Biomarker / Biochemical testing

INDIVIDUALIZE YOUR PATIENT’S THERAPY
Lysosomal storage disorders (LSD)

LSDs are a group of rare, inherited metabolic diseases characterized by abnormal accumulation of different metabolites in the cellular lysosomes, leading to impaired functioning of the affected cells. The overall incidence of LSDs as a group is ~1 in 5,000 individuals, with some specific LSDs being more common than others.¹

Lysosomal enzymes are involved in the degradation of complex molecules. Pathogenic variants in genes that encode these enzymes or transport proteins result in absent or impaired protein function. This leads to accumulation of molecules – first in the lysosome, then in the cytosol, and finally in the intracellular space, which leads to the various symptoms associated with LSDs.

More than 50 different monogenic LSDs have been reported with multisystemic effects involving the central nervous system, connective tissue, skin, heart or other organs.

![Lysosomal Storage Diseases](image)

Depending on the type, quantity and location of the stored and non-degraded cellular elements, LSDs are classified into different subtypes and result in specific phenotypic profiles.

- **Mucopolysaccharidoses**: Accumulation of incompletely degraded glycosaminoglycans (GAGs)
- **Sphingolipidoses**: Accumulation of sphingolipids
- **Oligosaccharidoses**: Accumulation of abnormal degradation products of glycoproteins
- **Neuronal ceroid lipofuscinoses**: Accumulation of ceroid lipopigments
- Lysosomal transport diseases, other lysosomal disorders

Role of enzymes and biomarkers in LSDs

**ENZYMES**
- Measurement of specific enzyme activity responsible for the disease
- Indirect measurement via synthetic substrates
- The “traditional” diagnostic tool for LSDs
- Enzyme instability is a limitation
  - The assay outcome does not always reflect activity in vivo
  - Substrates for testing available for only about 45% of LSDs

**BIOMARKERS**
- Measurement of accumulated primary or secondary metabolites or proteins
- Direct quantification of the amount of metabolite
- Can be used for both diagnosis and monitoring of disease
  - Reflects disease burden
  - Useful as a measure of therapy efficacy and guide for therapy dosage
- Requires low sample amount with highly sensitive techniques
  - Directly reflects the in vivo burden due to accumulated metabolites
  - Only a few LSDs have been characterized by specific biomarkers to date

Enzymatic assays and biomarker analyses are **complementary methods** (if both are available) for a LSD diagnosis.
Enzyme panel options

CENTOGENE offers LSD sub-type specific enzyme panel options and one comprehensive LSD enzyme panel that includes all the enzyme assays offered in one test (except for Krabbe disease and Metachromatic leukodystrophy). The different panel options are listed below:

1. CentoMPS
   8 enzymes

2. CentoSphingo
   12 enzymes

3. CentoNCL
   2 enzymes

4. CentoLSD
   21 enzymes

“ENZYME PANEL X-TRA” OPTION:

The enzyme panels listed above can be requested together with an automatic reflex to genetic testing if an enzyme deficiency is identified via CENTOGENE’s “Enzyme Panel X-TRA” option.

This testing strategy offers you and your patients a complete, biochemical-to-genetics solution, using CentoCard® sample, reducing the time to diagnosis, treatment and monitoring.

CENTOGENE ADVANTAGE:

- Proven expertise in the identification of new biomarkers, validated in epidemiological clinical trials
- Established biomarker tests for Gaucher disease, Niemann-Pick disease type A/B/C1/C2, Fabry disease and Farber disease
- Optimized and facilitated sample logistics with our CE-labeled filter cards, CentoCard®
- One single sample for complete patient diagnostics via enzyme assay, biomarker analysis and genetic testing
- Availability of biochemical analyses to assist appropriate classification of identified genetic variants
- Leverage the power of CentoMD® - a single database combining genotype, phenotype and biochemical information on thousands of individuals
Testing at CENTOGENE

CENTOGENE offers enzymatic assays for the diagnosis of several LSDs, including Fabry disease, Pompe disease, Gaucher disease, Mucopolysaccharidosis, Niemann-Pick diseases A/B and others. For the full list of enzyme analyses available please refer to the main table inside this brochure.

CENTOGENE has developed specific biomarkers for certain LSDs with therapeutic options. They can be analyzed from dried blood spots and are essential for early diagnosis of disease, as well as progression and therapeutic monitoring of a specific disorder.

<table>
<thead>
<tr>
<th>BIOMARKER DETERMINATION</th>
<th>DISEASE</th>
<th>GENES</th>
<th>DETECTION METHOD</th>
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<tbody>
<tr>
<td>Glucosylsphingosine (Lyso-Gb1)</td>
<td>Gaucher disease</td>
<td>GBA, PSAP</td>
<td>Tandem-MS</td>
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<tr>
<td>Lyso-Ceramide trihexoside (Lyso-Gb3)</td>
<td>Fabry disease</td>
<td>GLA</td>
<td>Tandem-MS</td>
</tr>
<tr>
<td>Lyso-SM509</td>
<td>Niemann-Pick disease</td>
<td>SMPD1, NPC1, NPC2</td>
<td>Tandem-MS</td>
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<tr>
<td>C26 Cer</td>
<td>Farber disease, cystic fibrosis</td>
<td>ASAH1, CFTR</td>
<td>Tandem-MS</td>
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</tbody>
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SAMPLE REQUIREMENTS:

Accepted sample types and minimum requirements are:
EDTA blood (≥ 1 ml) or 1 filtercard (CentoCard®)
Filtercards should reach CENTOGENE within 2 weeks of sample collection, EDTA blood within 5 days.

Exceptions:
- Arylsulfatase A enzyme (MLD) testing requires ≥5ml ETDA blood (testing in performed in leukocytes). Samples have to arrive within 72 hours of collection.
- CentoLSD Enzyme Panel and CentoLSD Enzyme Panel X-TRA require 2 full filtercards (2x10 blood spots).
Please visit our website for more information:

www.centogene.com

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