TRANSFERRING CODE TO DIAGNOSIS

Order Form 'Mitochondriopathies'

General Information

CeGaT Center for Genomics and Transcriptomics

Patient

Surname: _____

First name: _____

Date of birth: _____

Sex: ❑ male ❑ female

Material

❑ Blood ____ ml (min. 3 ml EDTA-blood)

❑ Dried blood spot cards (at least 10 spots)

❑ DNA ____ µg (min. 5 µg DNA, concentr. ≥ 50 ng/µl) DNA-No.: _____

❑ Other specimen _____

External ID: _____

Date of sample collection: _____

Samples can be sent by mail in a cardboard box or air cushion envelope. Samples should not be exposed to direct sunlight. Dried blood spot cards can be ordered for free (info@cegat.com).

Sender / Clinic

Surname:

First name:

Institution:

Street:

Postcode/City:

Country:

Phone:

Email:

If applicable, please include a VAT number or a copy of your business registration certificate.

VAT: _____

Invoice

❑ to patient ❑ to sender / clinic

Declaration of consent

By signing this form, I declare that I have received comprehensive information about the genetic background related to the disease in question as well as the possibilities and limitations of molecular genetic testing. I understand that I have the right to withdraw my consent to genetic analyses.

I have been informed, and agree, that the data obtained in the analysis will be recorded, evaluated, or stored in an anonymized form in scientific databases, and further, in accordance with data protection and medical confidentiality, that the request, or parts thereof, may be transmitted to a specialized cooperating laboratory. I have been informed, and agree, that all data collected by CeGaT GmbH is electronically stored, processed, and used. I also consent to the data being transmitted electronically (e.g. by e-mail or fax).

If you do not check these boxes, your answer will be recorded as "No".

I consent to the storage of my genetic material for additional tests and/or quality control (for max. 10 years). ❑ Yes ❑ No

I consent to the storage of my test results beyond the timespan of 10 years (as required by German law). ❑ Yes ❑ No

I consent to the anonymous storage and use of surplus genetic material and/or test results for scientific research. ❑ Yes ❑ No

Genetic variation may sometimes be identified, which does not fit within the scope of the requested genetic analysis (so-called secondary findings report). The reporting of these variants is limited to pathogenic alterations within selected genes, for which a treatment or course of action exists for you or your family (according to the current guidelines of the American College of Medical Genetics and Genomics; ACMG SF V2.0; Kalia et al., 2017, PMID: 27854360). There is no claim of a comprehensive analysis of the genes included within the secondary findings report. An absence of secondary findings cannot be used to indicate a reduced disease risk.

With regard to secondary findings I would like:

❑ to be informed

❑ to NOT be informed

Please Note

Our panels are regularly updated to reflect current scientific research. It should therefore be recognized that there is the possibility that the list of genes on the order form may have changed slightly (genes added or removed) by the time the sample is analyzed in the laboratory. By signing this form, the patient accepts that the list of genes actually analyzed may be slightly different from what is currently listed. When NGS is utilized more than the requested genes are sequenced for each sample.

This declaration of consent can be completely or partially withdrawn at any time. I have had sufficient time to consider giving my consent.

_____ Patient / Legal Guardian (Block letters)

_____ Doctor (Surname, First name)

X _____ Patient / Legal Guardian (Date, Signature)

X _____ Doctor (Date, Signature)

Doctor's stamp / Barcode

Contact

To discuss the diagnostic strategy please do not hesitate to contact us.
Phone: +49 7071 565 44-55
Email: diagnostic-support@cegat.de

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

CAP ACCREDITED COLLEGE of AMERICAN PATHOLOGISTS CLIA CERTIFIED ID: 99D2130225

CeGaT is accredited by DAkkS according to DIN EN ISO 15189:2014, by the College of American Pathologists (CAP) and CLIA.

Order Form 'Mitochondriopathies'

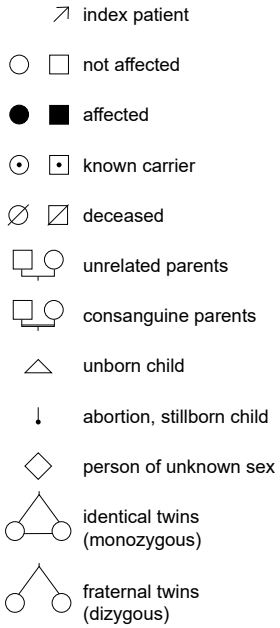
Indication & Medical history

CeGaT Center for Genomics and Transcriptomics

For targeted and effective processing, please complete the medical history form with as much detail as possible and include a copy of all existing reports.

Indication / Suspected Diagnosis

Pedigree



For a better description and illustration of the suspected familiy history, CeGaT offers a free Pedigree Chart Designer (PCD). You can find the PCD on our website or http://pedigree.cegat.de.

Additional information

Consanguinity: ❑ Yes ❑ No

Ethnic origin: _____ Age of father: _____ Age of mother: _____

Family medical history

Are there other family members who currently have or have had the same or a similar disease as the patient?

❑ Yes ❑ No Relationship to patient (e.g. mother): _____

Please list **family members** of the patient who are currently or have been affected by the following **neurological** (and other) **disorders**:

	Affected family members available?	Relationship to patient (e.g. mother)	Age of asset	**Diagnosis / Symptoms**
Muscle disorders/myopathy				
Movement disorders				
Epilepsy				
Stroke				
Inner-ear deafness				
Visual impairment				
Type II diabetes				
Other				

Order Form 'Mitochondriopathies'

Medical history of patient

Pregnancy clinical history

1. Complications during pregnancy ❑ No ❑ Yes; please describe: _____

2. Birth information Size: _____ Weight: _____ Head circumference: _____

Umbilical cord arterial pH: _____ Apgar score: _____

Due date: _____ ❑ On schedule ❑ No; birth in WOP: _____

3. Problems in neonatal period ❑ No ❑ Yes; please state: _____

4. Worsening of symptoms during infection ❑ No ❑ Yes; please describe? _____

5. Disease progression Age of onset: _____ Progressive course: ❑ No ❑ Yes

Symptoms

	Yes	No
1. Neurologic:		
Psychomotor development delay	❑	❑
Loss of psychomotor abilities	❑	❑
Stroke-like episodes	❑	❑
Muscular hypotonia	❑	❑
Ataxia	❑	❑
Dystonia	❑	❑
Spasticity	❑	❑
Difficulty in swallowing	❑	❑
Myoclonic twitches	❑	❑
Epilepsy	❑	❑
Peripheral neuropathy	❑	❑
2. Muscle:		
Muscle weakness	❑	❑
Rhabdomyolysis	❑	❑
Facies myopathica	❑	❑
3. Heart:		
Hypertrophic cardiomyopathy	❑	❑
Dilated cardiomyopathy	❑	❑
Conduction disturbance	❑	❑
4. Eyes:		
Ophthalmoplegia (CPEO)	❑	❑
Ptosis	❑	❑
Nystagmus	❑	❑
Retinitis pigmentosa	❑	❑
Optic atrophy	❑	❑
Cataract	❑	❑

	Yes	No
5. Ears:		
Sensorineural hearing loss/deafness	❑	❑
6. Gastro-intestinal system:		
Pseudoobstruction	❑	❑
Regular/cyclical vomiting	❑	❑
Chronic recurring diarrhea (>3 weeks)	❑	❑
Pancreatic insufficiency	❑	❑
7. Liver:		
Acute liver failure	❑	❑
Chronic liver failure (increased liver enzymes)	❑	❑
8. Kidney:		
Kidney failure	❑	❑
9. Endocrine system:		
Hypothyroidism	❑	❑
Adrenal failure	❑	❑
Type II diabetes	❑	❑
Other endocrine symptoms:		
10. Hematopoietic system:		
Pancytopenia	❑	❑
Hyporegenerative anemia	❑	❑
Neutropenia	❑	❑

11. Other symptoms:

Order Form 'Mitochondriopathies'

Medical history of patient

Tests previously performed (please attach copies)

Genetic tests

❑ Not performed

❑ Array-CGH

❑ Sequencing of following genes: _____

❑ Other (e.g. MLPA): _____

MRI

❑ Not performed ❑ Yes; date: _____

	Yes	No
Leukodystrophy	❑	❑
Brain atrophy	❑	❑
Symmetrical basal ganglia lesions	❑	❑
Symmetrical brain stem lesions	❑	❑
Cerebellar involvement	❑	❑

Other noticeable MRI findings: _____

EEG

❑ Not performed ❑ Yes; date:? _____ please include copy of report

Lab test – body fluids	not performed	normal	abnormal (please state values or attach test results)
Blood lactate			
Liquor lactate			
Creatine kinase			
Organic acids			
Alanine			
Other abnormal values			
Type II diabetes			

Tissue biopsies	not performed	normal	abnormal (please state values or attach test results)
Muscle			
Skin			
Liver			

Enzyme activity	not performed	normal	abnormal (please state values or attach test results)
Complex I			
Complex II			
Complex II/III			
Complex IV			
Complex V			
Pyruvate dehydrogenase			
Citrate synthase			
Other enzymes			

Findings from other tests (e.g. histology)

Inquiry Array-CGH

❑ Please perform Array-CGH before Panel Diagnostics
(Please attach a separate laboratory order)

❑ Array-CGH analysis has already taken place

❑ Array-CGH analysis not required

Inquiry

MIT: Mitochondriopathies
All genes listed on this order form, and the entire mitochondrial genome, are sequenced in parallel. This allows you to select multiple gene sets, or choose individual genes in addition to your selected gene set. As there is no additional laboratory expenditure, there is only a moderate price increase due to the subsequent analysis and interpretation. We are happy to answer your questions or send you an individual quote. Please contact us at info@cegat.com.

❑ **Large Panel Diagnostic Option (396 Genes, MIT-D45)**
In addition to the full analysis of the requested gene set(s), we will expand the analysis to all pathogenic and likely pathogenic variants (ACMG class 4 and 5) in genes which are related to the indication described for the proband on the entire diagnostic panel (396 genes in total).

❑ **Mitochondrial DNA (mtDNA) (37 Genes, MIT01)**
MT-ATP6, MT-ATP8, MT-CO1, MT-CO2, MT-CO3, MT-CYB, MT-ND1, MT-ND2, MT-ND3, MT-ND4, MT-ND4L, MT-ND5, MT-ND6, MT-RNR1, MT-RNR2, MT-TA, MT-TC, MT-TD, MT-TE, MT-TF, MT-TG, MT-TH, MT-TI, MT-TK, MT-TL1, MT-TL2, MT-TM, MT-TN, MT-TP, MT-TQ, MT-TR, MT-TS1, MT-TS2, MT-TT, MT-TV, MT-TW, MT-TY

❑ **Nuclear encoded mitochondrial diseases (359 Genes, MIT02)**
AARS2, ABCB7, ABHD5, ACAD8, ACAD9, ACADM, ACADS, ACADSB, ACADVL, ACAT1, ACO2, ADCK3, ADCK4, AFG3L2, AGK, AGL, AIFM1, ALDH4A1, ALDH6A1, AMACR, AMPD1, AMT, ANO10, APOPT1, APTX, ATAD3A, ATP5A1, ATP5E, ATP7B, ATPAF2, AUH, BCAT2, BCKDHA, BCKDHB, BCS1L, BOLA3, BTD, C10ORF2, C12ORF65, C19ORF70, CA5A, CARS2, CCDC115, CDKL5, CEP89, CHCHD10, CISD2, CLPB, CLPP, COA3, COA5, COA6, COA7, COASY, COG8, COQ2, COQ4, COQ6, COQ7, COQ9, COX10, COX14, COX15, COX20, COX4I1, COX4I2, COX6B1, COX7B, COX8A, CPS1, CPT1A, CPT2, CYB5R3, CYC1, CYP11B2, CYP24A1, CYP27A1, CYP27B1, D2HGDH, DARS, DARS2, DBT, DDHD1, DGUOK, DHTKD1, DLAT, DLD, DMGDH, DNA2, DNAJC19, DNM1L, DPAGT1, DPYD, EARS2, ECHS1, ECI1, ECSIT, EIF2AK3, ELAC2, ERCC6, ETFA, ETFB, ETFDH, ETHE1, FARS2, FASTKD2, FBP1, FBXL4, FDX1L, FH, FLAD1, FOXRED1, GAD1, GAMT, GARS, GATM, GBE1, GCDH, GCK, GCSH, GDAP1, GFAP, GFER, GFM1, GFM2, GK, GLDC, GLRX5, GLUD1, GNPAT, GPAM, GTPBP3, GYG2, HADH, HADHA, HADHB, HARS2, HCCS, HIBCH, HLCS, HMGCL, HMGCS2, HOGA1, HSD17B10, HSPD1, HTRA2, IARS, IARS2, IBA57, IDH2, ISCA2, ISCU, ITPA, IVD, KIF5A, KLC2, L2HGDH, LAMP2, LARS, LARS2, LIAS, LIPT1, LMBRD1, LRPPRC, LYRM4, LYRM7, MAOA, MARS2, MCCC1, MCCC2, MCEE, MFF, MFN2, MGME1, MGST3, MICU1, MIPEP, MLYCD, MMAA, MMAB, MMADHC, MPC1, MPV17, MRPL12, MRPL3, MRPL44, MRPS16, MRPS22, MRPS23, MRRF, MTFMT, MTO1, MTPAP, MUT, NADK2, NAGS, NARS2, NBAS, NDUFA1, NDUFA10, NDUFA11, NDUFA12, NDUFA13, NDUFA2, NDUFA4, NDUFA6, NDUFA8, NDUFA9, NDUFAF1, NDUFAF2, NDUFAF3, NDUFAF4, NDUFAF5, NDUFAF6, NDUFAF7, NDUFB1, NDUFB10, NDUFB11, NDUFB3, NDUFB8, NDUFB9, NDUFS1, NDUFS2, NDUFS3, NDUFS4, NDUFS5, NDUFS6, NDUFS7, NDUFS8, NDUFV1, NDUFV2, NDUFV3, NFS1, NFU1, NIPSNAP1, NIPSNAP3A, NPL, NR2F1, NSUN3, NUBPL, NUP62, OAT, OFD1, OGDH, OPA1, OPA3, OTC, OXCT1, PANK2, PARP10, PARS2, PC, PCCA, PCCB, PCK2, PDHA1, PDHB, PDHX, PDK3, PDP1, PDSS1, PDSS2, PET100, PHYH, PIGQ, PLA2G6, PNPLA2, PNPLA4, PNPT1, POLG, POLG2, PPA2, PPOX, PTCD1, PUS1, PYCR1, PYGM, QRSL1, RANBP2, RARS2, REEP1, RMND1, RNASEH1, RRM2B, RTN4IP1, RYR1, SAMHD1, SARS2, SBDS, SCO1, SCO2, SDHA, SDHAF1, SDHD, SERAC1, SFXN4, SLC19A2, SLC19A3, SLC22A5, SLC24A4, SLC25A1, SLC25A12, SLC25A13, SLC25A15, SLC25A19, SLC25A20, SLC25A22, SLC25A26, SLC25A3, SLC25A4, SLC25A46, SLC33A1, SLC35G2, SLC39A8, SLC52A2, SLC6A8, SPAST, SPG20, SPG7, STXBP1, SUCLA2, SUCLG1, SUGCT, SURF1, TACO1, TALDO1, TANGO2, TARS2, TAZ, TFAM, TFG, TIMM50, TIMM8A, TK2, TMEM126A, TMEM126B, TMEM70, TPK1, TRIT1, TRMT10C, TRMT5, TRMU, TSFM, TTC19, TUFM, TXN2, TYMP, UGT1A1, UQCC2, UQCC3, UQCRB, UQCRC2, UQCRQ, VARS2, WFS1, WWOX, XPNPEP3, YARS2, YME1L1

❑ **Leigh syndrome (nuclear genes) (45 Genes, MIT03)**
AARS2, ACAD9, ADCK3, BCS1L, C12ORF65, COX10, COX15, COX8A, ECHS1, FOXRED1, GFM2, GYG2, HIBCH, IARS2, LIPT1, MFF, MPV17, MTFMT, NARS2, NDUFA10, NDUFA12, NDUFA2, NDUFA9, NDUFAF2, NDUFAF5, NDUFAF6, NDUFS3, NDUFS4, NDUFS7, NDUFS8, NDUFV1, PDHA1, PDHB, PDSS2, PET100, SCO2, SDHA, SERAC1, SLC19A3, SLC25A46, SURF1, TACO1, TPK1, TSFM, TUFM

❑ **Mitochondrial encephalopathy / Mitochondrial Hepato(encephalo)pathy (204 Genes, MIT04)**
AARS2, ABHD5, ACAD8, ACAD9, ACADM, ACADS, ACADSB, ACADVL, ACAT1, ACO2, ADCK3, AGK, AGL, AIFM1, ALDH4A1, ALDH6A1, AMACR, AMT, ATP7B, ATPAF2, AUH, BCS1L, BOLA3, BTD, C10ORF2, C19ORF70, CA5A, CARS2, CCDC115, CDKL5, COA7, COASY, COG8, COQ2, COQ4, COQ6, COQ9, COX10, COX14, COX15, COX4I2, COX6B1, CPS1, CPT1A, CPT2, CYB5R3, CYP11B2, CYP27A1, CYP27B1, D2HGDH, DARS, DARS2, DGUOK, DLAT, DLD, DNAJC19, DPAGT1, DPYD, EARS2, ECHS1, EIF2AK3, ERCC6, ETFA, ETFB, ETFDH, ETHE1, FARS2, FASTKD2, FBP1, FBXL4, FLAD1, FOXRED1, GAMT, GATM, GBE1, GCDH, GCK, GCSH, GFAP, GFER, GFM1, GK, GLDC, GLRX5, GLUD1, HADH, HADHA, HADHB, HCCS, HLCS, HMGCS2, HSD17B10, HSPD1, IARS, IBA57, IDH2, ISCA2, ITPA, KIF5A, L2HGDH, LAMP2, LARS, LIAS, LMBRD1, LRPPRC, LYRM7, MARS2, MCCC1, MCCC2, MFF, MICU1, MLYCD, MMAA, MMAB, MMADHC, MPV17, MRPS16, MRPS22, MRPS23, MTFMT, MTO1, MTPAP, MUT, NADK2, NAGS, NBAS, NFU1, NUBPL, OAT, OFD1, OPA1, OTC, PANK2, PC, PCCA, PCCB, PCK2, PDHA1, PDHB, PDHX, PDP1, PDSS1, PDSS2, PLA2G6, PNPLA2, PNPT1, POLG, PTCD1, PUS1, PYGM, RARS2, RMND1, RRM2B, SAMHD1, SARS2, SBDS, SCO1, SCO2, SDHA, SDHAF1, SERAC1, SLC19A2, SLC19A3, SLC22A5, SLC25A1, SLC25A12, SLC25A13, SLC25A15, SLC25A19, SLC25A20, SLC25A22, SLC25A26, SLC25A3, SLC25A4, SLC33A1, SLC6A8, SPG20, SPG7, SUCLA2, SUCLG1, SURF1, TACO1, TALDO1, TANGO2, TARS2, TAZ, TFG, TIMM8A, TK2, TMEM70, TPK1, TRIT1, TRMU, TSFM, TTC19, TUFM, TYMP, UQCRB, UQCRC2, UQCRQ, VARS2, WFS1, XPNPEP3, YARS2

❑ **Mitochondrial DNA-depletion and deletion syndromes (33 Genes, MIT05)**
AARS2, AGK, C10ORF2, C12ORF65, CHCHD10, DGUOK, DNA2, FBXL4, GFER, MFN2, MGME1, MPV17, NDUFS1, OPA1, OPA3, PARS2, POLG, POLG2, RNASEH1, RRM2B, SLC24A4, SLC25A3, SLC25A4, SPG7, SUCLA2, SUCLG1, TFAM, TIMM50, TIMM8A, TK2, TMEM126A, TYMP, WFS1

❑ **Pyruvate Metabolism Disorders (9 Genes, MIT06)**
ATP5E, DLAT, DLD, MPC1, PDHA1, PDHB, PDHX, PDP1, TMEM70

❑ **Combined oxidative phosphorylation deficiency (COXPD) (32 Genes, MIT07)**
AARS2, AIFM1, ATP5A1, C12ORF65, CARS2, EARS2, ELAC2, FARS2, GFM1, GTPBP3, LYRM4, MARS2, MIPEP, MRPL3, MRPL44, MRPS16, MRPS22, MTFMT, MTO1, NARS2, NSUN3, PNPT1, RMND1, SFXN4, SLC25A26, TARS2, TRMT10C, TRMT5, TSFM, TUFM, TXN2, YARS2

For further information and advice please do not hesitate to contact our Diagnostic Support team.

www.cegat.de/en/diagnostic-support · diagnostic-support@cegat.de · Phone +49 7071 565 44-55

- ❑ **Complex I Deficiency (60 Genes, MIT08)**
  AARS2, ACAD9, AIFM1, C10ORF2, ECI1, ECSIT, FOXRED1, GAD1, GPAM, HOGA1, IVD, LRPPRC, MGST3, MRRF, MTFMT, NARS2, NDUFA1, NDUFA10, NDUFA11, NDUFA13, NDUFA2, NDUFA4, NDUFA6, NDUFA8, NDUFA9, NDUFAF1, NDUFAF2, NDUFAF3, NDUFAF4, NDUFAF5, NDUFAF6, NDUFAF7, NDUFB1, NDUFB10, NDUFB11, NDUFB3, NDUFB8, NDUFB9, NDUFS1, NDUFS2, NDUFS3, NDUFS4, NDUFS5, NDUFS6, NDUFS7, NDUFS8, NDUFV1, NDUFV2, NDUFV3, NFS1, NIPSNAP1, NIPSNAP3A, NPL, NUBPL, PHYH, PTCD1, SLC35G2, STXBP1, SUGCT, TMEM126B

- ❑ **Complex II Deficiency (6 Genes, MIT09)**
  FOXRED1, ISCU, NFS1, SDHA, SDHAF1, SDHD

- ❑ **Complex III Deficiency (12 Genes, MIT10)**
  BCS1L, CYC1, LYRM7, MT-CYB, NDUFS4, NFS1, TTC19, UQCC2, UQCC3, UQCRB, UQCRC2, UQCRQ

- ❑ **Complex IV Deficiency (26 Genes, MIT11)**
  AARS2, APOPT1, CEP89, COA3, COA5, COA6, COX10, COX14, COX15, COX20, COX4I1, COX4I2, COX6B1, ETHE1, FASTKD2, LRPPRC, MT-CO1, MT-CO2, MT-C03, MT-TL1, MT-TS1, PET100, SCO1, SCO2, SURF1, TACO1

- ❑ **Complex V Deficiency (6 Genes, MIT12)**
  ATP5A1, ATP5E, ATPAF2, MT-ATP6, MT-ATP8, TMEM70

- ❑ **CoQ10 Deficiency and Acyl-CoA-Dehydrogenase Deficiency (14 Genes, MIT13)**
  ADCK3, ADCK4, ANO10, APTX, COQ2, COQ4, COQ6, COQ7, COQ9, ETFA, ETFB, ETFDH, PDSS1, PDSS2

- ❑ **Methylglutaconic Aciduria (MGA) (18 Genes, MIT14)**
  AGK, ATP5E, ATPAF2, AUH, C19ORF70, CLPB, DNAJC19, HMGCL, HTRA2, MT-TL1, OPA3, POLG, SDHA, SERAC1, SUCLA2, TAZ, TIMM50, TMEM70

- ❑ **MELAS and MERRF syndrome (26 Genes, MIT15)**
  MT-CO1, MT-CO2, MT-CYB, MT-ND1, MT-ND3, MT-ND4, MT-ND5, MT-ND6, MT-NDUL, MT-TC, MT-TD, MT-TF, MT-TG, MT-TH, MT-TI, MT-TK, MT-TL1, MT-TP, MT-TQ, MT-TR, MT-TS1, MT-TS2, MT-TT, MT-TV, MT-TW, POLG

- ❑ **Progressive external ophthalmoplegia (PEO/CPEO) (34 Genes, MIT16)**
  ACO2, AUH, C10ORF2, C12ORF65, CISD2, DNA2, DNM1L, FH, ISCA2, KLC2, MFN2, MGME1, MTPAP, NDUFS1, NR2F1, OPA1, OPA3, POLG, POLG2, RNASEH1, RRM2B, RTN4IP1, RYR1, SLC19A3, SLC25A4, SLC25A46, SLC52A2, SPG7, TIMM8A, TK2, TMEM126A, TYMP, WFS1, YME1L1

Additional analyses

For further information and advice please do not hesitate to contact our Diagnostic Support team.

www.cegat.de/en/diagnostic-support · diagnostic-support@cegat.de · Phone +49 7071 565 44-55