



synlab[®]

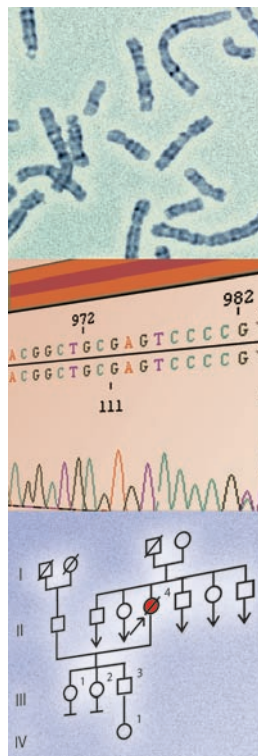
lab services

www.synlab.de

synlab Human Genetics Parameter Index

1. edition, 2007

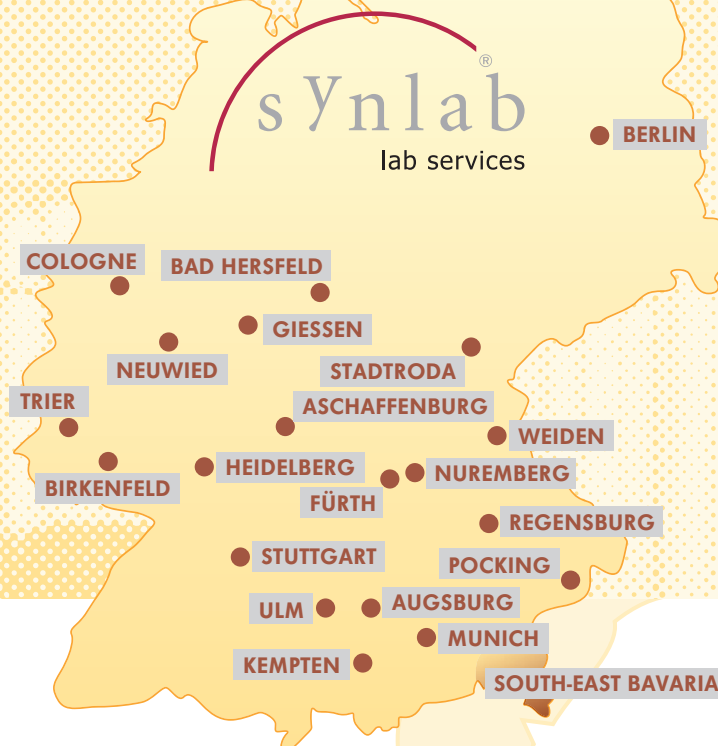
more than laboratory

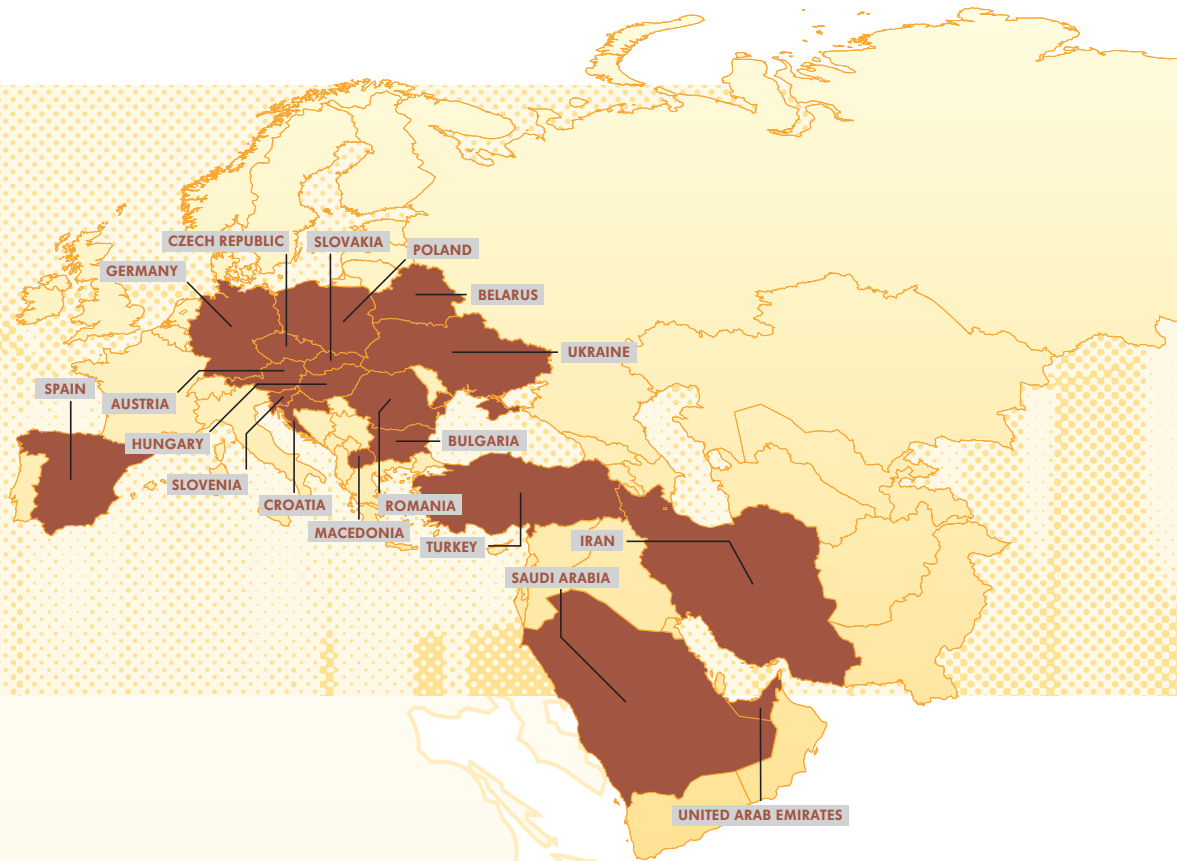


Facts

- Type of enterprise: synlab GmbH & Co. KG
- Founded: 1998 (synlab GmbH); 2005 (synlab GmbH & Co. KG)
- Enterprise objectives: Human, animal and environmental laboratory services, medical supplies, clinic consulting
- Turnover in 2006: € 145 Mio.
- N° analyses carried out in 2005: approx. 70 Mio.
- N° employees in Germany: approx. 1.500
- Employee structure: approx. 8% university graduates (doctors, natural scientists, engineers), largely laboratory-qualified trained professionals
- N° locations in Germany: 55
- N° locations abroad: 18
- QM: All specialist laboratories certified by the German Accreditation Council (DAR) and according to EN ISO standards.
- N° clients: approx. 11.000 in Germany
- Client structure: doctors' practices, hospitals, university hospitals, veterinary practices, business enterprises, research institutes.
- Board of Directors: Dr. Hans-Otto Frey (Leinfelden), Dr. Bartl Wimmer (Augsburg), Peter Thomsen (Augsburg).
- **synlab GmbH & Co. KG**
Max-Lang-Straße 58
70771 Leinfelden-Echterdingen
www.synlab.de

GERMANY





Profit orientated

synlab began as a cooperation of clinical pathologists focussing on central purchasing. The founders were aware that the economical savings whilst purchasing would immediately have a positive effect on the business profits. However, the growth of the group opened the door to other opportunities for synergies.

It always makes sense to streamline the laboratory where profits can be increased without endangering the security and quality of the analytics. Faithful to this maxim for years now, synlab has continuously gone through all business processes searching for the possibilities to reduce costs. Where possible, processes are reduced, the level of automation is increased and investments are made in both software and hardware. The aim is to boost the added value with the same resources.

High performance

Every day, approximately 4.000 different laboratory parameters are offered in the synlab laboratories. Every year, approximately 70 million analyses are carried out. A logistics network from partly own/partly subcontracted courier drivers, collects the samples – a complementary service for the client – and brings them to the laboratory. Included in the laboratory services are a free of charge inspection and dispatch of the samples and a transfer of the results online and also per courier.

The regional proximity of the laboratories to the samples being submitted enables short transport time to be guaranteed and the material can be processed immediately, resulting in a low error rate and rapid test results.

Preanalytics

Material and Preparations

Most genetic analyses require nuclei containing cells, which are further cultivated - or directly used for DNA extraction. Therefore patients do not need to fast. Blood and other material can be collected at any time and should be sent directly to the laboratory at room-temperature or slightly cooled (8–20 degrees).

Cytogenetics and Molecular Cytogenetics

5 ml sterile heparinized blood without other additives in collection tubes such as pearls. Those additives absorb active lymphocytes, so that cultivation of peripheral lymphocytes is not possible in some cases.

20 ml Amniotic Fluid
Chorion Villi
Abortion Material
Skin Biopsy

Molecular Genetics

5–10 ml EDTA-Blood
20 ml Amniotic Fluid
Chorion Villi
Abortion Material
Skin Biopsy

Paternity Testing

5 Buccal smears (infants)
5–10 ml EDTA-Blood (children and adults)

Identification of the samples and requests

The material must be identifiable by barcodes, ID numbers or correct writing of name and DOB of the patient.

Please use our Laboratory request forms. Detailed information about clinical symptoms of the patient as well as family history (affected family members?) will significantly support our experts to find the correct diagnosis.

Genetic investigations other than mentioned in this test list will be also offered by our collaborating laboratories.

Corresponding contact

synlab MVZ Humane Genetik

Frau Dr. med. Dr. rer. nat.

Claudia Nevinny-Stickel-Hinzpeter
Fachärztin für Humangenetik

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Quality Management

Our Quality Management bases on internal and external Quality Assessment Schemes. As a consequence, we establish structures which follow highest Quality and Security demands. In addition they support and allow us to permanently improve. Since the establishment of the Laboratory in 2000 it is our permanent and first objective to ensure our customers from our quality by regular participations in external Quality Assessment Schemes from the "Berufsverbandes Deutscher Humangenetiker e.V." (BVDH e.V.).

Department of Cytogenetics

Regular participation in external Quality Assessment Schemes from the "Berufsverbandes Deutscher Humangenetiker e.V." (BVDH e.V.) regarding Cytogenetics. Validation includes Turnaround Times (TAT) as well as resolution of chromosomal banding. According to the independent evaluation, our Laboratory ranks within the 10 best German Genetic Laboratories regarding TAT, reporting and Quality of Chromosomal Analyses. We were the only German Genetic Laboratory being asked to participate in a European pilot study regarding Quality Management Ensurance in 2006.

Molecular Genetics

Regular and very successful participation in external Quality Assessment Schemes from the "Cystic Fibrosis European Network", the DGKL (Deutsche Vereinte Gesellschaft für Klinische Chemie und Laboratoriumsmedizin e.V.), of the BVDH e.V. (Berufsverbandes Deutscher Humangenetiker e.V.) and of the INSTAND e.V. (Gesellschaft zur Förderung der Qualitätssicherung in medizinischen Laboratorien e.V.).

External Quality Assessment Schemes:

| | |
|------------------------------------|-----------------------|
| Myotonic Dystrophy | AZF |
| FraX | Chorea Huntington |
| DGKL FV1/05 | CF |
| Muscular Dystrophy Duchenne/Becker | Morbus Wilson (ATP7B) |
| HNPCC (MSH2/MLH1) | FII DGKL |
| Paternity Test (GEDNAP 30+31) | AGS |
| PWS / AS, TPMT | Sequencing (EMQN) |
| DGKL FV 2 / 05 | BRCA1, BRCA2 |
| MEN 2 | |

DACH-Accreditation

We are accredited by "DACH" (**Deutsche Akkreditierungsstelle Chemie GmbH**). All Investigations in **Molecular Genetics**, in **Cytogenetics** and **Investigations for Paternity Verification** are accredited according to **DIN EN ISO/IEC 17025**.

Aarskog Syndrome (Faziogenital Dysplasia)

OMIM: 305400
Gene: FGD1, Locus Xp11.21
Indications: faciogenital dysplasia
TAT: 3-4 weeks
Samples: 5 ml blood in EDTA tube
Method: PCR, sequencing of the FGD1-gene

Adrenal Hyperplasia (21-Hydroxylase Deficiency)

OMIM: 107400
Gene: CYP21, Locus 6p21.3
Indications: congenital adrenal hyperplasia, pseudopubertas praecox, hirsutism
TAT: around 4 weeks
Samples: 5 ml blood in EDTA tube
Method: Southern Blot analysis, PCR, sequencing

α 1-Antitrypsin Deficiency

OMIM: 201910
Gene: PI, Locus 14q32.1
Indications: emphysema of the lungs, liver cirrhosis, icterus prolongatus
TAT: 1 week
Samples: 5 ml blood in EDTA tube
Method: Real-time PCR (LightCycler); detection of S- and Z-mutation

Angelman Syndrome

OMIM: 105830
Gene: UBE3A, Locus 15q11-13
Indications: Severe motor and intellectual retardation, ataxia, hypotonia, epilepsy, absence of speech, and unusual facies
TAT: 2 weeks
Samples: 5 ml blood in EDTA tube; for requests with chromosomal analysis 5 ml blood in heparin tube
Method: Methylation-sensitive PCR, microsatellite analysis, FISH

Apolipoprotein B (Hypercholesterinemia)

OMIM: 107730
Gene: APOB, Locus 2p24
Indications: Familial hypercholesterinemia
TAT: 1 week
Samples: 5 ml blood in EDTA tube
Method: Real-time PCR (LightCycler); detection of the mutations R3500Q, R3500W, R3531C

Apolipoprotein E

OMIM: 107741
 Gene: APOE, Locus 19q13.2
 Indications: Dyslipoproteinemia, familial hypercholesterinemia; Morbus Alzheimer
 TAT: 1 week
 Samples: 5 ml blood in EDTA tube
 Method: Real-time PCR (LightCycler); detection of alleles E2, E3, E4

Azoospermia Factor (AZF)

OMIM: 415000
 Gene: AZF, Locus Yq11
 Indications: Infertility due to non-obstructive azoospermia or oligozoospermia
 TAT: 1 week
 Samples: 5 ml blood in EDTA tube
 Method: PCR; detection of microdeletions in the AZF-region

Cationic Trypsinogen/ Pancreatitis

OMIM: 276000
 Gene: PRSS1 , Locus 7q35
 Indications: Chronic pancreatitis before age 30 years, increased amylase and lipase in children
 TAT: 1 week
 Samples: 5 ml blood in EDTA tube
 Method: PCR, sequencing of exon 2 and 3; detection rate > 90%

Chromosomal Analysis

General: Infertility, due to

Unalanced chromosomal disturbances

47,XXY karyotype (Klinefelter syndrome)
 45,X karyotype (Turner-syndrom)
 47,XXX karyotype

Balanced chromosomal disturbances

Azoo-, oligozoospermia

Gene disturbances

Aplasia of vas deferentia (mutations in the cystic fibrosis gene, mucoviscidosis, CFTR gene), AZF. Azoospermia Factor (AZF), Y-chromosomal deletion

Recurrent Abortion

Mutations in the clotting factors V and II (Prothrombin), Methylen-Tetrahydro-Folate-Reductase (MTHFR)

The following investigations are available:

1. Chromosomal analysis from amniotic fluid

Indications: maternal age >35 years, previous abortions or missed abortions, paternal chromosomal structural abnormalities, malformation, diagnostic abnormal findings (PAPP-A, Triple-Test), abnormal ultrasound, previous

delivery (-ies) of children with chromosomal abnormalities, previous delivery (-ies) of children with malformation, mutagenic exposure during pregnancy.

TAT: 10 days up to three weeks
 Samples: 20 ml amniotic fluid
 Method: Cell culture of amniotic fluid cells; chromosomal analysis (Trypsin-Giemsa staining)

2. Chromosomal Analysis from Chorion Villi

Indications: early prenatal Diagnosis (from 10th week of gestation onwards), further procedures as with amniotic fluid

TAT: Direct preparation of trophoblast cells: 1–2 days,
 Cultivation of chorion cells: 2–3 weeks
 Samples: Chorion biopsy
 Method: Cell culture of chorionic cells; Chromosomal Analysis (High Resolution Trypsin-Giemsa-Banding)

3. Chromosomal Analysis from Abortion Material

Indications: Previous Abortion(s), known paternal chromosomal abnormalities, previous delivery(-ies) of children with chromosomal abnormalities

TAT: 3–4 weeks
 Samples: Abortion Material (very fresh!!, not in Formaline!!)
 Method: Cell Culture, Chromosomal Analysis (Trypsin-Giemsa-Banding); Microsatellite Analysis of female Karyotypes in order to exclude maternal contamination.

4. Chromosomal analysis from Peripheral Lymphocytes

Indications: Infertility, Delivery (ies) of children with chromosomal abnormalities, recurrent abortions, abnormal findings in prenatal Chromosomal Analysis, Suspicion of Dysmorphic Syndrome, Suspicion of gonosomal abnormalities.

TAT: around. 10 days
 Samples: 2–5 ml sterile Heparin blood (without adds for centrifugation such as plastic pearls or gel)
 Method: Cell Culture of peripeheral T-Cells; Chromosomal Analysis (Trypsin-Giemsa-Banding)

Chromosomal Rearrangements and Microdeletions

Indications: Suspicion of Microdeletion-Syndrome (e.g. Prader-Willi-Syndrome, Cri-du-chat-Syndrome, Wolf-Hirschhorn-Syndrome, Williams-Beuren-Syndrome, DiGeorge-Syndrome etc.), chromosomal Translocations

TAT: 5 days
 Samples: 2–5 ml sterile Heparin blood
 Method: Chromosome staining, Fluoreszenz-in-situ-Hybridization (FISH)

Collagen Type 1, alpha (COL1A1)

OMIM: 120150
 Gene: COL1A1, Locus 17q21.31-q22
 Indications: Osteoporosis, before hormone substitution therapy
 TAT: 1 week
 Samples: 5 ml blood in EDTA tube
 Method: PCR-RFLP; S/s-polymorphism

Congenital Bilateral Aplasia of Vas Deferens (CBAVD)

- OMIM: 277180
Gene: CFTR, Locus 7q31.2
Indications: Infertility
TAT: 1 to 6 weeks
Samples: 5 ml blood in EDTA tube
Method: 1. PCR, hybridisation; detection of 36 mutations, about 91.8% of the Middle European mutations are detected
2. sequencing of the CFTR-gene

Cystic Fibrosis Transmembrane Conductance Regulator (CFTR)

- OMIM: 602421
Gene: CFTR, Locus 7q31.2
Indications: Predisposition for hereditary pancreatitis
TAT: 1 to 6 weeks
Samples: 5 ml EDTA-Blut
Method: 1. PCR, hybridization (detection of the 36 most common german mutations; more than 91,8% of all mutations of the Middle European population are detected)
2. sequencing of the CFTR-gene

Cystic Fibrosis (Mukoviscidosis)

- OMIM: 219700
Gene: CFTR, Locus 7q31.2
Indications: Meconium ileus, chronic bronchopulmonary infection with emphysema, high electrolyte concentration in sweat, infertility; analysis of carrier status in families of risk
TAT: 1 to 6 weeks
Samples: 5 ml blood in EDTA tube
Method: depending on request and ethnic origin; Real-time PCR (Light-Cycler-Technique); detection of mutation F508del PCR, hybridisation; detection of 36 mutations, about 91.8% of the middle European mutations are detected by sequencing of the CFTR-gene

Cytochrome P450 (CYP1A1, CYP1A2)

- OMIM: 108330
Gene: CYP1A1, CYP1A2, Locus 15q22-q24;
Indications: Intoxication
TAT: 1 week
Samples: 5 ml blood in EDTA tube
Method: PCR, detection of polymorphisms

Factor V Leiden

| | |
|--------------|---|
| OMIM: | 227400 |
| Gene: | Factor V, Locus 1q23 |
| Indications: | Thrombosis, positive family history |
| TAT: | 3–5 days |
| Samples: | 5 ml blood in EDTA tube |
| Method: | Real Time PCR (Light Cycler), Detection of the mutation Leiden G1691A (R506Q) |

Factor XIII Gene

| | |
|--------------|--|
| OMIM: | 134570, 134570.0010 |
| Gene: | FXIII A, Locus 6p25-24 |
| Indications: | Factor XIII deficiency |
| TAT: | 3–5 days |
| Samples: | 5 ml blood in EDTA tube |
| Method: | Real Time PCR (Light Cycler), Detection of the polymorphism H1299R |

FAP (Familial adenomatous polyposis coli)

| | |
|-------------|---|
| OMIM: | 175100 |
| Gene: | APC, Locus 5q21-q22 |
| Indication: | Classic FAP with > 100 adenomas, attenuated FAP, Flat adenoma syndrome (5-100 adenomas: later onset than classic FAP) Gardner-Syndrome (like classic FAP with extracolonic manifestation: epidermoid cysts, Osteomas, desmoids) Turcot-Syndrome (like classic FAP with extracolonic manifestation (CNS-tumors: medulloblastomas) |
| TAT: | 4 months |
| Samples: | 5 ml blood in EDTA tube |
| Method: | DHPLC-analysis of all exons including exon-intron boundaries, if necessary sequencing |

Fragile X-Syndrome

1. Fragile Site Mental Retardation 1 Gene, FMR1

| | |
|--------------|--|
| OMIM: | 309550 |
| Gene: | FMR1, Locus Xq27.3 |
| Indications: | mental retardation (mainly boys, incidence 1:1250) |
| TAT: | 2 weeks |
| Samples: | 5 ml blood in EDTA tube |
| Method: | Southern Blot; PCR, determination of CGG-repeat-length |

2. Fragile Site Mental Retardation 2 Gene, FMR2

| | |
|-------|-------------------|
| OMIM: | 309548 |
| Gene: | FMR-2, Locus Xq28 |

Indications: mental retardation (mainly boys)
 TAT: 2 weeks
 Samples: 5 ml blood in EDTA tube
 Method: Southern Blot; determination of CGG-repeat-length

Glucose-6-phosphate-dehydrogenase deficiency

OMIM: 305900
 Gene: G6PD, Locus Xq28
 Indications: Anemia
 TAT: 2 weeks
 Samples: 5 ml blood in EDTA tube
 Method: PCR, sequencing of coding regions

Glutathione-S-Transferase M1 / T1

OMIM: 138350, 600436
 Gene: GSTM1, GSTT1, Locus 1p13.3; 22q11.2
 Indications: Intoxication
 TAT: 1 week
 Samples: 5 ml blood in EDTA tube
 Method: PCR; detection of homozygous deletion of GSTM1- and GSTT1-gene

Hereditary Breast and Ovarian cancer

OMIM: 13705, 600185
 Gene: BRCA1, Locus 17q21
 BRCA-2, Locus 13q12.3
 Indication: Hereditary Breast and Ovarian cancer
 TAT: 6 months
 Samples: 5 ml blood in EDTA tube, declaration of consent, family history or family tree with age at onset
 Method: Analysis of all coding exons including exon-intron boundaries, if necessary sequencing

Hereditary Hemochromatosis

OMIM: 235200
 Gene: HFE, Locus 6p21.3
 Indications: elevated transferrin saturation, increased serum ferritin levels, and liver iron content, liver cirrhosis, diabetes mellitus, hypermelanotic pigmentation of the skin, cardiomyopathy, positive family history
 TAT: 1–2 weeks
 Samples: 5 ml blood in EDTA tube
 Method: 1. Real-time PCR (LightCycler); detection of mutations C282Y, H63D, and S65C
 2. PCR, sequencing of all coding exons of the HFE-gene

Hereditary Hemochromatosis type 2B (juvenile type)

OMIM: 602390

Gene: Heparin Antimicrobial Peptide gene (HAMP, Heparin), Locus 19q13

Indications: juvenile hemochromatosis, age of onset 2. decade, adult hemochromatosis with heterozygous C282Y HFE-mutation; elevated transferrin saturation, increased serum ferritin levels, increased liver iron content, liver cirrhosis, diabetes mellitus, hypermelanotic pigmentation of the skin, cardiomyopathy, positive family history

TAT: 2 weeks

Samples: 5 ml blood in EDTA tube

Method: PCR, sequencing of all exons of the HAMP-gene

Hereditary Nonpolyposis Colorectal Cancer (HNPCC)

OMIM: 114500

Gene: MSH2, Locus 2p21-22
MLH1, Locus 3p21
MSH6, Locus 2p16
analysed microsatellite markers: BAT 25, BAT 26, D2S123, D5S346, D17S250

Indications: Colon cancer <45 years with familial disposition and HNPCC-associated tumor; histopathological criteria, adenomas < 40 years

TAT: Microsatellite analysis, around 6 weeks, gene analysis around 4 months

Samples: 5 ml blood in EDTA tube, tumor tissue

Method: PCR; detection of microsatellite instability in tumor-DNA compared to blood-DNA

HLA Typing

OMIM: 142800

Gene: Major Histocompatibility Complex (MHC), Locus 6p21.3

Indications: autoimmune disorders such as M. Bechterew, diabetes, arthritis, coeliac disease, narcolepsy

TAT: 2 days – 2 weeks

Samples: 5 ml blood in EDTA tube

Method: Sequence-specific PCR (SSP)

Huntington Disease

OMIM: 143100

Gene: IT15, Locus 4p16.3

Indications: Chorea, dementia, positive family history

TAT: 1 week

Samples: 5 ml blood in EDTA tube

Method: PCR; determination of the CAG-repeat-length

Hyperbilirubinemia (Gilbert Syndrome)

OMIM: 143500

Gene: UGT1A1, Locus 2q37

Indications: Hyperbilirubinemia of unclear etiology
 TAT: 2 weeks
 Samples: 5 ml blood in EDTA tube
 Method: PCR; detection of the TA-expansion in the promotor

Kearns-Sayre-Syndrome, Pearson Syndrome

Synonyme: Chronic Progressive External Ophthalmoplegia (CPEO)
 OMIM: 530000, 557000
 Gene: Mitochondrial genome
 Indications: Mitochondriopathy
 TAT: 1 week
 Samples: Muscle biopsy, buccal swabs, 5 ml blood in EDTA tube
 Method: Long PCR, quantification; detection of deletions/duplications

Lactose Intolerance (Adult Type)

OMIM: 223100
 Gene: Lactase-Phlorizin-Hydrolase gene (LPH), Locus 2q21
 Indications: Lactose intolerance, diarrhoe
 TAT: 1 week
 Samples: 5 ml blood in EDTA tube
 Method: PCR, sequencing of the promotor polymorphism -13910 of LPH-gene

Leber's Hereditary Optic Neuropathy (LHON)

OMIM: 535000
 Gene: ND1, ND4, ND6, mitochondrial genome
 Indications: bilateral or unilateral optic neuropathy
 TAT: 1 week
 Samples: 5 ml blood in EDTA tube
 Method: PCR-RFLP, quantification; detection of the three primary point mutations G11778A, G3460A, T14484A

Leigh Syndrome

Synonyme: NARP Syndrome, (Neuropathy, Ataxia, and Retinitis Pigmentosa)
 OMIM: 256000, 551500
 Gene: ATPase6, mitochondrial genome
 Indications: Myoclonic epilepsy, ragged-red fibers
 TAT: 1 week
 Samples: 5 ml blood in EDTA tube
 Method: PCR-RFLP, quantification; detection of the point mutation T8993G and T8993C

Leukemia

Synonyme: Philadelphia chromosome, translocation t(9;22), bcr-abl fusion gene
Gene: Translocation 9q and 22q; bcr-abl major and minor regions
Indications: CML, B-ALL
TAT: 2–3 working days
Samples: 5 ml blood (peripheral or bone marrow) in EDTA tube
Method: RT-PCR, nested PCR

Low Density Lipoprotein Receptor (LDLR)

OMIM: 606945
Gene: LDLR, Locus 19p13.2
Indications: Familial Hypercholesterinemia
TAT: 4 weeks
Samples: 5 ml blood in EDTA tube
Method: PCR, sequencing of the total LDLR-gene, MLPA; detection of point mutations and deletions

Marfan Syndrome

OMIM: 154700
Gene: Fibrillin-1 (FBN1), Locus 15q21.1
Indications: Weak connective tissue, increased height, disproportionately long limbs and digits, anterior chest deformity, mild to moderate joint laxity, vertebral column deformity (scoliosis and thoracic lordosis), subluxation of the lenses
TAT: 6 weeks
Samples: 5 ml blood in EDTA tube
Method: sequencing of all 65 exons

Mediterranean Fever

OMIM: 249100
Gene: Pylrin, Locus 16p13
Indications: Periodic fever, abdominal pain, peritonitis, amyloidosis
TAT: 2 weeks
Samples: 5 ml blood in EDTA tube
Method: PCR, sequencing of exons 1, 2, 3, 5, and 10

MELAS Syndrome

Synonyme: Mitochondrial Myopathy, encephalopathy, and lactic acidosis with stroke-like episodes
OMIM: 540000
Gene: tRNA genes, mitochondrial genome
Indications: Myopathy, lactic acidosis, mitochondriopathy

TAT: 1 week

Samples: Muscle biopsy, buccal swabs, 5 ml blood in EDTA tube

Method: PCR-RFLP, quantification; detection of the point mutation A3243G

Methylentetrahydrofolate-reductase

OMIM: 607093

Gene: MTHFR gene, Locus 1p36.3

Indications: Thrombosis, Neural tube defects, Folate metabolism, Hyperhomocysteinemia

TAT: 3–5 days

Samples: 5 ml blood in EDTA tube

Method: Real Time PCR (Light Cycler), Detection of the polymorphisms C677T (A222V) and A1298C

Mitochondrial Diabetes

OMIM: 520000, 590050

Gene: tRNA L(UUR), mitochondrial genome

Indications: Atypical diabetes, diabetes maybe associated with deafness or hypertrophic cardiomyopathy

TAT: 1 week

Samples: 5 ml blood in EDTA tube

Method: PCR-RFLP, quantification; detection of the point mutation A3243G

Multiple Endocrine Neoplasia Type II (MEN II)

OMIM: 171400

Gene: RET-protooncogene, Locus 10q11.2

Indications: Medullar thyroid carcinoma, isolated or associated with pheochromocytoma, hyperparathyroidism, ganglioneuromatosis, positive family history

TAT: 2 weeks

Samples: 5 ml blood in EDTA tube

Method: PCR, sequencing of exons 10, 11, 13, 14, 15, and 16

Muscular Dystrophy Type Duchenne/Becker

OMIM: 310200, 300376

Gene: Dystrophin, Locus Xp21

Indications: Muscular dystrophy, carrier status in families of risk

TAT: 2 weeks

Samples: 5 ml blood in EDTA tube

Method: Multiplex-PCR, microsatellite analysis, MLPA; detection of deletions and duplications

Myoclonic Epilepsy with ragged-red fibers

Synonyme: MERRF Syndrome

OMIM: 545000
Gene: tRNA genes, mitochondrial genome
Indications: Myoclonic epilepsy, ragged-red fibers
TAT: 1 week
Samples: Muscle biopsy, buccal swabs, 5 ml blood in EDTA tube
Method: PCR-RFLP, quantification; detection of the point mutation A8344G

Myotonic Dystrophy type 1

OMIM: 160900
Gene: DMPK, Locus 19q13.2-13.3
Indications: Myotonia, muscular dystrophy, cataract, hypogonadism
TAT: 3 weeks
Samples: 5 ml blood in EDTA tube
Method: PCR, fragment analysis, Southern Blot; determination of CTG-repeat-length

Myotonic Dystrophy type 2

Synonym: Proximal Myotonic Myopathy (PROMM)
OMIM: 602668
Gene: ZNF9, Locus 3q21
Indications: Adult-onset myotonia, muscular dystrophy, cataract, hypogonadism
TAT: 3 weeks
Samples: 5 ml blood in EDTA tube
Method: PCR, Long PCR, fragment analysis; determination of CCTG-repeat-length

N-Acetyltransferase (NAT2)

OMIM: 243400
Gene: NAT2, Locus 8p23.1-21.3
Indications: Intoxication, determination of acetylation activity (low or high)
TAT: 1 week
Samples: 5 ml blood in EDTA tube
Method: PCR, sequencing

Neuropathy, hereditary with liability to pressure palsies (HNPP)

OMIM: 162500
Gene: PMP22, Locus 17p11.2
Indications: Tomaculous neuropathy, peroneal neuropathy
TAT: 1 week
Samples: 5 ml blood in EDTA tube
Method: MLPA; screening for deletions

Neuropathy, hereditary, motor and sensory Type I (HMSN Type IA)/ Charot-Marie-Tooth Type I (CMT Type IA)

OMIM: 118200

Gene: PMP22, Locus 17p11.2

Indications: Neuropathy muscular atrophy, reduced motor and nerve conduction velocity, progressive distal weakness of arms and legs.

TAT: 1 week

Samples: 5 ml blood in EDTA tube

Method: MLPA; screening for duplications

Osteoporosis

Gene: COL1A1, Vitamine D receptor

Indications: Osteoporosis, before hormone substitution therapy

TAT: 1 week

Samples: 5 ml blood in EDTA tube

Method: PCR-RFLP, Real Time PCR (Light Cycler)

Paternity Testing

Gene: 16 polymorphic regions on different chromosomes

Indications: Paternity testing, twin analysis

TAT: 2 weeks

Samples: 5 ml blood in EDTA tube, buccal swab (esp. for children)

Method: PCR, microsatellite analysis

Note: for a request form please download the English documents (PDF) at our homepage: <http://www.humane-genetik.de/formulardownload2.html>

Phenylketonuria / Hyperphenylalaninemia

OMIM: 261600

Gene: PAH, Locus 11q22.3

Indications: Positive newborn screening, hyperphenylalaninemia

TAT: 3 weeks

Samples: 5 ml blood in EDTA tube

Method: PCR, sequencing of all 13 exons

Plasminogen activator inhibitor (PAI 1)

OMIM: 173360

Gene: PAI 1, Locus 7q21.3-q22

Indications: Thrombosis, positive family history

TAT: 3–5 days

Samples: 5 ml blood in EDTA tube
Method: Real Time PCR (Light Cycler), Detection of the 4G/5G-polymorphism

Platelet Glycoprotein IIb/IIIa

OMIM: 173470
Gene: GPIIIa (ITGB3), Locus 17q21.32
Indications: Thrombosis, Coronary Stenting, acute myocardial infarction
TAT: 3-5 days
Samples: 5 ml blood in EDTA tube
Method: Real Time PCR (Light Cycler), Detection of the polymorphism C1565T (L33P; HPA-1a/1b)

Prader-Willi Syndrome

OMIM: 249100
Gene: SNRPN, Locus 15q11-13
Indications: Newborn with muscular hypotonia, children with obesity, mental retardation, short stature, hypogonadotropic hypogonadism
TAT: 2 weeks
Samples: 5 ml blood in EDTA tube; for requests with chromosomal analysis 5 ml blood in heparin tube
Method: Methylation-sensitive PCR, microsatellite analysis, FISH

Prothrombin (Factor II)

OMIM: 176930
Gene: Factor II, Locus 11q11
Indications: Thrombosis, positive family history
TAT: 3-5 days
Samples: 5 ml blood in EDTA tube
Method: Real Time PCR (Light Cycler), Detection of the promotor-mutation G20210A

Rett-Syndrome

OMIM: 312750
Gene: MeCP2, Locus Xq28
Indication: Mental retardation, mainly in girls, autism, loss of motoric use of the hands
TAT: 2 weeks
Samples: 5 ml blood in EDTA tube
Method: PCR, dHPLC, sequencing of coding regions

Serine Protease Inhibitor, Kazal Type 1

OMIM: 167790
Gene: SPINK1 (Serin Protease Inhibitor, Kazal Type 1, Locus 5q32)

Indications: Predisposition for hereditary pancreatitis

TAT: 1 week

Samples: 5 ml blood in EDTA tube

Method: PCR-RFLP, detection of mutation N34S in exon 3; if necessary resequencing of all 4 exons

Sickle Cell Anemia

OMIM: 603903

Gene: HBB, Locus 11p15.5

Indications: suspicious for sickle cell anemia

TAT: 1 week

Samples: 5 ml blood in EDTA tube

Method: Real-time PCR (LightCycler), detection of mutation HbS and HbC Cholesterol Homeostasis

Spinal Muscular Atrophy Type I / II / III

Type I (Werdnig-Hoffmann) / II (intermediate) / III (Kugelberg-Welander)

OMIM: 253300, 253550, 253400

Gene: SMN1, Locus 5q12.2-q13.3

Indications: Muscular atrophy; Hypertrophic Cardiomyopathy, carrier status in families of risk

TAT: 1 week

Samples: 5 ml blood in EDTA tube

Method: Real-time PCR (LightCycler), microsatellite analysis; detection of homozygous deletions

Spinal and Bulbar Muscular Atrophy (Kennedy Disease)

OMIM: 313200

Gene: AR, Locus Xq11-q12

Indications: Muscular atrophy (spinal and bulbar), muscle weakness, fasciculations

TAT: 1 week

Samples: 5 ml blood in EDTA tube

Method: PCR; determination of CAG-repeat-length

Steroid 5- α -Reductase 2

OMIM: 607306

Gene: SRD5A2, Locus 2p23

Indications: Predisposition for prostate cancer

TAT: 1 week

Samples: 5 ml blood in EDTA tube

Method: PCR, sequencing of polymorphisms A49T and V89L

α-Thalassemia

OMIM: 141800
Gene: HBA1, HBA2, Locus 16pter-p13.3
Indications: Anemia, hypochromasia, microcytosis
TAT: 3–4 weeks
Samples: 5 ml blood in EDTA tube
Method: PCR; detection of deletions and point mutations

β-Thalassemia

OMIM: 141900
Gene: HBB, Locus 11p15.5
Indications: Microcytic anemia, HbA2-, HbF- increase
TAT: 3–4 weeks
Samples: 5 ml blood in EDTA tube
Method: PCR, sequencing of the total HBB-gene

Thiopurine S-Methyltransferase (TPMT)

OMIM: 187680
Gene: TPMT, Locus 6p22.3
Indications: Incompatibility of thiopurine-derivatives, 6-mercaptopurine sensitivity
TAT: 1 week
Samples: 5 ml blood in EDTA tube
Method: Real-time PCR (LightCycler); detection of the polymorphisms G460A and A719G

Thrombophilia

Gene: Factor V, Factor II (prothrombin), PAI 1, MTHFR etc.
Indications: Thrombophilia, embolisms, atherosclerosis, homocysteinuria
TAT: 3 days - 1 week, dependent on test
Samples: 5 ml blood in EDTA tube
Method: Real-time PCR (LightCycler), PCR-RFLP

Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS)

OMIM: 142680
Gene: TNFRSF1A, Locus 12p13.2
Indications: periodic fever, skin lesions, myalgia
TAT: 2–3 weeks
Samples: 5 ml blood in EDTA tube
Method: PCR, sequencing of exons 2, 3, 4, 6, and 7

UDP-Glucuronosyltransferase-Gene (UGT1A1)

OMIM: 191740

Gene: UGT1A1, Locus 2q37

Indications: Intoxication, hyperbilirubinemia of unclear etiology (Gilbert Syndrome)

TAT: 2 weeks

Samples: 5 ml blood in EDTA tube

Method: PCR; detection of the TA-expansion in the promotor

Vitamin D Receptor (VDR)

OMIM: 601759

Gene: VDR, Locus 12q12-q14

Indications: Osteoporosis, before hormone substitution therapy

TAT: 1 week

Samples: 5 ml blood in EDTA tube

Method: PCR-RFLP, VDR-b/B polymorphism

Wilson Disease

OMIM: 277900

Gene: ATP7B, Locus 13q14.3

Indications: Low ceruloplasmin in the serum, Kayser-Fleischer cornea ring

TAT: 1 week

Samples: 5 ml blood in EDTA tube

Method: Real-time PCR (LightCycler); detection of Mutation H1069Q

