Diagnostics Technologies 2009

NZOZ BioTe21

Genetic Diagnostics Unit

Jagiellonian Center of Innovation, room 6

Gronostajowa 7
30-387 Krakow

DEAR CUSTOMERS!

The BioTe21 laboratory was established as a result of implementation of the project co-funded by the European Regional Development Fund and 3.4 Integrated Regional Development Operational Program. It is located at the **Department of Biochemistry, Biophysics and Biotechnology of Jagiellonian University** at Gronostajowa 7 street in Krakow. Following specialized units are located in the BioTe21 laboratory:

- Genetic Identification unit,
- Genetic Diagnostics unit,
- Novel Biotechnologies unit,
- Nucleic Acid Sequencing and Synthesis unit.

OUR MISSION

The BioTe21 goal is to create technological and scientific foundation for development of state of the art bioinformatics and biotechnology techniques along with their implementation into the molecular medicine and PREVENTIVE GENETICS fields. The BioTe21 provides wide range of routine both and specialized services. This includes DNA synthesis and sequencing, genetic engineering, molecular diagnostic, genetic identification including paternity testing. Current progress in genetics and biochemistry fields results in generation of novel laboratory techniques. The BioTe21 provides services in translational research, bringing forth those pioneering discoveries at the forefront of medicine and biotechnology.

CREDIBILITY

The BioTe21 facility is certified by GEDNAP that attests credibility of genetic analysis. Moreover the laboratory has the NZOZ status and is officially recognized by National Council of Laboratory Diagnosticians. Analytical procedures performed in the facility are in accordance with analytical laboratory guidelines and certified according to PN-EN ISO/IEC 17025:2005/Ap1.

Moreover experience of our employees in biochemistry, biotechnology, genetics and molecular medicine guarantee high quality of performed tests and authenticity of their results. We are the only laboratory in Poland cooperating with NCBI's GeneTests database. We are also members of the prestigious international Gendia network, which associates the most innovative genetic laboratories in the world.

Dear Customer, considering your curiosity in provided services and medical expertise we would like to present you a brief list of our services endorsed by the current scientific knowledge.

Our experts will be happy to answer all your further questions.

PREVENTIVE MOLECULAR MEDICICE CUSTOMIZED TO YOUR GENETIC PROFILE!

DISEASE	OMIM™	Test denotation	Examined Gene	OMIM™	Mutations tested - range	Methodology, analytical sensitivity and specificity	Specimen required	Reported	UNIT PRICE gross [PLN]
ALZHEIMER DISEASE 	**Disease:** Alzheimer's disease is most common form of dementia. This disease leading to a degeneration of the brain tissue as a result of amyloid-beta protein deposition in the brain. The main symptoms are: progressing memory lapses, speech difficulties, irritations, difficulties focusing one's attention and dealing with even the simplest issues of everyday life often accompanied by depression. Polymorphisms of apolipoprotein E; the subtypes E2, E3, and E4; have been associated with hyperlipidaemia and Alzheimer disease. **Genetics:**The APOE gene consists of 3 exons. Preapolipoprotein E is the result translation. It contains 317 amino acids. 18 amino acids will be cleaved off the N-terminal end during secretion. The mature peptide contains exon 3 and partly exons 2 codons. Physiologically relevant is the receptor ligand coded in exon 3. Apolipoprotein E mutations can be found throughout the world. The most frequencies are: wildtype E3 then E2 and E4 10%. The apoE4 form of the gene has been associated with increased risk of Alzheimer's disease. The frequency of the apoE4 version of the gene in the general population varies, but is always less than 30% and frequently 8%-15%. Persons with one copy of the E4 gene usually have about a two to three fold increased risk of developing Alzheimer's disease. Persons with two copies of the E4 gene (usually around 1% of the population) have about a nine-fold increase in risk. Nonetheless, even persons with two copies of the E4 gene don't always get Alzheimer's disease. At least one copy of the E4 gene is found in 40% of patients with sporadic or late-onset Alzheimer's disease. **Indications:** 1) The test identifying the forms of the ApoE gene should be taken mainly by children, siblings relatives of people diagnosed with or suspected Alzheimer's disease, arteriosclerosis and strokes 2) People who have high blood pressure (hypertension), coronary artery disease, diabetes, and possibly elevated blood cholesterol. 3) Smokers carrying mutation in ApoE gene, In that case smoking is an additional environmental factor accelerating the disease progression. 4) Overweight people.								
ALZHEIMER DISEASE	104310	**APOE** ***Codons: 112, 158 145***	***APOE***	107741	Discovering characteristic alleles responsible too Alzheimer's disease and hyperlipoproteinemia type III	Analysis of 3 change SNP-type in double system of control of result certainty (PCR-SNP). Test allow detecting one out of three allele types in both homo- and hetero-zygotic state and detection of additional mutation in codon 145 of *ApoE* gene.	swab	***5***	**390**

SKIN CANCER (MALIGNANT SKIN MELANOMA)

Disease: Melanoma is a malignant tumor of melanocytes which are found predominantly in skin but also in the bowel and the eye. It is one of the rarer types of skin cancer but causes the majority of skin cancer related deaths. Malignant melanoma is a serious type of skin cancer. It is due to uncontrolled growth of pigment cells, called melanocytes. Around 160,000 new cases of melanoma are diagnosed worldwide each year, and it is more frequent in males and Caucasians. It is more common in Caucasian populations living in sunny climates than in other groups. Malignant melanoma accounts for 75% of all deaths associated with skin cancer.

Melanoma (*melanoma malignum*) is one of the most malignant tumors. This cancer originates in melanocytes and is very dangerous and resistant to treatment cancer of the skin, mucous membrane and vascular ocular membrane. In spite of the fact that melanoma accounts for merely 4% of malignant carcinomas, its growth rate, metastasis occurrence and treatment resistance lead to high rate, exceeding 79%, of melanoma related mortality. The risk for developing melanoma is associated with two groups of factors: intrinsic and environmental. The most relevant environmental factor is exposure to UV radiation whereas intrinsic factors depend on inherited genotype. Individuals with Red Hair Color (RHC) phenotype that includes green or blue eye color, clear and red hair color, clear complexion, freckles, hypersensitiveness to sunlight and UV radiation have higher risk of melanoma occurrence.

Genetics: The RHC phenotype together with *MC1R* isoform might increase two folds the risk of melanoma occurrence. Moreover the *MC1R* and*CDKN2A g*enes display interdependence in cancer related processes. At age 58 mutation in *CDKN2A* gene displays 50% penetration, individuals carrying that mutation and two normal alleles of *MC1R* are having 50% chance of melanoma occurrence at age 58. However if mutation in *CDKN2A* gene is presented together with mutation in *MC1R* gene the risk of melanoma is dramatically increased. Individuals carrying both mutations have 84% of chance of melanoma manifestation at age 38

Indications:

1) Individuals who are avid users of sun beds and quartz lamps
2) Individuals without the universal practice in using sun-blocking lotions.
3) Individuals having clear complexion, clear or red hair and green or blue eyes.
4) individuals having difficulties in getting a tan and prone to sunburns (RHC phenotype)
5) Individuals with reported occurrence of the melanoma in relatives
6) Generally all individuals however recently melanoma was manifested at higher frequency in young females,

Patients with diagnosed mutation will be directed to the genetic counselor where they will receive professional advice about the possible preventive or therapeutic approach.

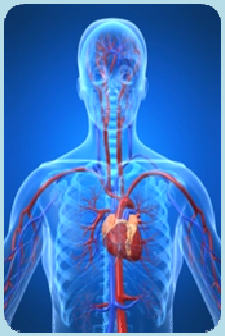
SKIN CANCER (MALIGNANT SKIN MELANOMA) DEPENDENT ON UV - RADIATION	155600	**MC1R-RHC** ***3 mutations***	***MC1R***	155555	Detection of gene variant (allele) responsible for basic genotype RHC, which has an influence on UV-radiation skin cancer predisposition.	Genetic analysis of three basic changes (polymorphism/mutation) in 1 type 1 melanocortin's receptor's gene.	swab	***10***	**440**
SKIN CANCER (MALIGNANT SKIN MELANOMA) DEPENDENT ON UV - RADIATION	155600	**MC1R** ***11-15 mutations***	***MC1R***	155555	Detection of gene variants (allele) responsible for basic genotype RHC and additional mutations increasing risk of dependent on UV - radiation skin cancer.	Genetic analysis of three basic and several other changes (polymorphism / mutation) in of melanocortin's receptor's gene.	swab	***10***	**780**

FAMILIAL MALIGNANT MELANOMA WITH PANCREAS CANCER	606719	**CDKN2A-2** *2 mutations*	***CDKN2A -2***	600160	Detection of basic mutation responsible for familial melanoma with pancreas cancer	Genetic analysis of two basic changes (polymorphism / mutation) in the gene of cyclin-dependent kinase inhibitor 2A.	swab	***10***	**220**
FAMILIAL MALIGNANT MELANOMA WITH PANCREAS CANCER	606719	**CDKN2A** *4-6 mutations*	***CDKN2A-2***	600160	Testing of mutation responsible for familial melanoma with pancreas cancer	Genetic analysis of several changes (polymorphism/mutation) in gene of cyclin-dependent kinase inhibitor 2A.	swab	***10***	**350**
SKIN CANCER (MALIGNANT SKIN MELANOMA) DEPENDENT ON UV - RADIATION AND FAMILIAL MALIGNANT MELANOMA WITH PANCREAS CANCER	155600 +606719	**MC1R+ CDKN2A** *15-21 mutations* *Recommended test!*	***MC1R CDKN2A***	155555	Complex genetic analysis of SNP polymorphism (mutation) in *MC1R* and *CDKN2A* gene, responsible for pronouncement dependent on UV - radiation skin cancer and familial melanoma predisposition.	Test includes all mutations mentioned above.	swab	***15***	**960**
RISK DIAGNOSIS OF THE ESTROGEN DEPENDENT CANCER DEVELOPMENT	**Test description:** Test allows to detect mutations in DNA-repair proteins (BRCA1 and CHEK2) and might determine the risk of cancer development caused by undesirable sex hormones activities. These mutations are responsible for estrogen hypersensitivity and their presence is associated with increased risk of some types of cancer occurrence. This includes breast, ovarian, pancreatic, prostate and colon cancers as well as melanoma cancer. Administration of birth control drugs containing hormonal specimen used by women under 35 are associated with higher frequency of mutations occurrence in genes *BRCA1* and *CHEK2*.Hormonal therapy might increase the risk of cancer development even ten times. **Indications:** 1) individuals administrating hormonal contraceptive therapy 2) females under 35 age of years administrating hormonal contraceptive therapy 3) individuals who want to determine if they have elevated risk of cancer development due to estrogen hypersensitivity								
RISK DIAGNOSIS OF THE ESTROGEN DEPENDENT CANCER DEVELOPMENT		**HTGR**	***BRCA1*** ***CHEK2***	113705 603078	Mutation testing in *BRCA1* and *CHEK2* genes responsible for increased risk of tumor occurence.	Genetic analysis of mutations in *BRCA1*gene: ***4153delA***, ***5382insC***, ***C61G*** and in *CHEK2 gene:* ***1100delC***.	swab	***15***	**315**

HEREDITARY HEMOCHROMATOSIS	**Disease:** Hereditary hemochromatosis is an autosomal recessive disorder of iron metabolism that varies in clinical severity and is one of the most common genetically determined metabolic diseases. Increased iron absorption leads to iron overload of the organs as manifested by liver cirrhosis, hepatocellular carcinoma, cardiomyopathy, arthritis, skin pigmentation and diabetes mellitus. Endocrinological, neurological and psychiatric symptoms may occur. Due to pregnancy, menstruation and nursing, women are much less affected than men. The disease can be treated by repetitive venesections. **Genetics:** Hereditary hemochromatosis is an autosomal recessive disease, i.e. there is a mutation in both parental genes on chromosome 6 (6p21.3). Three mutations (C282Y, H63D, and S65C) have been described in the majority of patients with hemochromatosis. The most common pathogenic mutation is the C282Y mutation in the *HFE* gene causing an amino acid change from cysteine to tyrosine at amino acid position 282. 80 to 90 % of the affected individuals are homozygous for the C282Y mutation. 4-8% of the patients carry different mutations on each of the alleles (compound-heterozygosity for the C282Y and H63D or S65C or Q283P mutations). In around 1% of the affected individuals only the C282Y mutation can be identified, whilst the second mutation is a very rare or yet unknown mutation. Homozygous mutation carriers are at increased risk for the clinical manifestation of hemochromatosis. In these individuals, serum ferritin and transferrin saturation should be screened regularly. Homozygosity for the C282Y mutation is responsible for up to 90% of hemochromatosis patients. Penetrance of C282Y is under debate. Current studies estimate penetrance as 80% for men and 35% for women over 40. Additional studies estimate much lower penetrance for liver disease (~1%).The second mutation (H63D) has been described in some patients when inherited with the C282Y mutation as a compound heterozygote (C282Y/H63D). This genotype, however, has a reduced penetrance of less than 2%. C282Y/ S65C compound heterozygotes have also been reported, but the penetrance of this genotype is not known. It may contribute to a mild form of hemochromatosis. Heterozygotes for C282Y (C282Y/WT), H63D (H63D/WT), or S65C (S65C/WT) are not significantly associated with hemochromatosis, although other undetected mutations in combination with these mutations may contribute to symptoms of hemochromatosis. Homozygous H63D genotypes (H63D/H63D) rarely show symptoms of hemochromatosis, but several cases have been reported. Mutations in unidentified genes or other mutations in the HFE gene which may cause hemochromatosis are not ruled out by this analysis. **Indications:** 1) Patients with symptoms as mentioned above and/or increased ferritin levels and increased transferrin saturation 2) Persons with a family history for hemochromatosis DD: primary or secondary hemochromatosis (e.g. patients with chronic virus hepatitis or toxic liver disease) Sensitivity and specificity for detection of this mutation are 99.9%.								
HEREDITARY HEMOCHROMATO-SIS (TYPE 1)	235200	**HFE**	***HFE***	235200	Detection of mutation in *HFE* gene responsible forhemochromatosis type 1.	Genetic analysis of 3 basic changes in *HFE* gene - ***C282Y, H63D, S65C.***	swab	***10***	**380**

		HFE-Seq	***HFE***	235200	Detection of mutation in *HFE* gene responsible too hemochromatosis type 1.	Sequencing analysis of all exons' codons: 1, 2, 3, 4, 5, 6 of *HFE* gene.	swab	***15***	**1160**

FAMILIAL HYPERCHOLE-STEROLEMIA



Disease: FAMILIAL HYPERCHOLESTEROLEMIA (FH) is due to loss-of-function mutations in the low-density lipoprotein receptor (LDLR), which mediates clearance of low-density lipoprotein (LDL), the main plasma reservoir of cholesterol, from the plasma. Binding of LDL to LDLR expressed on the cell surface leads to internalization of the LDLR-LDL complex. While LDLR is recycled to the membrane, LDL is disassembled into its components. Cholesterol derived from disassembled LDL then inhibits cholesterol biosynthesis within the cell. Loss-of-function mutations in LDLR lead to increased cholesterol biosynthesis and decreased plasma clearance of total and LDL-cholesterol. Mutations that completely prevent synthesis of a functional LDLR molecule are believed to cause a more severe elevation in plasma cholesterol than mutations that lead to synthesis of a defective LDLR with reduced activity. Classification of lipoproteins is based on their specific density, which reflects their protein and lipid composition. Low-density lipoprotein (LDL) is particularly rich in cholesterol. Excess plasma LDL can accumulate in arterial walls, where it becomes chemically modified and is taken up by macrophages. As the macrophages become engorged with modified LDL, they initiate the development of an atherosclerotic lesion, which, over time, can grow into an atherosclerotic plaque composed of cholesterol, cellular debris, and fibrous tissue. If the plaque ruptures, a blood clot can form and completely obstruct the artery; in a coronary artery, such an event leads to myocardial infarction. FH is typically characterized by a two to threefold increase in plasma levels of total and LDL-cholesterol. While hypercholesterolemia may be present from birth, symptoms of CHD appear on average at age 45 in men and at age 55 in women. Atherosclerosis, however, can already be detected in children and adolescents with FH. Tendon xanthoma, xanthelasma, and premature arcus corneae are present in some individuals with FH, but may not develop until later in life.

Genetics: is caused by autosomal dominant loss-of-function mutations in LDLR, the gene for LDLR. FDB is due to autosomal dominant loss-of-function mutations in APOB, the gene for Apo B-100. While heterozygotes usually express the phenotype, homozygotes are much more severely affected. Compound heterozygosity for an FH-associated mutation in LDLR and an FDB-associated mutation in APOB also leads to more severe symptoms (24, 25). Homozygosity for an FH-associated mutation in LDLR leads to much more severe hypercholesterolemia, with a three to six fold increase in total plasma cholesterol and a more than fivefold increase in plasma LDL-cholesterol. Homozygotes for FH-associated mutations in LDLR typically show planar xanthomata by age six, may exhibit symptoms of CHD by age 10, and, if untreated, usually die of myocardial infarction by age 20.

Indications:

1) Individuals who have reported occurrence of cardiovascular diseases, including heart attack and stroke, among their relatives
2) People who are overweight.
3) Individuals having relatives with diagnosed vascular atherosclerosis, hypertension, elevated level of cholesterol
4) Smokers. Smoking is and environmental factor accelerating disease development especially in case of individuals carrying mutations in *LDLR* and/or *APOB* genes.

FAMILIAL HYPERCHOLESTEROLEMIA	144010	**HCR-APOB** *2-4 codons*	***APOB***	107730	Detection of mutation in *APOE* gene responsible for hypercholesterolemia	Polymerase chain reaction and mini-sequencing 4 codons analysis: ***R3527Q (R3500Q), R3480W, R3531C, H3543Y***	swab.	***10***	**390**
		HCR-LDLR *12-18 codons*	***LDLR***	606945	Detection of mutations in the *LDLR* gene causing familial hypercholesterolemia and potential manifestation of cardiovascular disease	Genetic analysis of 18 primary *LDLR* codons and splicing acceptor site for the presence of 30 most frequent mutations *Test exclusively at BioTe21!*	swab	***10***	**580**
		HCR-LDLR-sek *Analysis of all examined codons*	***LDLR***	606945	Diagnosis of the mutations in the *LDLR* gene causing familial hypercholesterolemia and potential manifestation of cardiovascular disease	Genetic analysis of 16 *LDLR* exons, including examination of all *LDLR* codons	swab	***15***	**1750**
		HCR-2G *12-18 LDLR codons and 2-4 APOB codons* *Recommended test!*	***LDLR +APOB***	606945+ 107730	Diagnosis of the mutations in the *LDLR* and *APOB* genes causing familial hypercholesterolemia and potential manifestation of cardiovascular disease	Genetic analysis of 18 primary *LDLR* codons together with splicing acceptor site and 4 *APOB* codons for the presence of most frequent mutations Test exclusively at BioTe21!	swab	***10***	**790**

FAMILIAL HYPERLIPIDEMIA TYPE III

Disease: Hiperlipidemia is a disorder manifested by the presence of the abnormal apolipoprotein E isoforms (e2/e2). The APOE genotype, independently from the level of LDL, was linked with the increased risk of occurrence the ischemic heart disease and the carotid artery arteriosclerosis.

Genetics: The ApoE genotype was associated with the arteriosclerosis and Alzheimer disorders occurrence. Development of these two disorders depend on both intrinsic and environmental factors. ApoE is the major cholesterol carrier in the central nervous system. Despite being responsible for lipid homeostasis in the organism, it plays important role in brain development and repair. The ApoE polymorphisms caused by presence of three different alleles, named e2, e3, e4.Their combinations result in 6 different genotypes: e2/e2, e2/e3, e3/e3, e3/e4, e4/e4. The ApoE2/E2 genotype occurs in frequency of 1:100 and is linked to hyperlipidemia type III. However ApoE4 genotype is rare and is associated with risk of occurrence the familiar Alzheimer disorder.

Indications: Apolipoprotein E is included in lipoproteins rich in triglycerides (chylomikrons und VLDL). Apolipoprotein E holds the ligand for the receptor in hepatocytes. If this ligand part of the protein is mutated the above mentioned lipoproteins will increase in plasma. This takes place when the E2 allele is present. Clinical signs: The influence of E2-allel on clinical signs is dose dependent. In case of E2/E2 genotype the rare form of hyperlipimia may be deduced. According to Fredrickson this hyperlipemia is classifyed type III. This form is characterized by IDL and

remnants. In Diabetes there seems to be a correlation of E2 allele and albuminuria. There some more rare mutation affecting the ligand region of the gene have been found. These mutation have importance in lipid disorders. There is no evidence about correlation of these mutations to Alzheimer's disease. Interpretation: Epidemiologically there is a strong correlation between E2 genotype and lipid disorders. Nevertheless there are broad individual differences modified by environment and some other genes. That way an effective dietary education can be deduced by the evidence of the E2 allele. The mechanism leading to Alzheimer's disease is not quite clear yet. But apolipoprotein genotyping can provide useful additional information for early diagnosis.

1. Individuals with reported Alzheimer case in the family,
2. People who are overweight
3. Elderly individuals manifesting early Alzheimer symptoms
4. Individuals with hypothyroidism, diabetes or individuals with other genetic related co-lipid disorder such as a family hiperlipidemia
5. Individuals having family reported cases of arteriosclerosis, hypertension and elevated cholesterol level.
6. Smokers. Tobacco smoking is and environmental factor accelerating disease development especially in case of individuals carrying mutations in*ApoE* gene.

FAMILIAL HYPERLIPIDEMIA TYPE III	104310	**APOE** ***Codons: 112, 158 145***	***APOE***	107741	Detection of Alzheimer and hyperlipidemia type III related alleles.	Analysis of 3 types of SNP in a dual control system confidence result (PCR-SNP). The test enables detection of one of the 3 main alleles in the homo and heterozygous conformation and detection of additional mutations in codon 145 of the ApoE gene.	swab	***5***	**390**

HYPERPRO-THROMBI-NEMIA 20210A

Disease: Prothrombin also called coagulation factor II cleaves in its active form (thrombin) fibrinogen and hereby forms fibrin the final product of the coagulation process. But thrombin is not only essential for coagulation it has a function in interrupting of the coagulation process.

Genetics: The gene of Prothrombin or coagulation factor 2 (F2) is localized on chromosome 11 (11p11-q12). It is about 21kb in size and consists of 14 exons. The underlying mutation is a base transition G->A in position 20210 of the prothrombin gene. There is a mutation in the prothrombin gene G20210A that causes hypercoagulability. It is not known yet what the mechanism is. The precursor prothrombin is converted to thrombin which, in turn, is active in the process of conversion from fibrinogen to fibrin. Due to the genetic defect prothrombin levels increase, which disturbs the delicate equilibrium between coagulation cascade and fibrinolysis. The increased conversion from fibrinogen to fibrin thus leads to hypercoagulation.
Approx. 2% of our population carry a heterozygous genetic defect G20210A in the prothrombin gene increasing the risk for thrombosis 3- to 4-fold. Homozygous carriers of the G20210A mutation are very rare. Since thrombosis risk increases several fold in mutation carriers who simultaneously carry a factor V Leiden mutation, all carriers of the G20210A mutation should undergo analysis for the factor V Leiden mutation as well. Furthermore, additional risk factors such as smoking and hormonal contraception are to be avoided. The relative Risk for Thrombosis is 2-3.

Indications:
1) Individuals with preceding thrombosis and their relatives
2) individuals with increased risk for thrombosis
3) Family screening if a family member is a carrier.

HYPERPRO-THROMBI-NEMIA 20210A	176930	**F2**	***F2***	176930	Diagnosis of the *F2* gene mutations	Analysis of the mutation *20210* in the prothrombin gene	swab	***15***	**340**
HIRSCHSPRUNG DISEASE	**Disease:** Hirschsprung disease is a congenital disorder of the colon in which certain nerve cells, known as ganglion cells, are absent. The disorder result in chronic constipation. **Genetics:** The disease is caused by mutations in *RET* proto-oncogene that encodes membrane associated receptor tyrosine kinase. The RET kinase play important role in signal transduction being a receptor for numbers of extracellular signaling factors. Years of research performed in laboratories worldwide resulted in conclusion that Hirschsprung disorder is caused by mutation in four *RET* codons 609, 618, 620, 791. **Indications:** 1) Individuals with diagnosed thyroid cancer 2) Individuals having relatives with reported thyroid cancer or Hirschsprung disease (molecular screening of relatives)								
HIRSCHSPRUNG DISEASE	142623	**RET-3K17Z** *12-17 mutations in codons: 609, 618, 620, 7911*	***RET***	164761	Detection of specific genetic mutations responsible for occurrence of the Hirschsprung disorder..	Genetic analysis of the 17 most frequently occurring changes (mutations) in the four primary *RET* codons.	swab	***10***	**560**
		RET-Sek3E *codons in exons: 10, 11 and 13*	***RET***	164761	Detection of specific genetic mutations determining occurrence of the Hirschsprung disorder..	Gen sequence analysis of all codons of exons 10, 11 and 13 of the *RET* gene. Precise test performed when clinical results suggests Hirschprung disorder and mutations were not detected in codons 609, 618, 620, 791.	swab	***10***	**780**

		RET-Sek *All codons in sequenced exons*	***RET***	164761	Detection of specific genetic mutations determining occurrence of the Hirschsprung disorder.. In addition sequence analysis of the gene allowing detection of mutations determining medullary thyroid cancer and associated MEN2A and MEN2B syndromes as well as Hirschsprung disease.	Gene sequence analysis of codons of exons: 10, 11, 13, 14, 15, 16, 18 and *RET* gene splicing site. The most accurate test usually performed, when no mutations were detected in the most frequently mutated codons, in cases of diagnosed Hirschsprung disease or medullary thyroid cancer 1	swab	***15***	**1350**
HUNTINGTON DISEASE	**Disease:** Huntington disease (HD) is a neurodegenerative disorder of central nervous system manifesting by unintentional movements of any part of the body, called chorea, and cognition impairment. The disease is inherited dominantly autosomally at frequency of 1:15000 in Poland. **Genetics:** Molecular basis of the disease is mutation in gene IT15 encoding protein named Huntington (htt).Huntington disease belongs to the group of trinucleotide disorders, caused by the length of a repeated section of a gene, in HD CAG repeats, exceeding a normal range. Correct IT15 gene contains 9 to 35 repeats. Individuals having 36 to 39 repeats display reduced penetrance and may develop the disease symptoms. Individuals with over 39 repeats display full penetrance of the disease. **Indications:** 1) Female relatives of the sick patient to determine the risk of being a disease vector. 2) Individuals having relatives with diagnosed Huntington disease								
HUNTINGTON DISEASE	143100	**IT15**	***IT 15***	143100	Detection of mutations in gene *IT15.*	Gene sequence analysis of *IT15*	swab	***25***	**480**
THYROID HORMONES RESISTANCE	**Disease:** Thyroid hormone resistance (THR) is a rare syndrome manifested by tissue insensitiveness for thyroid hormones (TH). The disorder is very rare, an incidence is quotes as 1:50000, and is result of lack or damage of T3 receptors in cells. Disorder might display generalized character, affecting pituitary gland only. Contrary to the generalized manifestation, disorder manifested in peripheral tissues, pituitary gland is not affected, might display hormonal test deviations together with differentiated clinical image. THR is presented by elevated levels of FT4 and FT3 hormones (2-3 folds increase comparing to normal levels) together with slightly upraised TSH level.THR syndrome might be inherited either in recessive or dominant autosomal manner. If the disorder is inherited in dominant manner it might be run in a family. **Genetics**: Molecular basis of THR are in majority of cases point mutations in the *THRB* gene. THRB encodes receptor for thyroid hormones. Research shows that in THR structure of E domain, responsible for triiodothyronine T3 binding, is changed. These changes are caused by mutations within exons 6 to 10 (mutations in exons 9 and 10 uncovers 40% of the gene and were described in 85% investigated cases) **Indications:** 1)Individuals with chronic thyroid inflammation, Graves-Basedow disease or hyperthyroidism of unknown etiology 2) Individuals with increased levels of T4 or TSH								

THYROID HORMONES RESISTANCE	188570 274300	**TRB-sec**	***THRB***	190160		*THRB* gene sequence analysis of codons of exons 6, 7, 8, 9, 10	swab	***15***	**965**
GENETIC RESISTANCE TO HIV-1 INFECTIONS	**Genetics:** The test consists in identifying the CCR5 gene mutation which encodes the lymphocyte surface receptor. The mutated form of this receptor makes it impossible for viral molecules to adhere to the lymphocyte surface thus preventing the infection with the virus HIV-1. Carriers of a mutated form of the gene has a higher resistance to infection with HIV-1. People who have both gene copies in the mutated from (homozygote) are fully resistant to infection with this form of HIV virus. Survival analysis clearly shows that HIV disease progression is slower in CKR5 deletion heterozygotes than in individuals homozygous for the normal CKR5 gene. The chemokine receptor 5 (CKR5) protein serves as a secondary receptor on CD4+ T lymphocytes for certain strains of human immunodeficiency virus-type 1 (HIV-1). The CKR5 structural gene was mapped to human chromosome 3p21, and a 32-base pair deletion allele (CKR5Δ32) was identified that is present at a frequency of ~0.10 in the Caucasian population of the United States. An examination of 1955 patients included among six well-characterized acquired immunodeficiency syndrome (AIDS) cohort studies revealed that 17 deletion homozygotes occurred exclusively among 612 exposed HIV-1 antibody-negative individuals (2.8 percent) and not at all in 1343 HIV-1-infected individuals. The frequency of CKR5 deletion heterozygotes was significantly elevated in groups of individuals that had survived HIV-1 infection for more than 10 years, and, in some risk groups, twice as frequent as their occurrence in rapid progressors to AIDS. The CKR5Δ32 deletion may act as a recessive restriction gene against HIV-1 infection and may exert a dominant phenotype of delaying progression to AIDS among infected individuals.								
GENETIC RESISTANCE TO HIV-1 INFECTIONS	60423	**CCR5**	***CCR5***	601373	Detection of the deletion of the *CCR5* gene fragment that results in higher resistance to HIV-1 infections.	Gene deficiency analysis by double selection method (PCR-SNP).	swab	***10***	**340**

HEREDITARY BREAST AND OVARIAN CANCERS

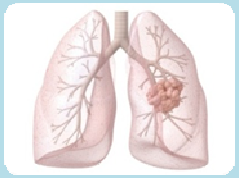
Disease: Breast cancer is a cancer that starts in the breast, usually in the inner lining of the milk ducts or lobules. There are different types of breast cancer, with different stages (spread), aggressiveness, and genetic makeup. With best treatment, 10-year disease-free survival varies from 98% to 10%. Treatment includes surgery, drugs (hormone therapy and chemotherapy), and radiation. In the United States, there were 216,000 cases of invasive breast cancer and 40,000 deaths in 2004. Worldwide, breast cancer is the second most common type of cancer after lung cancer (10.4% of all cancer incidence, both sexes counted) and the fifth most common cause of cancer death. In 2004, breast cancer caused 519,000 deaths worldwide (7% of cancer deaths; almost 1% of all deaths). Breast cancer is about 100 times as frequent among women as among men, but survival rates are equal in both sexes. Some breast cancers require the hormones estrogen and progesterone to grow, and have receptors for those hormones. Those cancers are treated with drugs that interfere with those hormones, usually tamoxifen, and with drugs that shut off the production of estrogen in the ovaries or elsewhere; this may damage the ovaries and end fertility. Low-risk, hormone-sensitive breast cancers may be treated with hormone therapy and radiation alone. Breast cancers without hormone receptors, or which have spread to the lymph nodes in the armpits, or which express certain genetic characeristics, are higher-risk, and are treated more aggressively. One standard regimen, popular in the U.S., is cycophosphamide plus doxorubicin (Adriomycin), known as CA; these drugs damage DNA in the cancer, but also in fast-growing normal cells where they cause serious side effects. Sometimes a taxane drug, such as docetaxel, is added, and the regime is then known as CAT; taxane attacks the microtubules in cancer cells. An equivalent treatment, popular in Europe, is cyclophosphamide, methotrexate, and fluorouracil (CMF). Monoclonal antibodies, such as trastuzumab, are used for cancer cells that have the HER2 mutation. Radiation is usually added to the surgical bed to control cancer cells that were missed by the surgery, which usually extends survival, although radiation exposure to the heart may cause damage and heart failure in the following years.

The most common form of ovarian cancer (≥80%) arises from the outer lining (epithelium) of the ovary. Other forms arise from the egg cells (germ cell tumor). In 2004, 25,580 new cases were diagnosed and 16,090 women died of ovarian cancer. The risk increases with age and decreases with pregnancy. Lifetime risk is about 1.6%, but women with affected first-degree relatives have a 5% risk. Women with a mutated BRCA1 or BRCA2 gene have a 25% risk. Ovarian cancer is the fifth leading cause of death from cancer in women and the leading cause of death from gynecological cancer.In early stages ovarian cancer is associated with abdominal distension. 10-year relative survival ranges from 84.1% in stage IA to 10.4% in stage IIIC. Ovarian cancer causes non-specific symptoms. Early diagnosis would result in better survival, on the assumption that stage I and II cancers progress to stage III and IV cancers (but this has not been proven). Most women with ovarian cancer report one or more symptoms such as abdominal pain or discomfort, an abdominal mass, bloating, back pain, urinary urgency, constipation, tiredness and a range of other non-specific symptoms, as well as more specific symptoms such as pelvic pain, abnormal vaginal bleeding or involuntary weight loss. There can be a build-up of fluid (ascites) in the abdominal cavity. Diagnosis of ovarian cancer starts with a physical examination (including a pelvic examination), a blood test (for CA-125 and sometimes other markers, and transvaginal ultrasound. The diagnosis must be confirmed with surgery to inspect the abdominal cavity, take biopsies (tissue samples for microscopic analysis) and look for cancer cells in the abdominal fluid. Treatment usually involves chemotherapy and surgery, and sometimes radiotherapy. In most cases, the cause of ovarian cancer remains unknown. Older women, and in those who have a first or second degree relative with the disease, have an increased risk. Hereditary forms of ovarian cancer can be caused by mutations in specific genes (most notably BRCA1 and BRCA2, but also in genes for hereditary nonpolyposis colorectal cancer). Infertile women and those with a condition called endometriosis, those who have never been pregnant and those who use postmenopausal estrogen replacement therapy are at increased risk. Use of combined oral contraceptive pills is a protective factor. The risk is also lower in women who have had their uterine tubes blocked surgically (tubal ligation).

Genetics: Carrier status for a BRCA1 or BRCA2 mutation coincides with a notably heightened risk of developing mamma and/or ovarian cancer in comparison to the general population. The average age of onset for carriers of mutations in the BRCA1 and/or BRCA2 gene is approximately 40 years - significantly below the average age of onset for sporadic mamma cancers with no positive family anamnesis. While ovarian cancers often occur alongside mamma cancers in BRCA1-positive families (approx. 40%), ovarian cancers are less frequent in BRCA2-positive families (approx. 11%). However, BRCA2 mutation carriers have an additional heightened risk of developing other tumors in comparison to the general population, especially pancreatic cancer, rare tumors of the oropharynx, colon cancer and lymphoma.

Mutations in *BRCA1* gene are causes of 64% familial cancers and are responsible for increased risk of breast and ovarian cancers development. The presence of mutations in *BRCA1* genes lowers the age of developing these cancers for age 42-45.The risk of developing cancer in individuals carrying mutations in *BRCA1* gene increase 35-50% in case of breast cancer and 10% in case of ovarian cancer. In addition mutations in *BRCA1* gene increase by about 10% risk of developing cancer of peritoneum and carcinoma of the fallopian tube. Mutations in *BRCA1* gene result in increased risk of developing colon cancer by about 2-folds, pancreatic cancer by about 3-folds and gastric cancer by about 7-folds.Mutations in the *BRCA2* gene were linked with increased risk of not only breast and ovarian cancer development, both in females and males, but also of cancers of prostate, pancreas, colon, other organs and melanoma. The risk of developing cancer, before age 70, in individuals carrying mutations in *BRCA2* gene. The risk of developing cancer, before age 70, in individuals carrying mutations in *BRCA2* gene is increased by about 35-84% in case of breast cancer and by about 10-50% in case of ovarian cancer. Males individuals carrying mutations in both *BRCA1* and *BRCA2* genes have 2 to 8 folds increased risk of pancreatic cancer development. However it doesn't involve individuals carrying mutations in *BRCA2* gene and having 2 to 5 folds increased risk of development of various types of melanomas, gastric cancer as well as cancer of gallbladder and the bile ducts. Breast cancer states for less than 1% of all type of tumors in males. However males individuals carrying mutation in *BRCA2* have 80-100-folds increased risk of developing breast cancer. Approximately

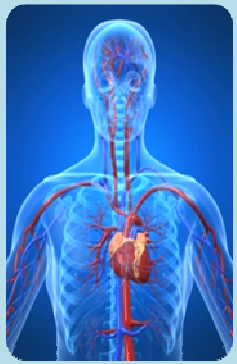
	6% of males individuals carrying these mutations will develop breast cancer before age 80. Some data present that males individuals carrying mutation in *BRCA1* gene have 60-folds increased risk of developing breast cancer. The early diagnosed mutations in these genes give a greater chance for an effective method of prevention. **Indications:** 1) individuals n the family with a minimum of three cases of breast and ovarian cancer reported (including first and second degree relatives) 2) Females below 25 years of age using oral contraceptives 3) Females using hormonal contraceptive therapy 4) Individuals in the family with at least two reported cases, one of which occurred before age of 50 5) Individuals and first degree relatives with diagnosed breast or ovarian cancer before age 40 6) In order to optimize the treatment process, all individuals with diagnosed breast and ovarian cancer should have *BRCA1* genotype studied 7) Anyone who wants to determine if has increased risk of developing breast and ovarian cancers								
HEREDITARY BREAST AND OVARIAN CANCERS	114480	**BRCA1-3**	***BRCA1***	113705	Detection of mutations in *BRCA1* gene predisposing to breast and ovarian cancers..	Analysis of 3 mutations in *BRCA1 gene*.	swab	***20***	**200**
		BRCA1-5	***BRCA1***	113705	Detection of mutations in *BRCA1* gene predisposing to breast and ovarian cancers..	Analysis of 5 mutations in *BRCA1 gene.*	swab	***20***	**249**
		BRCA1-12	***BRCA1***	113705	Detection of mutations in *BRCA1* gene predisposing to breast and ovarian cancers...	Analysis of 12 mutations in *BRCA1 gene.*	swab	***20***	**600**
		BRCA1/BRCA2 – 1 (7+4)	***BRCA1*** ***BRCA2***	113705 600185	Detection of mutations in *BRCA1* and *BRCA2* genes predisposing to breast and ovarian cancers..	Analysis of 7 most frequent mutations in *BRCA1* gene and 4 most frequent mutations in *BRCA2* gene	swab	***20***	**460**

		BRCA1/BRCA2-2 *Analysis of 19 mutations* *Test Recommended!*	***BRCA1 BRCA2***	113705 600185	Detection of mutations in *BRCA1* and *BRCA2* genes predisposing to breast and ovarian cancers. *The most precise test!*	Analysis of 12 mutations in *BRCA1* gene and 7 mutations in *BRCA2* gene.	swab	***20***	**960**
LUNG CANCER 	**Disease:** Lung cancer is one of the most common malignant tumors. This cancer usually has very aggressive progression and is poor in prognosis. Approximately 1,3 million of people dies every year due to lung cancer. This cancer is the most common cause of cancer deaths in men and is on 2 place in this respect in women. The current state of knowledge indicates that the greatest impact on the risk of lung cancer is long-term exposure to inhaled carcinogens, especially tobacco smoke. The risk of developing lung cancer is about 20-folds greater in smokers than in non-smokers. In contrast, in individuals who are passive smokers (e.g. children and spouses of smokers) the risk is 3 times higher. Smoking is responsible for 80-90% of all cases of lung cancer. In the case of a lung cancer in individuals who never smoke, the disease occurs mostly through a combination of genetic factors. **Genetics**: One of the reasons for the development of lung cancer are genetic polymorphism in *GSTP1* and *GSTM1* genes., Proteins encoded by these genes play important role in elimination of polycyclic aromatic hydrocarbons like benzopyrene, dibenzopyrene or methylbenzpyren. These compound are products of incomplete combustion of tobacco and they are carcinogens presented in tobacco smoke. Other genes that may contribute to the development of lung cancer are: ELA2, CHRNA3, CHRNA5. Research indicate that the diagnostic of the lung cancer related mutations in genes may be of great importance especially for smokers, for which the accumulation of environmental factors (tobacco smoke, carcinogens) in combination with the genetic load can be particularly dangerous! **Indications:** 1) Smokers, for which the accumulation of environmental factors (tobacco smoke, carcinogens) in combination with the genetic load may be especially dangerous. 2) Non-smokers with reported lung cancer cases in family 3) Anyone who wants to determine if has increased risk of developing lung cancer								
LUNG CANCER	182280 211980 608935 612052	**RP- 2G**	***GSTPI GSTM1***	134660 138350	Detection of primary mutations predisposing for the lung cancer	SNP analysis of 8 codons of*GSTP1*and *GSTM1*genes	swab	***10***	**490**
		RP-3G	***GSTPI, GSTM1, ELA2***	134660 138350 130130	Detection of mutations predisposing for the lung cancer	SNP analysis of 12 codons of *GSTP1* and *GSTM1* and *ELA2* genes	swab	***10***	**780**
		RP-CHRNA35	***CHRNA3CHRNA5***	118503 118505	Detection of mutations predisposing for the lung cancer	Sequence analysis of *CHRNA3*and*CHRNA5* genes	swab	***15***	**1350**

		RP-5G	***GSTPI, GSTM1, ELA2, CHRNA3CHRNA5***	134660 138350 130130 118503 118505	A comprehensive analysis of SNP polymorphisms in genes: GSTP1, GSTM1, ELA2, CHRNA3, CHRNA5 predisposing to the occurrence of lung cancer.	Analysis of all five genes:*GSTP1, GSTM1, ELA2,CHRNA3*and C*HRNA5.*	swab	***15***	**1750**
FAMILIAL MEDULLARY THYROID CANCER – FMTC 		**Disease:** Thyroid cancer is one of the most common malignant neoplasm of the endocrine secretion gland . Seventy-five percent of medullary thyroid carcinoma (MTC) occurs in individuals without an identifiable family history and is assigned the term "sporadic". MTC is a cancer with high hereditary predisposition that accounts for 25% of all cases. Familial Medullary Thyroid Carcinoma (FMTC) is inherited in the dominant autosomal manner and predominantly is characterized by high level of penetrance, exceeding 90%, in other words it means that individual carrying mutation will develop MTC together with multiple endocrine neoplasia type 2A (MEN2A).In addition to the MTC and MEN2A, in individuals carrying mutations, other type of disorders might manifest. These include: pheochromocytoma, adenoma folliculare, rarely Hirschprung disease, multiple endocrine neoplasia type 2B and others gastrointestinal adenomas (in that case excluding pheochromocytoma)Hirschsprung disease is a congenital disorder of the colon in which certain nerve cells, known as ganglion cells, are absent. The disorder result in chronic constipation. **Genetics**: mutations in the proto-oncogene *RET* are responsible for the development of medullary thyroid carcinoma. *RET* encodes surface associated tyrosine kinase protein receptor, which play important role in signal transduction into the cell. There are 190 described mutations in *RET* proto-oncogene. Interestingly all of them are localized in five exons: exon 10-19%, exon 11-43%, exon13-18%, exon 14-18%, rarely exon 16-12%. In the majority of cases these genetic defects have point mutation character and are localized in gene regions encoding motifs important for protein function. The presence of these mutations in *RET* proto-oncogene almost always result in development of MTC, just as often in women and men. Research performed in various centers allow determine, which mutations occur the most frequently. The presence of different mutations variants results in various clinical image manifested by different disorders, for instance 70% of MEN2A cases have mutation in exon 11 whereas for MEN2B disorder mutation in exon 16 was observed.. **Indications:** 1) Individuals with thyroid cancer in order to confirm or exclude a hereditary disease 2) Individuals with diagnosed thyroid cancer or Hirschsprung disease in family (molecular screen of relatives)) 3) Individuals with diagnosed thyroid disorder of not-known etiology.								
	155240 171400 162300	**RET-1K6Z** *3 mutations in codon 634*	***RET***	164761	Detection of the mutations responsible for inheritable form of MTC cancer and an associated with it MEN2A disorder	Genetic analysis of three most frequent mutations in codon 634 of the *RET* gene	swab	***10***	**420**
	191830	**RET-3K11Z** *9 to 11 mutations in three codons: 634, 618, 918*	***RET***	164761	Detection of the mutations resulting in inheritable form of MTC cancer and associated with it MEN2A, MEN2B and Hirschsprung disorders	Genetic analysis of 11 most frequent mutations in 3 *RET* codons	swab	***10***	**560**

		RET-13K37Z *31-37 mutations in 13codons* *Test Recommended!*	***RET***	164761	Detection of the mutations resulting in inheritable form of MTC cancer and associated with it MEN2A, MEN2B and Hirschsprung disorders.	Genetic analysis of 37 most frequent mutations in 13 *RET* codons.	swab	***10***	**780**
		RET-Sek *All codons in sequenced exons*	***RET***	164761	Detection of the mutations resulting in inheritable form of MTC cancer and associated with it MEN2A, MEN2B and Hirschsprung disorders. *The most precise test!*	Sequence analysis of all codons of exons: 10, 11, 13, 14, 15, 16, 18, additional splicing sites (acceptors and donors) and non-coding introns of the *RET* gene.	swab	***15***	**1350**

FAMILIAL DEFECTIVE APOLIPOPROTE-IN B-100



Disease: Familial hypercholesterolemia (FH) is among the most common disorders that are inherited in the dominant autosomal manner. In other words only one copy of mutated gene is sufficient to manifest the disease. Molecular basis of the FH are disorders of LDL transport and catabolism resulting in elevated levels of both LDL and cholesterol in the serum. Higher level of LDL is co-related with normal HDL and VLDL levels in the FH disorder. The cholesterol is deposited in the vascular walls what results in predisposition to development of arteriosclerosis and coronary disease. The cholesterol level is 2-3 folds elevated in heterozygote mutants whereas even 5 folds elevated in homozygous mutants. Approximately mutations in LDLR, in individuals after heart attack, are found at frequency of 1 to 25 cases!!!

Genetics: Mutations in *LDLR, APOB* genes results in disorders of cholesterol transport and catabolism in LDL lipoproteins. As a consequence of these disorders the level of cholesterol in serum is elevated due to inefficient removal of the LDL from blood. The LDL fraction favors deposition of the cholesterol, due to presence of mutated LDL receptor on surface of monocytes and macrophages, in smooth muscle fibers in walls of arteries. APOB protein is responsible for recognition of LDL by receptor and it removal from serum into the cells. Familial hypercholesterolemia (FH) is among the most common disorders that are inherited in the dominant autosomal manner. In other words only one copy of mutated gene is sufficient to manifest the disease. Heterozygotic variant of *LDLR* gene is found at frequency of 1:500 in Polish population (approx. 76000 of patients). Homozygotic variant of *LDLR* gene is found at frequency 1:1000000. Mutations in *LDLR* gene was detected at frequency 1:20 in individuals after the heart attack, which indicates enormous preventive potential of FC diagnostic. In Polish FC population mutations in *LDLR* gene were found in 55% of cases, whereas mutation in *APOB* (R3500Q) gene were found in 10.4% of cases. Mutations in both *LDLR* and *APOB* genes determine inclination for inheritable arteriosclerosis.

Indications:

1) Individuals having reported cases of cardiovascular diseases, including heart attacks and strokes, in family.
2) Obese individuals, anyone who wants to determine if they have increased risk of developing disorder
3) Individuals with reported cases of vascular arteriosclerosis, hypertension and elevated cholesterol levels in family
4) Smokers, smoking is an additional environmental factor accelerating progression of the disease, especially in individuals carrying mutations in either *LDLR* or *APOB* genes.

FAMILIAL APOLIPOPROTEIN Y B-100 DISORDER	144010	**HCR-APOB** *analysis of 2-4 codons*	***APOB***	107730	Detection of mutations in *APOB* gene predisposing to familial hypercholesterolemia	analysis of four codons for presence of following mutations: ***R3527Q (R3500Q), R3480W, R3531C, H3543Y***	swab	***10***	**390**
THROMBOPHI-LIA	**Disease:** Factor V Leiden mutation is the most common cause of inherited thrombophilia and accounts for over 90 percent of activated protein C resistance. The expression of Factor V Leiden thrombophilia is impacted by coexisting genetic thrombophilic disorders, acquired thrombophilic disorders (malignancy, hyperhomocysteinemia, high factor VIII levels), and circumstances including: pregnancy, oral contraceptive use, hormone replacement therapy, selective estrogen receptor modulators, travel, central venous catheters, surgery, transplantation and advanced age. Thromboembolic events may be acquired or inherited. The genetically determined resistance of coagulation factor V against activated protein C (APC resistance) shows a higher prevalence. The mutation in the factor V gene disturbs the inactivation of protein C by factor V leading to hypercoagulation. **Genetics:** The gene F5 is about 70kb in size. It is located on Chromosome 1 (1q23). It consists of 25 exons. The structure is similar to coagulation factor VIII. We have the same domains (A1-A2-B-A3-C1-C2). The B domain is very much glycosylated. The factor V Leiden mutation is a point mutation at nucleotide position 1691 which results in the amino acid exchange Arg506Gln. Heterozygosity for the factor V mutation is present in around 5% of the population and increases the risk for thrombosis by 5 to 10 times. Homozygosity (only in around 0.05-0.5% of the population) increases the risk by 50 to 100 times. This disease they are inheriting incomplete autosomal dominant. Additional susceptibility factors such as smoking, exsiccosis or hormonal contraception are to be avoided. Drug-based antithrombotic prophylaxis is advisable if further risk factors are present such as immobilization, pregnancy or other diseases affecting the coagulation system (e.g. prothrombin gene, MTHFR gene). **Indications:** 1) Individuals with preceding thrombosis 2) Individuals with increased risk for thrombosis by, e.g., defects in the coagulation system, and their first-grade relatives.								
THROMBOPHILIA	227400	**V Leiden**	***F5***	227400	Detection of mutation in*F5*gene type Leiden of clotting blood factor V	Analysis for the presence of following mutation (R506Q) in heavy chain.	swab	***10***	**280**
PROSTATE CANCER	**Disease:** Prostate cancer is a form of cancer that develops in the prostate, a gland in the male reproductive system. The cancer cells may metastasize (spread) from the prostate to other parts of the body, particularly the bones and lymph nodes. Prostate cancer may cause pain, difficulty in urinating, problems during sexual intercourse, or erectile dysfunction. Other symptoms can potentially develop during later stages of the disease. Rates of detection of prostate cancers vary widely across the world, with South and East Asia detecting less frequently than in Europe, and especially the United States. Prostate cancer tends to develop in men over the age of fifty and although it is one of the most prevalent types of cancer in men, many never have symptoms, undergo no therapy, and eventually die of other causes. This is because cancer of the prostate is, in most cases, slow-growing, symptom free and men with the condition often die of causes unrelated to the prostate cancer, such as heart/circulatory disease, pneumonia, other unconnected cancers, or old age. Many factors, including genetics and diet, have been implicated in the development of prostate cancer. The presence of prostate cancer may be indicated by symptoms, physical examination, prostate specific antigen (PSA), or biopsy. **Genetics:** The mutations in BRCA1 and BRCA2 genes are associated with higher risk of prostate cancer occurrence. Mutations in BRCA2 gene cause even 5-times higher risk of prostate cancer occurrence, up to 7-times higher for individuals till the age of 65, and even up to 20-times till the age of 56. The average life span of mutations carriers is 10 years shorter. Still, the BRCA2 (or BRCA1) mutations are very rare and may be responsible for a small amount of cases. **Indications:** 1) Individuals having reported cases of prostate cancer in family 2) Anyone who wants to determine if has increased risk of developing prostate cancer								

PROSTATE CANCER	176808	**CHEK2-3**	***CHEK2***	113705	Detection of mutations in *CHEK2* gene predisposing to prostate cancer occurrence.	Analysis of 3 mutations in *CHEK2 gene*.	swab	***10***	**390**
		NBS1-1	***NBS1-1***	113705	Detection of mutations in *NBS1* gene predisposing to prostate cancer.	Analysis of mutations in *NBS1 gene*.	swab	***10***	**220**
		BRCA1-2	***BRCA1***	113705 600185	Detection of mutations in *BRCA1* gene predisposing to prostate cancer.	Analysis of 2 mutations in *BRCA1 gene.*	swab	***10***	**340**
		RP-3	***BRCA1*** ***CHEK2*** ***NBS1***	113705 602667 603078	Detection of mutations in 3 genes predisposing to prostate cancer.	Analysis of up to 7 mutations in *BRCA1, CHEK2 and NBS1 genes.*	swab	***15***	**560**