CENTOGENE
THE RARE DISEASE COMPANY

CentoMetabolic®

CentoMetabolic® – A one-test solution for all medically relevant metabolic disorders

CENTOGENE is committed to developing innovative solutions to help end the diagnostic odyssey of patients suffering from rare genetic diseases. Our CentoMetabolic® panel has been designed to test for a wide range of metabolic disorders. It integrates genetic and biochemical testing, including enzyme assays as well as a selection of proprietary biomarkers. When genetic variants relevant to your patient are detected via CentoMetabolic®, we will automatically complement with biomarker and/or enzyme testing (if applicable) and include the results in your medical report. In addition, CentoMetabolic® includes an evaluation of copy number variants (CNV) at no extra cost.

CentoMetabolic® gives the confidence of a thorough evaluation for a potential metabolic diagnosis while simultaneously providing an opportunity to prove the consequences of the identified genetic variant.

Who should consider CentoMetabolic®?

Physicians providing treatment for patients matching any of the following criteria:

- Suspected metabolic disorder
- Babies with lethargy or abdominal pain or vomiting or jaundice or metabolic acidosis
- Developmental delay
- Admission to a neonatal intensive care unit (NICU), especially due to epilepsy of unclear origin and disturbed consciousness

What genes and disorders are targeted by CentoMetabolic®?

CentoMetabolic® targets close to 200 metabolic disorders. The content and design of the panel is based on our continuously enhanced medical expertise and knowledge in rare metabolic diseases.

The following table shows the distribution of genes and targeted metabolic disorders depending on 19 different disease categories.

TYPE OF METABOLIC DISORDERS COVERED	NUMBER OF GENES
Congenital disorders of glycosylation and other disorders of protein modification	2
Defects in Cholesterol and Lipoprotein Metabolism	2
Defects in Hormone Biogenesis or Function	7
Disorder of phosphate, calcium and vitamin D metabolism	3
Disorders in the metabolism of purines, pyrimidines and nucleotides	6
Disorders in the metabolism of trace elements and metals	6
Disorders in the metabolism of vitamins and (non-protein) cofactors	10
Disorders of amino acid and peptide metabolism	33
Disorders of carbohydrate metabolism	35
Disorders of energy metabolism	6
Disorders of fatty acid and ketone body metabolism	3
Disorders of lipid and lipoprotein metabolism	8
Disorders of neurotransmitter metabolism	1
Disorders of porphyrin and haem metabolism	8
Disorders of the metabolism of sterols	16
Lysosomal disorders	48
Peroxisomal disorders	16
Porphyria and Bilirubinemia	1

GENES INCLUDED

ABCA1, ABCB4, ABCC2, ABCD1, ABCD4, ABCG5, ABCG8, ACAT1, ADA, AGA, AGL, AGPS, AGXT, ALAD, ALAS2, ALDH4A1, ALDOA, ALDOB, ALG3, ALPL, ANTXR2, APOA2, APOA5, APOB, APOC2, APOE, ARG1, ARSA, ARSB, ASAH1, ASL, ASS1, ATP7A, ATP7B, BCKDHA, BCKDHB, BTD, CBS, CD320, CETP, CLN3, CLN5, CLN6, CLN8, CPOX, CPS1, CPT1A, CTNS, CTSA, CTSD, CTSK, CYP11B1, CYP17A1, CYP19A1, CYP21A2, DBT, DDC, DHCR7, DIABLO, DLX4, DNAJC5, DPYD, ENO3, ENPP1, EPHX2, ETHE1, FAH, FBP1, FECH, FGF23, FUCA1, G6PC, G6PD, GAA, GALC, GALE, GALK1, GALNS, GALT, GAMT, GATM, GBA, GBE1, GHR, GK, GLA, GLB1, GM2A, GNPAT, GNPTAB, GNPTG, GNS, GUSB, GYG1, GYS1, GYS2, HCFC1, HEXA, HEXB, HFE, HJV, HGD, HGSNAT, HLCS, HMBS, HPD, HPRT1, HSD3B2, HYAL1, IDS, IDUA, ITIH4, IVD, KHK, LAMP2, LCAT, LDHA, LDLR, LDLRAP1, LIPA, LIPC, LIPI, LMBRD1, LPA, LPL, MAN2B1, MANBA, MCOLN1, MFSD8, MMAA, MMAB, MMACHC, MMADHC, MMUT, NAGA, NAGLU, NAGS, NEU1, NPC1, NPC2, OTC, PAH, PCSK9, PDHB, PEX1, PEX10, PEX12, PEX13, PEX14, PEX16, PEX19, PEX2, PEX26, PEX3, PEX5, PEX6, PEX7, PFKM, PGAM2, PGK1, PGM1, PHKA1, PHKA2, PHKB, PHKG2, PKLR, PNPO, POR, PPOX, PPP1R17, PPT1, PRKAG2, PSAP, PYGL, PYGM, RBCK1, SGSH, SI, SLC17A5, SLC22A5, SLC25A13, SLC25A15, SLC25A20, SLC25A36, SLC2A1, SLC2A2, SLC2A3, SLC37A4, SLC3A1, SLC3A2, SLC40A1, SLC6A19, SLC6A8, SLC7A7, SLC7A9, SLCO1B1, SLCO1B3, SMPD1, SUMF1, TAT, TFR2, TPP1, UGT1A1, UMPS, UROD, UROS

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CENTOGENE´s biomarkers and enzyme testing

Biomarkers serve as measureable indicators of pathological processes. They are typically directly linked to genetic variants in specific genes and can predict, diagnose, monitor, and assess the severity of a disease. Measuring the cellular activity of an enzyme can also be used as a tool for the diagnosis and monitoring of a disease. Our multiomic- and big data-based approaches allow us to continuously discover new highly specific biomarkers. Any new biomarker will be included in this panel and represents an opportunity to advance our understanding of metabolic diseases as well as develop better tailored therapies for patients.

COMPLEMENTARY ENZYMES

SPHINGOLIPIDOSES AND OLIGOSACCHARIDOSES

- Acid lipase - **Wolman disease**
- Acidic alpha-glucosidase - **Pompe disease**
- Acidic sphingomyelinase - **Niemann-Pick disease types A and B**
- Alpha-fucosidase - **Alpha-fucosidase deficiency**
- Alpha-galactosidase - **Fabry disease**
- Alpha-mannosidase - **Alpha-mannosidase deficiency**
- Alpha-N-acetylgalactosaminidase - **Schindler/Kanzaki disease**
- Arylsulfatase A* - **Metachromatic leukodystrophy**
- Beta-glucocerebrosidase - **Gaucher disease**
- Beta-hexosaminidase - **Tay-Sachs disease**
- Beta-mannosidase - **Beta-mannosidase deficiency**
- Galactocerebrosidase - **Krabbe disease**
- Total hexaminidisase - **Sandhoff disease**

NCLs

- Palmitoyl-protein thioesterase - **NCL1**
- Tripeptidyl peptidase - **NCL2**

MPS

- Alpha-L-iduronidase - **MPS I**
- Arylsulfatase B - **MPS VI**
- Beta-galactosidase - **MPS IVB**
- Beta-glucuronidase - **MPS VII**
- Iduronate-2-sulfatase - **MPS II**
- N-acetyl-alpha-glucosaminidase - **MPS IIIB**
- N-acetylgalactosamine-6-sulfate-sulfatase - **MPS IVA**

COMPLEMENTARY BIOMARKERS

- C26-ceramide - **Farber disease**
- Glucosylsphingosine (lyso-Gb1)[1] - **Gaucher disease**
- Globotriaosylceramide (lyso-Gb3) - **Fabry disease**
- Lyso-SM509 - **Niemann-Pick disease type A/B/C**
- 3-O-Methyldopa (3-OMD) - **AADC deficiency**

AADC = Aromatic L-amino acid decarboxylase
MPS = Mucopolysaccharidosis
NCLs = Neuronal Ceroid Lipofuscinosis

[1] A method using Lyso-Gb1 is covered by US Patent No. 10,859,580, other pending US applications, and pending applications and patents in other jurisdictions.

* Patients who qualify for Arylsulfatase A enzyme (MLD) testing will be contacted for submission of additional sample. Arylsulfatase A enzyme (MLD) testing requires ≥5ml EDTA blood (testing is performed in leukocytes). Samples have to arrive within 72hrs of collection.

CentoMetabolic® – Key features

- Bidirectional next-generation sequencing of target regions of all genes in the panel, including coding regions and +/- 10 bp exon/intron boundaries
- All relevant deep intronic variants described in CentoMD® and HGMD® are included
- Coverage: ≥99.5% of targeted regions covered at ≥ 20x
- Low quality single nucleotide variants (SNVs) and all relevant deletion/insertion variants are confirmed by Sanger sequencing prior to reporting
- **CNV included**
- Fast and precise diagnostic with a TAT of 15 business days
- **Specificity of >99.9% for all reported variants**
- Our test combines genetic and biochemical testing for the widest range of rare metabolic diseases
- Complementary biochemical testing by proprietary biomarkers and enzyme-activity assays when applicable
- **Only 1** CentoCard® is sufficient for **all** tests

› Contact Details

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