Overview

Useful For
Determining the specific apolipoprotein E (APOE) genotypes in patients with type III hyperlipoproteinemia

APOE genotyping has been used to assess susceptibility for Alzheimer disease. However, the use of APOE analysis for predictive testing for Alzheimer disease is not currently recommended by the American College of Medical Genetics due to limited clinical utility and poor predictive value.

Special Instructions

- Informed Consent for Genetic Testing
- Molecular Genetics: Neurology Patient Information
- Informed Consent for Genetic Testing (Spanish)

Method Name
Polymerase Chain Reaction (PCR), Including Restriction Digest

(PCR is utilized pursuant to a license agreement with Roche Diagnostic Systems, Inc.)

NY State Available
Yes

Specimen

Specimen Type
Varies

Shipping Instructions
Specimen preferred to arrive within 96 hours of draw.

Specimen Required

Patient Preparation: A previous bone marrow transplant from an allogenic donor will interfere with testing. Call 800-533-1710 for instructions for testing patients who have received a bone marrow transplant.

Specimen Type: Whole blood

Container/Tube:

Preferred: Lavender top (EDTA) or yellow top (ACD)

Acceptable: Any anticoagulant

Specimen Volume: 3 mL

Collection Instructions:

1. Invert several times to mix blood.
2. Send specimen in original tube.
Test Definition: APOEG
Apolipoprotein E Genotyping, B

Forms
1. **New York Clients-Informed consent is required.** Document on the request form or electronic order that a copy is on file. The following documents are available in Special Instructions:

- [Informed Consent for Genetic Testing](T576)
- [Informed Consent for Genetic Testing-Spanish](T826)

2. **Molecular Genetics: Neurology Patient Information** in Special Instructions

3. If not ordering electronically, complete, print, and send a [Neurology Specialty Testing Client Test Request](T732) with the specimen.

Reject Due To
All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

Specimen Stability Information

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<tr>
<th>Specimen Type</th>
<th>Temperature</th>
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Clinical and Interpretive

Clinical Information
Apolipoproteins are structural constituents of lipoprotein particles that participate in lipoprotein synthesis, secretion, processing, and metabolism. Apolipoproteins have critical roles in blood lipid metabolism. Defects in apolipoprotein E (Apo E) are responsible for familial dysbetalipoproteinemia, or type III hyperlipoproteinemia, in which increased plasma cholesterol and triglycerides result from impaired clearance of chylomicron and very-low-density lipoprotein (VLDL) remnants.

The human \( APOE \) gene is located on chromosome 19. The 3 common \( APOE \) alleles are designated e2, e3, and e4, which encode the Apo E isoforms E2, E3, and E4, respectively. E3, the most common isoform in Caucasians, shows cysteine (Cys) at amino acid position 112 and arginine (Arg) at position 158. E2 and E4 differ from E3 by single amino acid substitutions at positions 158 and 112, respectively (E2: Arg158->Cys; E4: Cys112->Arg). The allele frequencies for most Caucasian populations are as follows:

- \( e2 = 8\% \text{ to } 12\% \)
- \( e3 = 74\% \text{ to } 78\% \)
- \( e4 = 14\% \text{ to } 15\% \)

E2 and E4 are both associated with higher plasma triglyceride concentrations. Over 90% of individuals with type III hyperlipoproteinemia are homozygous for the e2 allele. However, <10% of individuals homozygous for the e2 allele have overt type III hyperlipoproteinemia. This suggests that other genetic, hormonal, or environmental factors must

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contribute to the phenotypic expression of the disease. The e4 allele has been linked to pure elevations of low-density lipoproteins (LDL). Patients with a lipid profile consistent with type III hyperlipidemia are candidates for analysis of their APOE genotype.

The APOE gene is also a known susceptibility gene for Alzheimer disease. The e4 allele is associated with an increased risk for Alzheimer disease, particularly late-onset disease, in a dose-dependent manner. This risk is also influenced by other factors. It is estimated that individuals with the APOE e3/e4 genotype have a 4-fold relative risk for Alzheimer disease, while homozygotes for e4 allele have a 12-fold relative risk. Several studies have suggested a protective effect of the APOE e2 allele.

The APOE e4 allele, however, is neither sufficient nor necessary for the development of Alzheimer disease.

Approximately 50% of individuals with Alzheimer disease carry an e4 allele and many individuals who have an e4 allele will never develop Alzheimer disease. The use of APOE analysis for predictive testing for Alzheimer disease is not currently recommended by the American College of Medical Genetics due to limited clinical utility and poor predictive value.

**Interpretation**

An interpretive report will be provided.

**Cautions**

This assay will not detect all of the mutations that cause type III hyperlipoproteinemia. Therefore, the absence of a detectable mutation does not rule out the possibility that an individual is a carrier of or affected with this disease.

This assay cannot predict or rule out the development of Alzheimer disease in an individual.

Test results should be interpreted in the context of clinical findings, family history, and other laboratory data. Errors in our interpretation of results may occur if information given is inaccurate or incomplete.

Rare polymorphisms exist that could lead to false-negative or false-positive results. If results obtained do not match the clinical findings, additional testing should be considered.

In rare cases, DNA alterations of undetermined significance may be identified.

This assay does not identify all of the less common apolipoprotein E alleles. Thus, an individual who appears to be homozygous for e2, e3, or e4 may carry 1 of the rare alleles that cannot be detected by this assay.

**Clinical Reference**


Performance

Method Description
A PCR-based assay, which includes HhaI digestion of the amplified product, is utilized to identify the 3 most common apolipoprotein E alleles (e2, e3, e4). (Unpublished Mayo method)

PDF Report
No

Day(s) and Time(s) Test Performed
Friday; 10 a.m.

Analytic Time
5 days

Maximum Laboratory Time
10 days

Performing Laboratory Location
Rochester

Fees and Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information

LOINC® Information
### Test Definition: APOEG
Apolipoprotein E Genotyping, B

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