Lysosomal Storage Disorders: Deletion/Duplication Panel

**Test Code:** MD120  
**Turnaround time:** 2 weeks  
**CPT Codes:** 81228 x1, 81401 x1

### Condition Description

Lysosomal storage disorders (LSDs) are a heterogeneous group of mostly autosomal recessive disorders with the exception of mucopolysaccharidosis type II (MPS II) also known as Hunter syndrome, Danon disease, and Fabry disease which show X-linked inheritance. LSDs comprise more than 50 metabolic disorders including defects in degradative and synthetic enzymes, lysosomal membrane defects, the neuronal ceroid lipofuscinoses (NCLs) and disorders of lysosome biogenesis and endosome–lysosome traffic.

Clinical and biochemical features continue to be used reliably to assign patients to this general disease category. Identification of the precise genetic defect is important, however, to permit carrier testing and early prenatal diagnosis. Molecular analysis is likely to expand the clinical spectrum of LSD and may also provide data relevant to prognosis and future therapeutic intervention. The overall incidence of LSDs as a group is estimated to be 1 in 5,000 births.

Although each LSD results from pathogenic variants in a different gene leading to a deficiency of enzyme activity or protein function, LSDs share one common biochemical characteristic: an accumulation of substrates within lysosomes. The particular substrates that are stored and the site(s) of storage vary. The substrate type is used to group the LSDs into broad categories, including the MPSs, the lipidoses, the glycogenoses, the oligosaccharidoses, and NCLs. Despite this categorization, many clinical similarities are observed between groups as well as within each group. Common clinical features of LSDs include coarse hair and facies, bone abnormalities, organomegaly, and central nervous system dysfunction.

### References:

- OMIM

### Genes

ADAMTS10, AGA, ARSA, ARSB, ASAH1, ATP13A2, CLN3, CLN5, CLN6, CLN8, CTNS, CTSA, CTSD, DNAJC5, FBN1, FUC1, GAA, GALC, GALNS, GLA, GLB1, GM2A, GNE, GNPTA, GNPTB, GUS, HEXA, HEXB, HSNSAT, HYAL1, IDS, IDUA, KCTD7, LAMP2, LIPA, LTBP2, MAN2B1, MANBA, MCOLN1, MFSD8, NAGA, NAGLU, NEU1, NPC1, NPC2, PPT1, PSAP, SGSH, SLC17A5, SMPD1, SUMF1, TPP1

### Indications

- With clinical features such as bone abnormalities, organomegaly, central nervous system dysfunction and coarse hair and facies.
- In which NCLs are suspected (presenting with neurocognitive decline, blindness, seizures and premature death.
- Abnormal biochemical results suggestive of an LSD.

### Methodology

**Deletion/Duplication Analysis:** DNA isolated from peripheral blood is hybridized to a gene-targeted CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes that cover the entire genomic region. Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants cause two of disease may be identified that may or may not be related to the patient’s phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

### Detection

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**Deletion/Duplication Analysis:** Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient's clinical and/or biochemical phenotype.

**Specimen Requirements**

Submit only 1 of the following specimen types

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Ship sample at room temperature with overnight delivery.

**Type: Isolated DNA**

Specimen Requirements:

In microtainer: 10 ug

Isolation using the Qiagen™ Puregene kit for DNA extraction is recommended.

Specimen Collection and Shipping: Refrigerate until time of shipment in 100 ng/ul of TE buffer. Ship sample at room temperature with overnight delivery.

**Related Tests**

- Lysosomal Storage Disorders: Sequencing Panel
- Biochemical enzyme assay for lysosomal storage disorders