Lysosomal Acid Lipase Deficiency: (LALD) is an autosomal recessive disorder caused by mutations in the LIPA gene which lead to decreased lysosomal acid lipase (LAL) activity. Lysosomal acid lipase is responsible for the breakdown of lipids in the lysosome; deficiency of this enzyme leads to accumulation of cholesteryl esters and triglycerides, particularly in the liver, spleen, and macrophages. LALD is classified into two subtypes.

The early-onset subtype, or Wolman’s disease (WD), is rapidly progressive and fatal in infancy. It is characterized by prominent GI and liver manifestations (persistent vomiting, profound growth failure, hepatosplenomegaly, and liver failure) and adrenal calcification. The later-onset subtype, cholesteryl ester storage disease (CESD), is more variable and symptoms may present from childhood through adulthood. CESD is characterized by prominent hepatic manifestations (fatty liver, fibrosis) ultimately leading to liver failure. CESD results in significant morbidity and a shortened lifespan.

Genetics: Lysosomal acid lipase deficiency is inherited in an autosomal recessive manner. If an individual is affected, it is implied that each parent is a carrier of one mutated gene and the risk of having future affected offspring is 25% with each pregnancy. A person who is a carrier for an autosomal recessive condition does not manifest features of the disorder. LIPA mutations that result in little or no LAL activity lead to the early-onset phenotype, while mutations which result in some amount of residual enzyme activity lead to later-onset CESD.

While over 40 mutations have been identified, an exon 8 splice site mutation (c.894G>A) is estimated to account for 60% of reported mutations among CESD patients.

Biochemical Analysis: LAL activity is measured in leukocytes using fluorogenic 4-MU olate substrate and LAL inhibitor lalistat. The LAL activity is calculated by subtracting the lalistat inhibited lipases (non LAL lipase) from the total lipases. A normal LAL activity can rule out WD or CESD. Significant enzyme activity reduction (<5-10% of normal mean) can establish the biochemical diagnosis for either WD or CESD, which should be confirmed by LIPA sequencing to identify the disease causing mutation. Results are reported to the referring physician within 7 to 10 days from the receipt of the specimen.

Molecular Analysis: DNA is extracted and molecular analysis is performed by Sanger sequencing of the coding regions of the LIPA gene. All sequencing is bi-directional. The technological and analytical test sensitivity for identifying alterations in the LIPA gene is ~92% as some large deletions and rearrangements and intronic alterations may be missed using this technique. Results are reported to the referring physician within 3 to 4 weeks from the receipt of the specimen.

Specimen and Shipping requirements:
Biochemical Analysis:
- 2 yellow-top (ACD-A or ACD-B) 5-10 ml tubes of blood from the patient are required. Note that lavender-top (EDTA), and green-top (NaHp) tubes are also acceptable. Tubes of blood should be kept and shipped at room temperature (do NOT freeze) within 48 hours of collection or frozen on dry ice.
- White blood cell pellet (at least 1 pellet) can be sent frozen on dry ice

Molecular Analysis:
- 2 yellow-top (ACD-A or ACD-B) or 2 lavender-top (EDTA), 5-10 ml tubes of blood kept and shipped refrigerated or at room temperature (do NOT freeze).