Isovaleric Acidemia Mutation Panel

Test Code	D0409
Test Summary	This test analyzes 1 variant of the IVD gene
Turn-Around-Time (TAT)*	3 - 5 weeks
Acceptable Sample Types	DNA, Isolated (Preferred sample type)
Acceptable Billing Types	Self (patient) Payment Institutional Billing Commercial Insurance

Indications for Testing

- Individuals with symptoms of a distinctive odor, poor feeding, vomiting, seizures, lethargy, organic acidemia, organic aciduria, coma, early death, failure to thrive, and developmental delay
- Individuals with a family history of isovaleric acidemia

Test Description

This test detects the A282V variant of the *IVD* gene associated with isovaleric acidemia.

Condition Description

Isovaleric acidemia is a disease that prevents the body from breaking down the amino acid leucine. The onset is typically in early infancy and includes symptoms of a distinctive odor, poor feeding, vomiting, seizures, lethargy, organic acidemia, organic aciduria, coma, and premature death. Later onset of the disease is associated with symptoms of failure to thrive and developmental delay. The condition can be managed with a strict diet. The incidence of isovaleric acidemia is estimated to be ~ 1 in 250,000.

Test Methods and Limitations

Gene analysis for the various targeted mutations is performed by polymerase chain reaction and melting curve analysis to detect the mutant and wild-type forms of the gene. Sequence-specific oligonucleotide probes are labeled with fluorescent dyes, which hybridize to their complementary sequence target in PCR products. The fluorescence resonance energy transfer (FRET) from one fluorophore to another adjacent fluorophore is measurable and is directly proportional to the amount of target DNA generated during PCR. Allele-specific melting curves are generated by slow thermal denaturing of the probe: template hybrid. Melting curves are generated by monitoring fluorescence throughout denaturation, and melting peaks are generated by plotting the inverse derivative of fluorescence versus temperature (?dF/dT).

Detailed Sample Requirements

DNA, Isolated (Preferred sample type)

Collection:

Required DNA Quantity by Test Type*:

- **Next Generation Sequencing (NGS):** Send >1000 ng total gDNA @ >15 ng/?L. Please ship samples in 10mM Tris. Do not use EDTA.
- **Sanger Sequencing:** Send >500 ng total gDNA @ >15 ng/?L (varies by the size of the gene and the variants requested).

- **Non-Sanger Sequencing Tests:** Send >500 ng total gDNA @ >15 ng/?L.

Sample Condition: * Required DNA Quality: High molecular weight DNA (>12kb). A260/A280 reading should be ? 1.8. A260/230 a ratio range of 1.8 to 2.2. Contact the laboratory for specific amounts if total ng cannot be met.
Shipping: Ship overnight at ambient temperature.

SPECIAL INSTRUCTIONS:

- **Research Laboratories:** DNA extracted in research laboratories is not acceptable. Only under exceptional circumstances (e.g., proband not available) will DNA extracted in a research laboratory be accepted for clinical testing. Additional testing (e.g., of other family members) may be required to confirm results.
- **Laboratories outside the United States:** Non-US laboratories are not subject to CLIA regulations and will be reviewed on a case-by-case basis. Please call to speak with a laboratory genetic counselor prior to submitting a DNA sample from any non-CLIA certified laboratory.
- **Special Notes**: If extracted DNA is submitted, information regarding the method used for extraction should be sent along with the sample.