Apolipoprotein B Mutation Detection

Apolipoprotein B (apoB) is a protein product of the *APOB* gene and is the main protein of chylomicrons and low density lipoproteins (LDLs). ApoB occurs in two isoforms, intestinal apoB-48 and hepatic apoB-100. *APOB* gene variants that induce a conformational change in the apoB-100 protein result in reduced binding of the LDL complex to its receptor. Such variants cause the heritable condition familial defective apolipoprotein B-100 (FDB), which is associated with increased risk for hypercholesterolemia and coronary artery disease (CAD). Genetic testing may be useful when the diagnosis of FDB is unclear or to identify at-risk relatives when the causative familial variant is known.

Disease Overview

Incidence

- R3500Q: occurs in 1/500-1/700 White individuals of North America and Europe
- R3500W: described in Scottish population and in ~2% of Asian individuals with FDB
- 1.5% of familial hypercholesterolemia is due to FDB
- Variants in *LDLR*, *PCSK9,* or *APOB* genes result in indistinguishable phenotypes for hypercholesterolemia

Symptoms

- Elevated cholesterol, triglycerides
- Premature CAD

Genetics

Gene

APOB

Inheritance

Autosomal dominant with reduced penetrance

Penetrance

- 40% of males and 20% of females heterozygous for an APOB variant will develop CAD
- Patients who are homozygotes or compound heterozygotes for R3500Q/R3500W are at greater risk

Variants Tested

- *APOB* c.10580G>A; p.Arg3527Gln (R3500Q)
- *APOB* c.10579C>T; p.Arg3527Trp (R3500W)

Tests to Consider

Apolipoprotein B (APOB) Mutation Detection 0055654

Method: Polymerase Chain Reaction/Fluorescence Monitoring

Assesses for the *APOB* p.Arg3527Gln (R3500Q) and p.Arg3527Trp (R3500W) variants

Indications for testing:

- Use to confirm a diagnosis of familial defective Apo B-100 (FDB)
- Use to identify genetic etiology for inherited hypercholesterolemia
- Use to screen individuals with a family history of FDB to assess risk of coronary artery disease

Related Tests

Apolipoprotein B/A Ratio 0050028

Method: Quantitative Nephelometry

- Not usually recommended for cardiovascular disease risk assessment
- May be used concurrently with cholesterol/HDL-C ratio in individuals with elevated triglycerides (≥200 mg/dL)

Apolipoprotein B 0050029

Method: Quantitative Nephelometry

- Acceptable nontraditional secondary cardiovascular disease risk screen for specific populations
- May be useful in addition to LDL-C monitoring in individuals with elevated triglycerides

Test Interpretation

Sensitivity/Specificity

Analytical sensitivity/specificity: 99.9%

Results

- Negative: R3500W and R3500Q not detected
- Positive: R3500W and/or R3500Q detected
  - Associated with hypercholesterolemia and increased risk for CAD

Limitations

- Other *APOB* gene variants will not be detected
- Variants in other genes that may cause familial hypercholesterolemia are not detected
- Diagnostic errors can occur due to rare sequence variations
- Not recommended for asymptomatic individuals <18 years

Additional Resources

Andersen LH, Miserez AR, Ahmad Z, et al. Familial defective apolipoprotein B-100: A review. J Clin Lipidol. 2016;10(6):1297-1302. PubMed

Youngblom E, Pariani M, Knowles JW. Familial hypercholesterolemia. In: Adam MP, Ardinger HH, Pagon RA, et al, editors. GeneReviews, University of Washington; 1993-2020. [Last update: Dec 2016; Accessed: Sep 2020]

Related Information

Atherosclerotic Cardiovascular Disease Risk Markers

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