Lysosomal Storage Disorders: Sequencing Panel

Test Code: MM120
Turnaround time: 6 weeks
CPT Codes: 81406 x1, 81404 x1, 81405 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, AP3B1, ARSA, ARSB, ASAH1, ATP13A2, CLN3, CLN5, CLN6, CLN8, CTNS, CTSA, CTSD, CTSK, DNAJC5, FBN1, FUC1, GAA, GALC, GALNS, GBA, GLA, GLB1, GM2A, GNE, GNPTAB, GNPTG, GNS, GRN, GUSB, HEXA, HEXB, HGSNAT, HYAL1, IDS, IDUA, KCTD7, LAMP2, LIPA, LTBP2, LYST, MAN2B1, MANBA, MCOLN1, MFSD8, MYOSA, NAGA, NAGLU, NEU1, NPC1, NPC2, PPT1, PSAP, Rab27A, SGSH, SLC17A5, SMPD1, SUMF1, TPP1

Indications

This test is indicated for individuals:

- 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

Next Generation Sequencing: In-solution hybridization of all coding exons is performed on the patient's genomic DNA. Although some deep intronic regions may also be analyzed, this assay is not meant to interrogate most promoter regions, deep intronic regions, or other regulatory elements, and does not detect single or multi-exon deletions or duplications. Direct sequencing of the captured regions is performed using next generation sequencing. The patient's gene sequences are then compared to a standard reference sequence. Potentially causative variants and areas of low coverage are Sanger-sequenced. Sequence variations are classified as pathogenic, likely pathogenic, benign, likely benign, or variants of unknown significance. Variants of unknown significance may require further studies of the patient and/or family members.

Detection

Next Generation Sequencing: Clinical Sensitivity: Unknown. Mutations in the promoter region, some mutations in the introns and other regulatory element mutations cannot be detected by this analysis. Large deletions/duplications will not be detected by this analysis. Results of molecular analysis should be interpreted in the context of the patient's clinical/biochemical phenotype.

Analytical Sensitivity: ~99%.

Specimen Requirements
Submit only 1 of the following specimen types

Type: Saliva

Specimen Requirements:
Oragene™ Saliva Collection Kit
Oragene™ Saliva Collection Kit used according to manufacturer instructions. Please contact EGL for a Saliva Collection Kit for patients that cannot provide a blood sample.

Specimen Collection and Shipping:
Please do not refrigerate or freeze saliva sample. Please store and ship at room temperature.

Type: Whole Blood (EDTA)

Specimen Requirements:
EDTA (Purple Top)
Infants and Young Children (2 years of age to 10 years old): 3-5 ml
Older Children & Adults: 5-10 ml
Autopsy: 2-3 ml unclotted cord or cardiac blood

Specimen Collection and Shipping:
Ship sample at room temperature for receipt at EGL within 24 hours of collection. Do not refrigerate or freeze.

Type: DNA, Isolated

Specimen Requirements:
Microtainer
15µg
Isolation using the Perkin Elmer™ Chemagen™ Automated Extraction method or Qiagen™ Puregene kit for DNA extraction is recommended.

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

Related Tests

- Biochemical enzyme assay for lysosomal storage disorders
- Lysosomal Storage Disorders: Deletion/Duplication Panel