HENRY FORD HEALTH
CENTER FOR PRECISION DIAGNOSTICS

Familial Amyloidosis (hATTR)(TTR) Gene Sequencing Panel

Hereditary transthyretin amyloidosis (ATTR) is a disorder where proteins fold improperly leading to harmful amyloid buildup in organs. Symptoms usually start between the 3rd and 5th decades of life, with around 1 in 100,000 individuals in the US affected. Pathogenic variants in the TTR gene account for nearly 90% of hereditary amyloidosis cases.

Testing Method and Background

This test utilizes **Next Generation Sequencing (NGS) technology,** which provides coverage of all coding exons and noncoding DNA in exon flanking regions (on average 50 bp) enriched using hybrid capture methodology. This assay can detect >99% of described mutations in the included genes, when present, including single nucleotide variants (point mutations), small insertions/deletions (1-25 bp), larger deletions and duplication (<100 bp), complex insertions/deletions, splice site mutations, whole-gene deletions/duplications and exon-level intragenic deletions/insertions in each gene targeted for analysis. All reportable copy number variants are confirmed by independent methodology.

Most ATTR is inherited and about 90% of hereditary amyloidosis cases stem from mutations in the TTR gene, inherited in an autosomal dominant (AD) manner with incomplete penetrance. Only rarely ATTR is inherited in an autosomal recessive (AR) manner, which typically has higher penetrance, greater severity and earlier onset. More than 95% of the causative variants in TTR are missense mutations. These changes are linked to neuropathic, cardiac, or leptomeningeal forms of amyloidosis, although there can be overlap in symptoms. Since hereditary ATTR amyloidosis occurs through a gain-of-function mechanism and large intragenic deletion or duplication has not been reported, testing for intragenic deletions or duplication is unlikely to identify a disease-causing variant. Pathogenic variants in the TTR gene account for nearly 90% of hereditary amyloidosis cases. TTR gene sequence analysis detects 99% of pathogenic variants in the gene.

Highlights of Familial Amyloidosis (hATTR)(TTR) Gene Sequencing Panel

Targeted Region

TTR

- **Wide-ranging Coverage of Variants**
  Detects and provides coverage of all coding exons and noncoding DNA in exon flanking regions.
- **Accurate Results Using Clinically Validated Computational Data Analysis**
  A variety of mutation types (point, indels and duplications) are confirmed using computational data analysis for sequence variant calling, filtering and annotation.

Ordering Information

Get started (non-HFHS): Print a Germline/Non-Cancer Hereditary Test requisition form online at www.HenryFord.com/HFCPD

Get started (HFHS): Order through Epic using test "Familial Amyloidosis (hATTR)(TTR) Gene Sequencing Panel" (DNA2100037)

Specimen requirements:

- Peripheral Blood - 1-3ml in lavender top tube (EDTA) **Specimen stability: Ambient - 72 hours; Refrigerated - 1 week**
- Extracted DNA - from a CLIA-certified Laboratory

Cause for Rejection: Clotted, hemolyzed, or frozen specimens, improper anticoagulant, tubes not labeled with dual patient identification, non-dedicated tubes.

TAT: 10-14 business days (after Prior Authorization obtained)

Mail test material to:
Henry Ford Center for Precision Diagnostics
Pathology and Laboratory Medicine
Clinic Building, K6, Core Lab, E-655
2799 W. Grand Blvd., Detroit, MI 48202

CPT Codes: 81404 (TTR), G0452

Contact us: Client Services, Account and Billing Set-up, and connect with a Molecular Pathologist at (313) 916-4DNA (4362)

For more information on Comprehensive Molecular Services, visit our website www.HenryFord.com/HFCPD

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