familial cancer genes in those without such a history.
It is recommended to analyze approximately 200 genes associated with cancer and around 600 candidate genes. Monitoring familial cancers reduces risk, and treatment strategies differ in such cases. For cancer prevention and in every cancer case, familial cancer screening should be performed. The cost of limited screening (e.g., BRCA1-2) is similar to that of broader panel testing.

Whole Genome Sequencing (WGS)

Whole Genome Sequencing (WGS) is a DNA sequencing technique that determines the complete genetic material of an organism, meaning its entire genome. This technique aims to identify the full DNA sequence of an individual or organism.
In recent years, this method has begun to be used in the diagnosis of diseases and in research for identifying genetic variants. In addition to patients who cannot be diagnosed through exome sequencing, genome sequencing is particularly used to determine drug sensitivities and to perform haplotype analyses.

In Which Diseases/Conditions Is Whole Genome Sequencing (WGS) Used?
Monogenic Diseases: WGS is an effective tool in diagnosing genetic diseases caused by a mutation in a single gene. It is especially used to identify and understand the causes of rare genetic disorders.
Cancer: Genomic analysis of cancer cells can be performed using WGS. This can be used to determine familial cancer risks, identify cancer types, detect potential therapeutic targets, and personalize treatment strategies.
Genetic Variants and Polymorphisms: WGS is effective in identifying numerous mild variants and carrier states in individuals. When evaluated together with genetic polymorphisms, it enables the determination of risk scores for many diseases. It can provide solutions for multifactorial diseases and conditions with unclear etiology.
Carrier Status: WGS is an important tool for identifying genetic diseases that an individual may carry. This information allows for early diagnosis of diseases that may appear later in life and enables planning before marriage or having children.
Genomic Regions with Rearrangements: WGS can effectively detect large-scale changes in genetic structure, such as structural variations, chromosomal alterations, and translocations. (Long-read whole genome sequencing has a higher detection rate for these changes.)
Pharmacogenetic Applications: WGS can be used to identify genetic factors that influence drug metabolism. This plays a crucial role in personalized medicine applications.

Long-Read Whole Genome Sequencing (LRS)

Long-read whole genome analysis is the most advanced technology that enables access to an individual's entire genetic information by reading long DNA fragments. This method can directly read DNA sequences ranging from 10,000 to 100,000 base pairs in length and covers nearly the entire genome. It is expected to replace other technologies in the near future.

- Detection of complex variants that cannot be identified by standard WGS/WES
- Identification of genomic rearrangements and translocations
- Clarification of rare or uncertain genetic findings
- Diagnosis of previously undiagnosed diseases
- Evaluation of methylation disorders

Today, sequencing individuals' genetic data and determining clinically significant disease risks is increasingly recommended. During the initial evaluation, certain carrier states and risk factors that should be assessed in everyone are identified and reported. As individuals age, newly emerging clinical findings can be re-evaluated in light of existing genetic data.

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BabySEQ (NIPT)

BabySEQ, a Non-Invasive Prenatal Testing (NIPT) method, is a next-generation screening test that analyzes fetal DNA using only a maternal blood sample, without requiring any invasive procedures. It screens for chromosomal aneuploidies such as Down Syndrome and Trisomy 13, as well as smaller but clinically significant alterations known as microdeletions and microduplications. BabySEQ is based on shotgun whole genome sequencing technology. There are four different BabySEQ panels available.

	BabySEQ BASIC PANEL	BabySEQ EXPANDED PANEL	BabySEQ RARE	BabySEQ XL
Common Aneuploidies (T21, T18, T13, X/Y)	✓	✓	✓	✓
All Other Aneuploidies	✓	✓	✓	✓
Deletion and Duplication Syndromes		✓	✓	✓
Cystic Fibrosis + SMA + Fragile X Carrier Screening			✓	✓
Carrier Screening for 700+ Diseases				✓

Preimplantation Genetic Testing (PGT)

Preimplantation Genetic Testing (PGT) enables the detection of genetic disorders in embryos before they are transferred to the uterus and allows the selection of healthy embryos that do not carry these disorders. Commonly described as “eliminating bad genes,” the actual process works as follows: genetic testing is performed on biopsies taken from all embryos to determine which embryo is healthy, and only that embryo is transferred. No treatment is applied to the embryo. Today, it is not legally permitted worldwide to treat embryos or even conduct research on embryos that will not be used. However, rapid advancements in genetic science may change this situation in the near future, and embryo-based treatments may become a topic of discussion.

In vitro fertilization (IVF) combined with PGT is a highly effective and successful method for helping families have healthy babies when indications are correctly determined. If there is a known genetic disease in the family, planning can be made specifically for that condition. However, with current technologies, if a family is considering PGT for any disease, they should обязательно consult a genetic specialist beforehand. Comprehensive genetic screening of both partners, along with the identification of risks for other genetic conditions within the family, and evaluating these in embryos, can significantly reduce the likelihood of having a child with a genetic disorder.

It should not be forgotten that natural conception is always the preferred and healthiest process from a medical perspective. It is not appropriate to pursue IVF solely to achieve a “healthier” pregnancy when there is no medical indication. Every pregnancy carries certain risks. No center can guarantee that a baby will be born 100% healthy, and the same applies to IVF pregnancies. However, advanced prenatal follow-up methods, detailed screening during pregnancy, and preconception screening of parents can significantly reduce the risk of disease in the baby.

Genetic Approach to Infertility

What is Infertility?

Infertility is defined as the inability to achieve pregnancy within 12 months despite regular, unprotected sexual intercourse.
In women over the age of 35, this period is considered as 6 months.
Infertility may result from problems in either the female or the male partner, and genetic factors play a significant role among the causes of infertility. It is a condition that can arise from many different factors and may present with various clinical manifestations, ranging from impaired sperm production to decreased ovarian reserve and premature menopause, from recurrent pregnancy loss to repeated IVF failures.
Certain genetic variants carried by partners can affect embryo formation, implantation, and placental development, ultimately preventing couples from having children.

Why is Genetic Evaluation Performed?

Genetic testing is performed to clarify the cause of infertility, determine treatment approaches based on the underlying cause, and guide families toward the most appropriate method to achieve pregnancy and have a healthy baby.
Each individual has a unique genetic makeup. Even identical twins do not have completely identical genetic structures. Since genetic differences exist among individuals, treatments should also be personalized to improve success rates. This approach is known as “personalized medicine.”
Therefore, identifying genetic predispositions, underlying conditions, and potential responses to medications before starting treatment can significantly increase treatment success.

Who Should Undergo Genetic Testing?

In men, genetic testing is recommended in cases of azoospermia, severe oligozoospermia (very low sperm count), or a high rate of abnormal sperm (morphology disorder), as well as in the presence of delayed puberty, small testes, or gynecomastia. In women, it is recommended in cases of premature ovarian insufficiency or early menopause and menstrual irregularities. Additionally, genetic evaluation should be considered if there is a history of infertility in the family, the presence of any genetic disease in the family, delayed puberty, small testes, or gynecomastia, a history of pregnancy loss, unsuccessful IVF attempts, a history of pregnancy or a child with a genetic anomaly, or consanguinity between partners. In all of these situations, couples should receive genetic counseling and appropriate tests should be planned.

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Autism and Genetics

"Autism is not a disease diagnosis. It is a finding that results from many different conditions. There is sometimes a single underlying cause, but more often multiple factors are involved. Identifying the underlying causes can provide treatment recommendations that directly impact the lives of the child and, consequently, their families. Today, 'personalized medicine' is being discussed across all diseases. No patient is the same as another. We have approximately 20,000 genes, and variations in these genes lead to our individual differences and predispositions to certain diseases. If we are all different, then our treatment outcomes will also differ. Determining these differences is extremely valuable."
In children with autism, identifying the underlying mechanisms through these gene panels can significantly improve treatment success.

Gluten Sensitivity

Individuals who experience discomfort after consuming gluten should be evaluated genetically. It presents quite differently from celiac disease. Antibody tests and intestinal biopsy results may not be abnormal. It is important for individuals showing signs of gluten-related disorders to undergo genetic testing and adjust their diet accordingly. Dietary and lifestyle changes can help manage symptoms and prevent disease progression.
This condition, which can present with very different findings in each individual, can significantly affect quality of life and may lead to irreversible problems in later years. In some individuals, symptoms such as diarrhea, constipation, frequent bowel movements (more than 2–3 times per day), and gas complaints may be prominent, while in others, skin manifestations may be more noticeable (such as itching, small blisters, redness, and rashes). In some individuals, migraine may be the most prominent symptom. In others, persistent fatigue and waking up tired may be the main complaint.
Genetic counseling is strongly recommended.

Genetic Panels for Athletes

When athletes and individuals who actively engage in sports carry certain "genetic predispositions," especially if they participate in high-performance sports, they may encounter problems that can lead to much more serious health issues than minor injuries. According to current scientific data, certain variants present in more than 2,000 genes, which affect the functioning speed of genes, are known to be associated with serious injuries and even the risk of sudden death.

In studies conducted to understand and prevent the causes of injuries and sudden deaths during sports, our knowledge about genetic risk factors that may lead to injuries or sudden death in adults is increasing exponentially day by day. A significant portion of these risk factors are variants in genes associated with heart muscle and cardiac rhythm disorders, connective tissue diseases, bleeding and clotting disorders, immune system diseases, brain and nervous system disorders, or metabolic diseases. Although individuals with personal or family history of these conditions are at higher risk, genetic risks can also be identified in people with no family history or clinical symptoms. For this reason, genetic screening has become increasingly important for both professional and amateur athletes to ensure safe and healthy participation in sports.

As a result, today, gene mutations that may cause death or injury during sports activities in athletes and active individuals can be easily detected with the advancement of genetic technologies. Knowing genetic predispositions has become an important step in taking preventive measures to ensure athlete health and safety.

Pregnarisk – Pre-Marital and Pre-Pregnancy Genetic Risk Assessment

What is Pregnarisk? When Should It Be Performed?
Are Genetic Diseases Destiny?
There are approximately 20,000 protein-coding genes in the human genome. In all of us, there are genetic variations in these genes that may cause carrier states for certain diseases. For autosomal recessive genetic diseases, both partners being carriers; for X-linked diseases, the woman being a carrier; and for autosomal dominant diseases, the presence of a disease-associated genetic variation in one of the partners can create risks for their children.
Especially in consanguineous marriages, the risks are significantly increased due to shared genes and genetic carrier states between partners. While the risk is much higher in close consanguineous marriages, even marriages within the same or nearby villages can increase the risk of having a child with a genetic disease due to genetic similarities. With the use of expanded gene panels, it is possible to detect these genetic variations associated with disease risks.
Families who think, "I want to undergo all tests that can identify potential genetic disease risks in my baby before pregnancy," should be informed about these panels. Identifying risks before pregnancy makes it possible to take preventive measures; therefore, informing families during the preconception period is of great importance.
Even in the absence of consanguinity between partners, common carrier states in the population may still pose risks for their children. In addition, for dominant diseases, some genetic variations present in parents may not affect them but can cause health problems in their children. Detecting these is also important. Furthermore, if a mother carries a pathogenic variant in genes located on the X chromosome, there is a 50% risk of disease in male offspring, even though the mother is usually asymptomatic.
In summary, all couples planning to have children should be informed about these tests. Although risks cannot be completely eliminated due to technical limitations of current methods and the possibility of new (de novo) genetic mutations occurring in the child, these tests can identify a large proportion of parental risks, allowing preventive measures to be taken and reducing the likelihood of these diseases.

What Tests Can Be Performed Before Pregnancy to Ensure a Healthy Baby?

1. Couples can be screened for carrier states of diseases that are very common in the population, have severe clinical outcomes, or are life-threatening. (PregnaRisk Panel 1) Compared to expanded panels, this evaluates a more limited number of genes to determine whether there are any changes that may pose a risk for the baby.
2. Couples can also undergo expanded gene panel testing to assess carrier status for approximately 8,000 known diseases (PregnaRisk Panel 3). Based on the results, genetic counseling can be provided to guide the planning of pregnancy.

lifemap

Every individual is unique. Even identical twins do not have exactly the same genetic structure. Twins are born with more than 100 differences arising from mitochondrial inheritance from the mother, epigenetic influences, or newly developed variants in that individual. These differences continue to increase throughout life. In other words, there is no one exactly like us, and our genetic code is the most fundamental map that defines who we are.

Although this map should serve as our primary guide in the diagnosis and treatment of diseases, it has remained unread and silent until now. One of the main reasons for this is the difficulty of accessibility, and another is the lack of awareness about this subject. In many panels developed so far and presented as “genetic check-ups,” only certain “known” variants in selected genes are included, typically analyzing 200–300 variants, and interpretations are made based on these results. Panels that provide recommendations such as “What should we avoid eating?” or “How much exercise should we do?” do have an impact on people’s lives.

We scientifically support making recommendations that improve an individual’s quality of life, whether or not they are directly related to the test results. If, after a test, you are advised to stay active and maintain a healthy diet, this will positively affect your life regardless of which test you have taken. However, such data can only reflect a very small portion of your life map.

If each of us is truly unique, then both our predisposition to diseases and our responses to medications will also differ from others. Yet, in practice, nearly everyone who becomes ill is given the same medications at the same doses. Personalized and preventive medicine is now possible. Genetic knowledge has significantly advanced in helping us understand what we should pay attention to in order to live longer, maintain quality of life, and age well, as well as identifying conditions we often accept as part of aging but that limit our independence.

These data cannot be generated by every system, and more importantly, generating and interpreting such data requires time. Therefore, producing and securely storing these data while an individual is still healthy has become an urgent need. This allows immediate access to all genetic data without delay in cases of emergency, accidents, or when a new diagnosis is made.

Lifemap has been designed to make this previously unread and silent map visible. Its goal is to transform complex and extensive genetic data into a clear, meaningful, and actionable format, and to establish a comprehensive system that goes beyond a simple genetic test by integrating personalized risk analysis, counseling, and re-analysis services. Rather than functioning as a conventional “check-up,” these panels can be positioned as a biological awareness platform.

With the guidance of your genetic information, Lifemap acts as a compass to help direct your life more accurately—transforming data into awareness, prioritizing knowledge over fear, planning over chance, anticipating risks, and enabling a healthier future. Under the guidance of science and technology, it brings the most advanced methods of personalized medicine to an accessible level for everyone.

Screening panel tests can be performed with different scopes. By consulting with a genetic specialist, you can receive guidance in selecting the most appropriate panel for your needs.

lifescan Colon

Lifescan is a screening test designed for the early detection of colorectal cancer and certain advanced adenomas by analyzing DNA methylation levels of the SDC2 and TFPI2 genes in stool samples. This test aims to detect abnormal methylation changes in DNA shed from intestinal cells into the stool.

Who is this test suitable for?

Colonoscopy is recommended for individuals aged 45 and over with average risk. This test should be recommended to all individuals over the age of 45 who are reluctant to undergo colonoscopy, who postpone it, or who have limited access to it.

Patients with positive fecal occult blood (FOB) test: Fecal occult blood tests can be affected by diet and certain medications. Therefore, to increase sensitivity, it is recommended—if feasible—to perform both the FOB test and the methylation test together. If either test result is positive, colonoscopy is recommended.

Pre-test preparation: Fasting, dietary restrictions, or discontinuation of medications are not required. However, in cases of severe diarrhea or active hemorrhoid episodes, although the DNA test itself is not affected, the quality of the analysis may be impacted.

Interpretation of results:

Positive result: Does not establish a definitive diagnosis of cancer. Lifescan is a highly reliable screening test. Colonoscopy and/or evaluation by a specialist physician is recommended.

Negative result: Follow-up or alternative screening methods may be planned according to clinical risk factors and physician recommendation. In the literature, it is recommended to repeat the test every 1–3 years. The screening interval should be determined by your physician, as each individual’s risk factors and family history are different.

lifescan Liver

Hepatocellular carcinoma (HCC) is one of the six most common cancers worldwide and typically ranks third among cancer-related deaths. Due to its high prevalence among liver cancers and its high mortality rate, early diagnosis and screening are of great importance, especially in individuals at risk such as those with cirrhosis or hepatitis carriers. When liver cancer is detected at an early stage, curative treatment options (surgery, ablation, transplantation) become possible, and survival rates increase significantly. Therefore, effective screening methods are particularly important for at-risk individuals.

Lifescan Liver is a blood test that aims to qualitatively detect DNA methylation of the GNB4 and RIPLET genes associated with hepatocellular carcinoma in circulating cell-free DNA (cfDNA).

Who should take this test?

The Lifescan Liver test is particularly suitable for individuals in the following risk groups:

- Individuals with chronic hepatitis B or C infection
- Patients with liver cirrhosis
- Individuals with advanced liver fibrosis
- Individuals with non-alcoholic fatty liver disease (NAFLD / NASH)
- Individuals with type 2 diabetes accompanied by liver disease
- Individuals with a history of long-term and heavy alcohol use
- Individuals with a family history of liver cancer

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Genetic Testing in Cancer

The TMB Panel is performed using the NGS method and includes the analysis of single nucleotide variants (SNVs), copy number variations (CNVs), and gene fusions. Within this panel, Tumor Mutational Burden (TMB), MSI, and PD-L1 are also evaluated. The report includes drug-related information based on the variants detected in the patient, as well as pharmacogenetic data (drug resistance, sensitivity, and toxicity). In addition to smart drug selection, sensitivity, resistance, and side effect evaluations for chemotherapeutic agents are also performed.
The Tumor Mutational Burden (TMB) test is used to measure the number of genetic mutations in cancer cells. The number of genetic mutations in cancer cells is associated with increased recognition by the immune system, which may result in a better response to immunotherapy.

The MSI (Microsatellite Instability) test detects genetic changes resulting from defects in DNA repair mechanisms. Microsatellites are short, repetitive DNA sequences. Normally, cells repair errors in these regions. However, when DNA repair systems fail, mutations accumulate in these repetitive regions, leading to microsatellite instability. MSI is most commonly associated with colorectal cancer but is also observed in many other cancer types. This test helps determine treatment options and is particularly important for planning targeted therapies such as immunotherapy.
Genetic changes have now become critically important in the diagnosis and treatment of cancer patients. There is a common misconception that genetic testing is only performed abroad and is difficult to access. However, cancer genetic tests are widely available in many public and private centers in our country. When a genetic cause is identified, it can have a highly positive impact on treatment decisions and outcomes.

What is RNASEQ?
RNA sequencing (RNASEQ) is a technology that enables the sequencing of all RNA molecules expressed in a cell at a given time and allows quantitative comparisons based on specific parameters. Compared to DNA-based data, RNA-based studies provide insights into the dynamic structure of the cell and ongoing biological processes. RNA sequencing has now become an integral part of both routine diagnostics and research.

It is routinely used in the diagnosis, treatment, and prognosis of leukemia and lymphoma. In these diseases, RNA sequencing can identify not only known gene fusions but also novel immunotherapy candidate genes, as well as genes and variants that may influence prognosis and follow-up. Particularly in cases with unclear diagnosis, unexpected clinical course, lack of response to treatment, or complications during treatment, RNA sequencing can provide highly successful outcomes.

Familial Cancers
Approximately 10% of all cancers are associated with hereditary cancer predisposition syndromes. In individuals with familial cancer predisposition, treatment options and preventive strategies differ. Other family members are also at risk in such cases. Therefore, identifying familial cancer is crucial both for guiding treatment and for protecting other family members.

It is important to perform genetic testing in all individuals diagnosed with cancer, whether they are currently undergoing treatment or have had cancer in the past. Additionally, individuals with a family history of cancer may undergo these tests to reduce their own cancer risk.

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