TEST ID: LYSDU
LYSOSOMAL STORAGE DISORDERS SCREEN, URINE

USEFUL FOR
Screening patients suspected of having a lysosomal storage disorder

GENETICS TEST INFORMATION
This is a general urine screening test for a broad array of lysosomal storage (LSD) and related disorders. Not all LSDs are detectable by this method.

CLINICAL INFORMATION
Lysosomal storage disorders (LSD) are a diverse group of inherited diseases characterized by the intracellular accumulation of macromolecules leading to cell damage and organ dysfunction. Approximately 50 lysosomal storage disorders have been described with a wide phenotypic spectrum and ranging in severity from neonatal lethal to later onset milder variants.

Although classification is not always straightforward, LSDs are generally categorized according to the type of storage material that accumulates in the cells and tissues. Major categories include mucopolysaccharidoses, oligosaccharidoses, neuronal ceroid lipofuscinoses, and sphingolipidoses. In many cases, accumulating analytes can be detected in urine. Screening for these disorders typically begins with an analysis to detect disease-specific metabolite patterns or profiles indicative of an LSD. The combined analysis of disease-specific markers for LSDs in multiple tests can allow for the identification of additional disorders that may not be picked up using any of the single tests alone.

Disorders detectable by this approach include the oligosaccharidoses alpha-mannosidosis, aspartylglucosaminuria, fucosidosis, Schindler disease, and sialidosis; the sphingolipidoses GM1 gangliosidosis, Sandhoff disease, galactosialidosis, Saposin B deficiency, metachromatic leukodystrophy, multiple sulfatase deficiency, Fabry disease, Gaucher disease, and Krabbe disease; the mucopolysaccharidoses excluding MPS IX (hyaluronidase deficiency); the glycogen storage disorder Pompe disease and the mucolipidoses types II and III. Additionally, other disorders such as CDG types IIb and de-glycosylation disorders such as NGLY1-CDG may also be detected.

The mucopolysaccharidoses (MPS) are a subset of lysosomal storage disorders caused by the deficiency of any of the enzymes involved in the stepwise degradation of dermatan sulfate, heparan sulfate, keratan sulfate, or chondroitin sulfate (glycosaminoglycans: GAGs). Undegraded or partially degraded GAGs (also called mucopolysaccharides) are stored in lysosomes and excreted in the urine. Accumulation of GAGs in lysosomes interferes with normal functioning of cells, tissues, and organs resulting in the clinical features observed in MPS disorders. There are 11 known enzyme deficiencies that result in MPS. In addition, abnormal GAG storage is observed in multiple sulfatase deficiency and in I-cell disease. Finally, an abnormal excretion of GAGs in urine is observed occasionally in other disorders including active bone diseases, connective tissue disease, hypothyroidism, urinary dysfunction, and oligosaccharidoses.
The oligosaccharidoses (glycoproteinoses) are a subset of lysosomal storage disorders caused by the deficiency of any one of the lysosomal enzymes involved in the degradation of complex oligosaccharide chains. They are characterized by the abnormal accumulation of incompletely degraded oligosaccharides in cells and tissues and the corresponding increase of related free oligosaccharides in the urine. Clinical features can include bone abnormalities, coarse facial features, corneal cloudiness, organomegaly, muscle weakness, hypotonia, developmental delay, and ataxia. Age of onset ranges from early infancy to adult and can even present prenatally.

The sphingolipidoses are a subset of lysosomal storage disorders caused by a defect in any one of the enzymes that degrade complex ceramide containing lipids. They are characterized by the excessive accumulation of sphingolipids in the tissues, particularly in the central nervous system resulting in progressive neurodegeneration and developmental regression. In 2 conditions, Fabry disease and Gaucher disease type I, there is only systemic involvement. In many cases, sphingolipidoses can be detected by through oligosaccharide analysis in urine.

Because of the similarity of features across disorders and their variability, clinical diagnosis of LSDs can be challenging; therefore, urine screening and the combined analysis of multiple urine screening tests is an important tool for the initial workup of an individual suspected of having a lysosomal storage disorder. Abnormal results can be followed up with the appropriate enzyme or molecular analysis.

**INTERPRETATION**

Abnormal results are not sufficient to conclusively establish a diagnosis of a particular disease. Follow-up testing is recommended to confirm a diagnosis.

When abnormal results are detected with characteristic patterns, a detailed interpretation is given, including an overview of the results and their significance, a correlation to available clinical information, elements of differential diagnosis, recommendations for additional biochemical testing, and in vitro confirmatory studies (enzyme assay and molecular test).

**CLINICAL REFERENCE**

