CENTOGENE
THE RARE DISEASE COMPANY

CentoMetabolic MOx

More Answers Today.
More Options Tomorrow.

PRODUCT SHEET

CentoMetabolic MOx

Inherited metabolic disorders (IMDs) are a group of rare conditions caused by genetic defects that disrupt the cellular metabolism. A growing number of IMDs are treatable if diagnosed early, but can be quickly fatal without prompt identification. With a multiomic approach, we can help you and your patients to accelerate the critical journey from symptoms to diagnosis by avoiding stepwise testing – saving time, resources, and pivotal years amid often rapid IMD progression.

CENTOGENE's multiomic panel – CentoMetabolic MOx – has been designed to test for a wide range of IMDs – integrating 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 MOx, we will automatically complement the analysis with biomarker and/or enzyme testing (if applicable) and include the results in your medical report. CentoMetabolic MOx provides you with the most valuable information for diagnosis decisions, prognosis and therapeutic approaches, laying the roadmap to personalized treatment options.

The CENTOGENE Advantage

MOx

Multiomic panel integrating genetic and biochemical testing in a **single solution, for fast and accurate diagnosis of a wide range** of rare inherited metabolic disorders

Best-in-class medical reports powered by by CENTOGENE'S Biodatabank, the world's largest real-world data repository for rare and neurodegenerative diseases

Biochemical testing to support variant classification, leading to **higher diagnostic yields**

Dedicated team of rare disease experts to provide **best clinical interpretation** and **life-long support**

Who Should Consider CentoMetabolic MOx?

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

- Suspected metabolic disorder
- Infants with overlapping symptoms, lethargy, abdominal pain, vomitting, jaundice or metabolic acidosis
- Developmental delay
- Abnormal newborn screening results
- Infants admitted to a neonatal intensive care unit (NICU), especially due to epilepsy of unclear origin and disturbed consciousness
- Symptoms related to neurological conditions of unknown etiology

What Genes and Disorders Are Targeted?

CentoMetabolic MOx targets close to 200 IMDs. The content and design of the panel is based on our continuously enhanced medical expertise and knowledge of rare metabolic disorders, including the latest medical and in-house findings.

The table below shows the distribution of genes and targeted metabolic disorders based on 18 different disease categories:

TYPE OF METABOLIC DISORDERS COVERED	# 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

TYPE OF METABOLIC DISORDERS COVERED	# GENES*
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 heme metabolism	8
Disorders of the metabolism of sterols	16
Lysosomal disorders	48
Peroxisomal disorders	16
Porphyria and bilirubinemia	1

Genes Included (206)

ABCA1, ABCB4, ABCC2, ABCD1, ABCD4, ABCG5, ABCG8, ACAT1, ADA, AGA, AGL, AGPS, AGXT, ALAD, ALAS, 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

CENTOGENE´s Biomarker and Enzyme Testing — Going Beyond Genetics

CentoMetabolic MOx panel includes biomarkers and enzymatic assays for over 20 metabolic disorders. Biomarkers serve as measurable 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, as well as treatment efficacy.

Our multiomic- and big data-based approaches allow us to continuously discover new highly specific biomarkers. All new biomarkers and biochemical assays clinically relevant for metabolic disorders will be included in this panel, advancing the understanding of metabolic disorders, accelerating the path from diagnosis to personalized treatment.

Diseases and Complementary Enzymes

Sphingolipidoses and Oligosaccharidoses

- Wolman disease
  Acid lipase
- Pompe disease
  Alpha-glucosidase
- Fucosidosis
  Alpha-fucosidase
- Fabry disease
  Alpha-galactosidase
- Alpha-mannosidosis
  Alpha-mannosidase
- Schindler/Kanzaki disease
  Alpha-N-acetylgalactosaminidase
- Gaucher disease
  Beta-glucocerebrosidase
- Tay-Sachs disease
  Beta-hexosaminidase
- Beta-mannosidosis
  Beta-mannosidase
- Sandhoff disease
  Total-hexosaminidase

Neuronal Ceroid Lipofuscinosis

- Santavuori-Haltia disease
  Palmitoyl-protein- thioesterase
- Jansky-Bielschowsky disease
  Tripeptidyl-peptidase

Mucopolysaccharidosis

- Hurler syndrome (MPS I)
  Alpha-L-iduronidase
- Hunter syndrome (MPS II)
  Iduronate-2-sulfatase
- Sanfilippo syndrome B (MPS III B)
  Alpha-N-acetylglucosaminidase
- Morquio syndrome A (MPS IV A)
  N-acetylgalactosamine-6-sulfate-sulfatase
- Morquio syndrome B (MPS IV B)
  Beta-galactosidase
- Maroteaux-Lamy syndrome (MPS VI)
  Arylsulfatase B
- Sly syndrome (MPS VII)
  Beta-glucuronidase

Diseases and Complementary Biomarkers

- Gaucher disease
  Glucosylsphingosine (lyso-Gb1)**
- Fabry disease
  Lyso-ceramide trihexoside (lyso-Gb3)
- Niemann-Pick disease type A/B/C
  Lyso-SM-509
- Aromatic L-amino acid decarboxylase (AADC)
  3-O-methyldopa (3-OMD)

Key Features and Performance

MULTIOMIC APPROACH	206 genes, and over 20 enzymes and biomarkers associated with more than 180 IMDs
COVERAGE	• Mean depth ~ 200x • ≥ 99.5% targeted regions covered at ≥ 20x • For each gene, all clinically relevant variants described in HGMD® and the CENTOGENE Biodatabank are covered, including deep intronic and regulatory variants
IMPROVED INTERPRETATION	Extra insights supported by CENTOGENE's Biodatabank, which contains curated unique variant data and omics data from a wide range of ethnicities from more than 120 countries, are used to confirm results and validate pathogenicity of the variants found
DELETION/DUPLICATION	High resolution NGS-based CNV analysis to detect deletions and duplications is included at no extra cost. Deletion/duplications constitute 5 – 10% of disease-causing variants. By including CNV analysis, the potential of providing the most accurate diagnosis increase
SPECIFICITY	≥ 99.9% guaranteed for all reported variants. Variants with low quality and/or unclear zygosity are confirmed by orthogonal methods (Sanger, MLPA, qPCR) ***
MATERIAL	≥ 1 CentoCard® or 4ml EDTA blood
TAT	15 business days

* Due to overlapping phenotypes, particular genes are listed in more than one category as they are associated with more than one disorder.
** 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.
*** MLPA: Multiplex ligation-dependent probe amplification; qPCR: quantitative polymerase chain reaction.