Condition Description

Glycogen storage disorders (GSDs) are a group of inherited genetic defects of glycogen metabolism. Most of them have autosomal recessive inheritance, however there are a few exceptions. There are more than 20 subtypes classified by the specific enzyme deficiency, affected tissue, and disease phenotype. 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, as molecular analysis is likely to expand the clinical spectrum of GSDs, may provide data relevant to prognosis and future therapeutic intervention and is important for carrier testing and early prenatal diagnosis.

The overall incidence of GSDs as a group is estimated to be 1 in 20,000-43,000 births. GSDs primarily affect the liver, the muscle, or both. Although the phenotype range is broad, the majority of clinical manifestations are hepatomegaly, failure to thrive, hypoglycemia, hyperlactatemia, hyperuricemia, and hyperlipidemia. This GSD panel covers 15 genes in which pathogenic variants cause the muscle isoforms of GSD and disorders that have overlapping phenotype with GSDs.

References:
- Burwinkel et al. (2005), Am J Hum Genet, 76:1034-1049.

Genes
AGL, ENO3, GAA, GBE1, GYS1, LAMP2, PFKM, PGAM2, PGM1, PHKB, PRKAG2, PYGM

Indications

This test is indicated for:
- Confirmation of a clinical diagnosis of glycogen storage disorders (GSDs).
- Carrier testing in adults with a family history of glycogen storage disorders (GSDs).

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: 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: 60 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

- Pompe (dry blood spot - test code DZ; leukocytes - DW).
- Glycogen Storage Disorders- Muscle: Deletion/Duplication Panel