MAYO CLINIC
Mayo Medical Laboratories

TEST ID: LSDP

LYSOSOMAL STORAGE DISEASE PANEL BY NEXT-GENERATION SEQUENCING

USEFUL FOR

- Follow up for abnormal biochemical results and confirmation of suspected lysosomal storage disease (LSD)
- Identifying mutations within genes known to be associated with lysosomal storage disease, allowing for predictive testing of at-risk family members

CLINICAL INFORMATION

Lysosomal storage diseases (LSDs) encompass a group of over 40 inherited biochemical diseases in which genetic mutations cause defective lysosomal functioning. Lysosomes perform catabolic functions for cells, which is accomplished through activity of various proteins such as lysosomal enzymes, transport proteins, and other proteins. Functional deficits in these proteins cause an accumulation of substrates in cells leading to progressive organ dysfunction.

This leads to variable clinical features that can affect the cardiovascular, neurological, ocular, and skeletal systems, among others. Clinical features are dependent on the amount and location of the substrate accumulation, but may include the following: characteristic facial features (coarse features), hepatomegaly, deafness, vision loss, abnormal skeletal findings, hydrops fetalis, ataxia, hypotonia, developmental delay/regression, and intellectual disability. Age of onset is variable, with symptoms presenting from the prenatal period to adulthood, but generally LSDs are progressive and cause significant morbidity and mortality with a decreased lifespan. Enzyme replacement therapy and oral substrate inhibitors are therapeutic options for some LSDs.

LSDs are inherited in an autosomal recessive manner with the exception of Hunter, Fabry, and Danon diseases, which are X-linked. There are some founder mutations associated with particular LSDs in the Ashkenazi Jewish and Finnish populations, leading to an increased carrier frequency for some. Overall, the prevalence of LSDs is estimated at 1/7000 to 1/8000.

Neuronal ceroid lipofuscinoses (NCLs) are a subset of lysosomal storage diseases that involve defective cellular processing of lipids. NCLs are clinically characterized by epilepsy, intellectual and motor decline, and blindness. Electron microscopy typically shows a characteristic accumulation of granular osmophilic deposits (GROD), curvilinear profiles (CVB), or fingerprint profiles (FP). Enzymatic testing may show deficiency in palmitoyl-protein thioesterase 1 (PPT1), tripeptidyl-peptidase 1 (TPP1), or cathepsin D (CTSD). Currently there are at least 14 genetically distinct forms.

Age of onset and clinical features can be variable, from congenital to adult onset. NCL is typically inherited in an autosomal recessive manner, although one adult onset form (ANCL; *DNAJC5* gene) has been shown to be autosomal dominant.

First-tier biochemical testing is available for the 2 most common types of enzyme deficiency resulting in NCL: **TPPTL / Tripeptidyl Peptidase 1 (TPP1) and Palmitoyl-Protein Thioesterase 1 (PPT1), Leukocytes**; and **TPPTF / Tripeptidyl Peptidase 1 (TPP1) and Palmitoyl-Protein Thioesterase 1 (PPT1), Fibroblasts**.

This panel includes sequencing of 43 genes related to various LSDs, as well as 15 genes specific to neuronal ceroid lipofuscinosis, for a total of 58 genes.

REFERENCE VALUES

An interpretive report will be provided.

ANALYTIC TIME

4 weeks

05/2017

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See gene table below for genes and conditions that are included on the panel. Recommended first-tier biochemical testing is also provided.

GENE	DISEASE NAME	OMIM ID	INHERITANCE
ACP2	Lysosomal acid phosphatase deficiency (ACPHD)	200950	AR
AGA	Aspartylglucosaminuria (AGU)	208400	AR *Finnish Founder mutation
ARSA	Metachromatic leukodystrophy	250100	AR
ARSB	Mucopolysaccharidosis Type VI maroteaux-lamy	253200	AR
ARSH	Multiple sulfatase deficiency	300586	AR
ASAH1	Farber lipogranulomatosis	228000	AR
CHIT1	Chitotriosidase deficiency (with Gaucher 1)	600031, 614122	AR
CTNS	Cystinosis	219800	AR
CTSA	Galactosialidosis	256540	AR
FUCA1	Fucosidosis	230000	AR
GAA	Pompe disease-glycogen storage disease type II	232300	AR
GALC	Krabbe disease	245200	AR
GALNS	Mucopolysaccharidosis Type IVA Morquio A	612222	AR
GBA	Gaucher Disease	230800, 230900, 231000	AR
GFAP	Alexander disease	203450	AR
GLA	Fabry disease	301500	X linked
GLB1	Mucopolysaccharidosis type IVB-MorquioB	253010	AR
GM2A	GM2-gangliosidosis, AB variant	272750	AR
GNPTAB	Mucolipidosis II, and III	252500, 252600	AR
GNPTG	Mucolipidosis III gamma	232605	AR
GNS	Mucopolysaccharidosis type IIID Sanfilippo D	252940	AR
GUSB	Mucopolysaccharidosis type VII Sly	253220	AR
HEXA	Tay-Sachs disease	272800	AR
HEXB	Sandhoff disease	268800	AR
HGSNAT	Mucopolysaccharidosis type IIIC (Sanfilippo)	252930	AR
HYAL1	Mucopolysaccharidosis type IX: Hyaluroindase deficiency	601492	AR
IDS	Mucopolysaccharidosis type II Hunter disease	309900	X linked
IDUA	Mucopolysaccharidosis type I (Hurler/Scheie)	607014	AR
LAMP2	Glycogen Storage Disease Type IIB-Danon Disease	300257	AR
LIPA	Lysosomal acid lipase deficiency/Wolman disease	278000	AR
MAN2B1	Alpha-mannosidase deficiency	248500	AR
MANBA	Beta-mannosidosis	248510	AR
MCOLN1	Mucolipidosis type IV	252650	AR
NAGA	Schindler disease	609241	AR
NAGLU	Mucopolysaccharidosis Type IIIB	252920	AR
NEU1	Sialidosis	256550	AR
NPC1	Niemann-Pick type C1 and C2	257220	AR
NPC2	Niemann-Pick type C1 and C3	607625	AR
PSAP	Prosaposin Deficiency (Variants of other disorders as well)	611721, 610539, 611722, 249900	AR
SGSH	Mucopolysaccharidosis Type IIIA Sanfilippo	252900	AR
SLC17A5	Sialic acid storage disease	269920	AR
SMPD1	Niemann-Pick type A/B	257200, 607616	AR
SUMF1	Multiple Sulfatase Deficiency	272200	AR

AR = autosomal recessive