CentoMetabolic

CentoMetabolic™ – A one test solution for rare metabolic disorders

We are committed to providing solutions to help end the diagnostic odyssey of patients suffering from rare diseases. We have developed CentoMetabolic™, a panel that integrates genetic and biochemical testing to diagnose a wide range of rare metabolic disorders. Our panel includes a comprehensive range of genes combined with biochemical testing — including enzyme assays and a selection of proprietary biomarkers. When variants relevant to your patient are detected, we will automatically complement the genetic testing with biomarker and/or enzyme testing and include the results in your medical report.

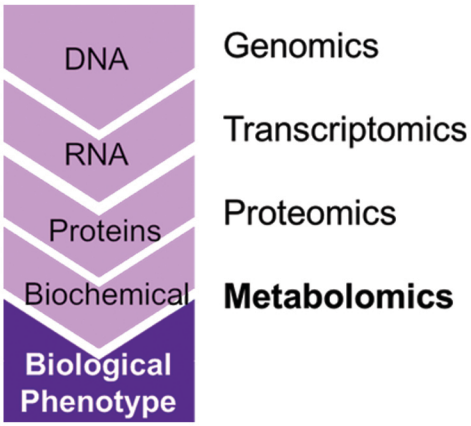
CentoMetabolic™ gives the confidence of a thorough evaluation for a potential metabolic diagnosis while at the same time providing an opportunity to validate the consequences of the identified genetic variant.*

*when applicable

Who should consider CentoMetabolic™?

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

- Suspected metabolic disorder
- Complex, overlapping symptoms with broad differential diagnosis
- Metabolic crisis
- Abnormal newborn screening results
- Admission to a neonatal intensive care unit
- Symptoms related to neurological conditions of unknown etiology



What genes and disorders are targeted by CentoMetabolic™?

CentoMetabolic™ includes 166 genes and targets more than 150 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 11 different disease categories.

TYPES OF METABOLIC DISORDERS COVERED	TARGETED DISORDERS	NUMBER OF GENES*
Disorders of Carbohydrate Metabolism	31	33
Disorders of Cholesterol and Lipoprotein Metabolism	29	31
Disorders of Amino and Organic Acid Metabolism	19	24
Disorders of Glycolipid and Glycoprotein Metabolism	18	17
Transmembrane Protein Defects	17	17
Peroxisomal Disorders	17	16
Porphyrias and Bilirubinemia	12	13
Disorders of Hormone Biogenesis or Function	6	6
Disorders of Nucleotide Metabolism	4	4
Disorders of Metal Metabolism and Transport	3	6
Disorders of Phosphate Metabolism	3	3

*Due to overlapping phenotypes, particular genes are listed in more than one category as they are associated with more than one disorder

CENTOGENE´s biomarkers and enzyme testing

Biomarkers serve as measureable indicators of normal biological or 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 rare metabolic diseases as well as to develop better tailored therapies for patients.

COMPLEMENTARY ENZYMES

SPHINGOLIPIDOSES AND OLIGOSACCHARIDOSES

- Acid lipase - **Wolman disease**
- Acidic alpha-glucosidase - **Pompe disease**
- Acidic sphingomyelinase - **Niemann-Pick Type A and Type B disease**
- Alpha-galactosidase - **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**
- Chitotriosidase - **Gaucher disease (unspecific)**
- 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 IVA**
- N-acetylgalactosamine-6-sulfate-sulfatase - **MPS IIIB**

COMPLEMENTARY BIOMARKERS

- C26-ceramide - **Farber disease**
- Glucosylsphingosine (lyso-Gb1) - **Gaucher disease**
- Lyso-ceramide trihexoside (lyso-Gb3) - **Fabry disease**
- Lyso-SM509 - **Niemann Pick disease type A/B/C**

NCLs = Neuronal Ceroid Lipofuscinosis
MPS = Mucopolysaccharidosis

* 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 166 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
- Fast and precise diagnostic with a TAT of 6–10 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
- Required Material: ≥ 1 filter card

GENES INCLUDED

ABCA1, ABCC2, ABCD1, ABCD4, ADA, AGA, AGL, AGPS, ALAD, ALAS2, ALDOA, ALDOB, ALPL, APOA2, APOA5, APOB, APOC2, APOE, ARG1, ARSA, ARSB, ASAH1, ASL, ASS1, ATP7A, ATP7B, BCKDHA, BCKDHB, CBS, CETP, CLN3, CLN5, CLN6, CLN8, CPOX, CPS1, CTNS, CTSA, CTSD, CTSK, CYP11B1, CYP17A1, CYP19A1, CYP21A2, DBT, DHCR7, ENO3, ENPP1, EPHX2, FECH, FGF23, FUCA1, G6PC, G6PD, GAA, GALC, GALE, GALK1, GALNS, GALT, GBA, GBE1, GHR, GK, GLA, GLB1, GM2A, GNPAT, GNPTAB, GNPTG, GNS, GUSB, GYG1, GYS2, HCFC1, HEXA, HEXB, HFE, HFE2, HGD, HGSNAT, HMBS, HPRT1, HSD3B2, HYAL1, IDS, IDUA, ITIH4, KHK, LAMP2, LCAT, LDHA, LDLR, LIPA, LIPI, LMBRD1, LPA, LPL, MAN2B1, MANBA, MCOLN1, MFSD8, MMACHC, MMADHC, NAGA, NAGLU, NAGS, NEU1, NPC1, NPC2, OTC, PAH, PEX1, PEX10, PEX12, PEX13, PEX14, PEX16, PEX19, PEX2, PEX26, PEX3, PEX5, PEX6, PEX7, PFKM, PGAM2, PGK1, PGM1, PHKA1, PHKA2, PHKB, PHKG2, PKLR, POR, PPOX, PPP1R17, PPT1, PRKAG2, PYGL, PYGM, RBCK1, SGSH, SLC17A5, SLC25A13, SLC25A15, SLC25A36, SLC2A1, SLC2A2, SLC2A3, SLC3A1, SLC3A2, SLC40A1, SLC6A19, SLC7A7, SLC7A9, SLCO1B1, SLCO1B3, SMPD1, SUMF1, TFR2, TPP1, UGT1A1, UMPS, UROD, UROS

ISO9001:2015 TÜV NORD

تلفن: ۴۳۹۳۶-۰۲۱
فکس: ۸۹۷۷۰۰۱۱-۰۲۱

تهران، خیابان ولیعصر، بالاتر از بیمارستان دی،
نرسیده به پل همت، سمت چپ، خیابان نیلو،
www.DNA-Lab.ir

آزمایشگاه دنا
D©NA Laboratory