Request for Molecular Genetic Testing

Diagnostic Laboratories Department of Pediatrics and Adolescent Medicine
Medical Director: Prof. Dr. K.-M. Debatin
Prof. Dr. Georgia Lahr
Molecular Diagnostics Laboratory
University Medical Center Ulm
Eythstrasse 24 - D-89075 Ulm
Germany

Informed consent of patient

The German law (**Gendiagnostikgesetz – GenDG**) defines under which circumstances genetic testing of a human individual is legal. *Diagnostic* testing can only be conducted with the patient's informed consent which requires documented consultation with a doctor. *Predictive* testing requires genetic counselling by a human genetics specialist prior to and after the investigation, or the patient's written renunciation.
Please fill out the informed consent carefully and completely and sign it. Otherwise no molecular genetic testing can be performed!

Molecular Genetic Testing

3-5 ml EDTA-blood (send by normal mail)
Turnaround time: 2-4 weeks, more than one analysis and rare analyses may take up to 8 weeks

	OMIM	Disease	Gene
	Immunology		
	Immunodeficiency SCID (T-B+)		
❑	OMIM 300400	Severe Combinined Immunodeficiency (SCID, X-chromosomal, T-, B+, NK-)	IL2RG
❑	OMIM 606367	Severe Combinined Immunodeficiency, CD25 deficiency	IL2RA
❑	OMIM 600802	Severe Combinined Immunodeficiency (SCID, T-, B+, NK-), JAK3 deficiency	JAK3
❑	OMIM 608971	Severe Combinined Immunodeficiency (SCID, T- B+ NK+), IL7R deficiency	IL7R
❑	OMIM 608971	Severe Combinined Immunodeficiency (SCID, T- B+ NK+), CD3D deficiency	CD3D
❑	OMIM 608971	Severe Combinined Immunodeficiency (SCID, T- B+ NK+), CD3E deficiency	CD3E
	Other defined immune disorders		
❑	OMIM 109535	Immunideficiency - Hyper-IgM-Syndrome (HIGM 3)	CD40
❑	OMIM 300386	Hyper-IgM-Syndrome, X-linked (HIGM 1), (SCID, T- B-)	CD40L
❑	OMIM 176947	Severe Combinined Immunodeficiency (SCID, T-, B-), ZAP70 deficiency, CD8 deficiency	ZAP70
❑	OMIM 301000	Wiskott-Aldrich Syndrome	WASP
❑	OMIM 603553	familial hemophagocytic lymphohistiocytosis (FHL2; HLH2)	PRF1
❑	OMIM 240300	autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APS1), APECED	AIRE
❑	OMIM 304790	immune dysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX)	FOXP3
❑	OMIM 209950	familial disseminated atypical mycobacterial infection and disseminated BCG infection (FDAMI)	IFNGR1
❑	OMIM 601859	Autoimmune lymphoproliferative syndrome (ALPS1a), Canale-Smith-Syndrome	APO1
❑	OMIM 601859	Autoimmune lymphoproliferative syndrome (ALPS1b), Canale-Smith-Syndrome	FASL
❑	OMIM 603909	Autoimmune lymphoproliferative syndrome (ALPS2a), Canale-Smith-Syndrome	CASP10
❑	OMIM 607271	Autoimmune lymphoproliferative syndrome (ALPS2b), Canale-Smith-Syndrome	CASP8
❑	OMIM 164790	Autoimmune lymphoproliferative syndrome (ALPS4); N-RAS exon 2	N-Ras
❑	OMIM 308240	X-linked lymphoproliferative syndrome (XLP), Purtillo-Syndrome (SH2D1A)	SAP
❑	OMIM 613011	EBV-associated lymphoproliferative diseases, autosmal-rezessive; IL2-inducible T-cell kinase, ITK deficiency	ITK
❑	OMIM 300079	X-linked lymphoproliferative syndrome (XLP2), BIRC4 deficiency	BIRC4
❑	OMIM 154545	infections, recurrent, with chronic diarrhea and opsonisation defect (low MBL2), including susceptibility to meningococcal disease, MBL2 deficiency; polymorphisms in promotor and exon 1: -550 C/G, -221 C/G; p.T24A, p.R52C, p.G54D >	MBL2
❑	OMIM 123890	Graves disease, susceptibility locus 5 (GD5S), T-cell defect	CTLA4
❑	OMIM 305000	Dyskeratosis congenita; X-linked; Codon: p.A353V	DKC1
❑	OMIM 305000	Dyskeratosis congenita-1; X-linked	DKC1
❑	OMIM 266100	epilepsy, pyridoxine-dependent (EPD); pyridoxine dependency with seizures, ALDH7A1 deficiency	ALDH7A1
❑	OMIM 606609	Aicardi-Goutieres Syndroms AGS, chilblain lupus CHBL, hereditary endotheliopathy with retinopathy, nephropathy and	TREX1
❑	OMIM 300645	chronic granulomatous disease 1 (CGD1); X-linked granulomatous disease; cytochrome b-245, beta polypeptide	CYBB
❑	OMIM 608508	CGD; Chronic Granulomatosis; Cytochrome b-245 Alpha Kette - CYBA	CYBA
❑	OMIM 612301	CGD; Chronic Granulomatosis; neutrophile cytosolic factor 2 - NCF2	NCF2
❑	OMIM 102582	Hyper-IgE-Syndrome, autosomal-dominant (exons 13, 21 und 23; p.K392R; pN646K; pK658N; p.T715M)	STAT3
❑	OMIM 300248	*incontinentia pigmenti, hypohidrotic ectodermal dysplasia, (EDA-ID); X-chrom. recessive (NEMO); not: Incontinentia Pigmenti -del. Ex 4-10!	IKBKG
	Osteopetrosis	* not accreditated	
❑	OMIM 602727	osteopetrosis, Albers-Schonberg disease 4 (OPTB4), recessive	CLCN7
❑	OMIM 602727	osteopetrosis, type II (OPTA2), autosomal dominant, ADOII, Albers-Schoenberg disease	CLCN7
❑	OMIM 604592	osteopetrosis, lethal B1 (OPTB1)	TCIRG1
❑	OMIM 607649	osteopetrosis type 1B 5 (OPTB5), malignant infantile	OSTM1
❑	OMIM 602642	osteopetrosis type B2 (POTB2), TNFSF11 deficiency	RANKL
❑	OMIM 612301	Osteopetrosis, (TNFRSF11A), Hypogammaglobulinämia	RANK
❑	OMIM 612301	Osteopetrosis, (SNX10), Typ B7	SNX10
	Periodic Fever Syndromes		
❑	OMIM 249100	Familial Mediterranean fever (FMF)	MEFV
❑	OMIM 142680	TNF receptor associated periodic syndrome, benign autosomal dominant familial periodic fever (FPF), Hibernian fever	TRAPS
❑	OMIM 260920	Hyperimmunoglobulinemia D with recurrent fever (HIDS), mevalonate kinase deficiency	MVK
	Hematology		
❑	OMIM 300367	dyserythropoietic anemia with thrombocytopenia (X-linked), CDATX	GATA-1
❑	OMIM 603474	Diamond-Blackfan anemia (DBA)	RPS19
❑	OMIM 603634	Diamond-Blackfan anemia (DBA5)	RPL5
❑	OMIM 611184	Dehydrated hereditary Stomatocytosis 1 (DHD1); Hereditary Xerozytosis	PIEZO1
❑	OMIM 602754	Dehydrated hereditäre Stomatocytosis 2 (DHD2); Hereditary Xerozytosis	KCNN4
❑	OMIM 159530	congenital amegakaryocytic thrombocytopenia (CAMT)	MPL
❑	OMIM 600044	thrombocythemia, essential (THPO)	THPO

Request for Molecular Genetic Testing

Diagnostic Laboratories Department of Pediatrics and Adolescent Medicine
Medical Director: Prof. Dr. K.-M. Debatin
Prof. Dr. Georgia Lahr
Molecular Diagnostics Laboratory
University Medical Center Ulm
Eythstrasse 24 - D-89075 Ulm -Germany

	OMIM	Disease	Gene
	Hematology		
❑	OMIM 137295	*MonoMAC Syndrome; acute myeloid Leukmia, AML	GATA2
❑	OMIM 615888	*LADIII leukocyte adhesion deficiency	RASGRP2
❑	OMIM 206200	iron-refractory iron deficiency anemia (IRIDA)	TMPRSS6
❑	OMIM 600424	disturbance in MTX clearance, high MTX levels	SLC19A1/GGH
❑	OMIM 249270	thiamine responsive megaloblastic anemia (TRMA)	SLC19A2
❑	OMIM 600523	pseudo-iron deficiency anemia (PIDA), microcytic anemia with liver iron overload , DMT1 deficiency	SLC11A2/DMT1
❑	OMIM147700	isocitrate dehydrogenase 1 (NADP+), soluble, associated with brain tumors and secondary Glioblastoma	IDH1
❑	OMIM 613657	isocitrate dehydrogenase 2 (NADP+), mitochondrial; D-2-hydroxyglutaric aciduria (D2HA2)	IDH2
❑	OMIM 613673	congenital dyserythropoietic anemia, TYPE IV; CDAN4	KLF1

*not akkreditated

	Endocrinology and Diabetology		
	Disturbance in glucose regulation		
❑	OMIM 125850	Maturity-Onset Diabetes of the Young, MODY-Diabetes, MODY type 1 (MODY1)	HNF4a
❑	OMIM 125851	Maturity-Onset Diabetes of the Young, MODY-Diabetes, MODY type 2 (MODY2)	GCK
❑	OMIM 600496	Maturity-Onset Diabetes of the Young, MODY-Diabetes, MODY type 3 (MODY3)	HNF1a/TCF1
	Disturbance in body weight regulation		
❑	OMIM 155541	severe obesity (OBS3)	MC4R
❑	OMIM 164160	severe early-onset obesity (OBS1)	LEP
❑	OMIM 601007	*early-onset morbid obesity (only after having consulted Prof. Wabitsch)	LEPR
❑	OMIM 601047	Berardinelli-Seip congenital generalized lipodystrophy type (BSCL3)	CAV1
❑	OMIM 613327	congenital generalized lipodystrophy type 4 (CGL4)	PTRF
	Disturbance of growth		
❑	OMIM 117550	Sotos syndrome (STO)	NSD1
❑	OMIM 610978	congenital thyroglobulin defect with respiratory distress (TGDRD)	NKX2-1
❑	OMIM 118700	benign hereditary chorea (BHC)	NKX2-1
	Polymorphisms (possibly clinical relevant)		
❑	OMIM 174800	McCune-Albright Syndrome (MAS); polymorphisms in exons 8 & 9: p.R201C,p. R201H, p.R201G, p.Q227H, p.Q227R	GNAS
❑	OMIM 167413	*Diabetes; polymorphism in exon 9: rs712701(c.962A>C; p.P321H)	PAX4
❑	OMIM 173360	*Obesity; polymorphism in promotor: rs1799768 (NG_013213.1:g.4328_4329insC; -675 4G/5G)	PAI1
❑	OMIM 601487	*Obesity and thromboembolism; polymorphism in exon 1: rs1801282 (c.34C>G; p.Pro12Ala)	PPARg2
❑	OMIM 151750	*Obesity; polymorphism in IVS6 : rs57282318 (rs71167395; NM_005357.3:c.2365+142_2365+145delGTGT)	HSL
❑	OMIM 170290	*Obesity;polymorphism in IVS6 : rs894160 (NM_002666.3:c.772-799A>G)	PLIN
❑	OMIM 190220	*Obesity and Diabetes; polymorphism in exon 1: rs1800470 (c.17T>C; p.Leu10Pro)	TGFB1
❑	OMIM 601283	*Obesity; Diabetes Mellitus, Noninsulin-dependent, 1 (NIDDM1); intronisc polymorphisms: IVS6; rs3842570 (NM_023083.4:c.997+116Indel), IVS3 rs3792267 (NM_021251.3:c.141+4705G>A) und IVS1 3rs5030952 (NM_023089.1:c.274-13102G>C)	CAPN10
❑	OMIM 605441	*Obesity, Adipocyte, C1q, and Collagen Domain containing,(ADIPOQ); polymorphism in exon 9: rs2241766 (NM_004797.2:c.45T>G; p.Gly15Gly)	APM1
❑	OMIM 601693	*Obesity; polymorphism in promoter: rs659366 (NG_011478.1:g.4136G>A)	UCP-2
❑	OMIM 600716	*Diabetes (type 1); polymorphism in exon 9: rs2476601 (NM_012411.2; c.1858C>TArg620Trp)	PTPN22
	Gastroenterology		
❑	OMIM 608374	hemochromatosis, type 2, Hämojuvelin (HVJ); HFE2	HVJ
❑	OMIM 604250	hemochromatosis, type 3 ; transferrin receptor 2, TFR2	HFE3/TFR2
❑	OMIM 606069	hematochromatosis, type 4 ; solute carrier family 40 (iron-regulated transporter), member 1, FPN1 / SLC40A1	HFE4/FPN1
❑	OMIM 602390	hemochromatosis, juvenile, (JH), (HFE2B)	HAMP
❑	OMIM 143500	Gilbert-Syndrom (GBTS)	UGT1A1
❑	OMIM 146933	chronic inflammatory bowel disease, interleukin 10 receptor, alpha; IL10RA	IL10Ra
❑	OMIM 123889	chronic inflammatory bowel disease, interleukin 10 receptor, beta; IL10RB	IL10Rb
❑	OMIM 124092	chronic inflammatory bowel disease, interleukin 10; early onset	IL10
❑	OMIM 610370	congenital malabsorptive diarrhea 4 (DIAR4); T2DM; hyperproinsulinaemia	NEUROG3
	Polymorphisms (possibly clinical relevant)		
❑	OMIM 266600	chronic inflammatory bowel disease, 1 (IBD1), Morbus Crohn	NOD2
❑	OMIM 605956	Hepatic veno-occlusive disease or veno-occlusive disease (VOD)	NOD2
❑	OMIM 235200	hemochromatosis (HFE1); polymorphism p.H63D, p.S65C und p.C282Y	HFE
❑	OMIM 235200	hemochromatosis (HFE1)	HFE
❑	OMIM 613282	*nonalkoholic fatty liver disease ; polymorphism in exon3 and 9: rs738409 (c.444C>G;p.I148M) & rs6006460 (c.1358G>T; p.S453I)	PNPLA3
❑	OMIM 107720	*Insulin resistance in nonalcoholic fatty liver disease (NG_008949.1:g.4546C>T (c.-482C>T; c.-455T>C)	APOC3
❑	OMIM 156845	*Waardenburg syndrome, type 2A", WS2, WS2A; polymorphism in exon 9: rs149617956 (p.E318K; p.Glu318Lys)	MITF

Information about the indication of molecular diagnostis can be achieved via "**The portal for rare diseases and orphan drugs**" - ***orphanet-*** : http://www.orpha.net/consor/cgi-bin/index.php or http://www.orpha.net/consor/cgi-bin/Disease_Genes.php?lng=EN

External quality assurance (EQA):

our laboratory participates regulary on „Ringversuche" of the national Reference Institute for Bioanalytics (RfB). These RfB-laboratories determine method-independent target values, so called reference methods values, in control materials for external quality control. In addition we routinely perform laboratory exchanges.