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: 1/500 European Caucasians
- R3500W: described in Scottish population and in ~2% of Asian individuals with FDB
- Up to 15% 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

Variants Tested

- APOB c.10580G>A; p.Arg3527Gln (R3500Q)
- APOB c.10579C>T; p.Arg3527Trp (R3500W)
- ~40% of males and 20% of females heterozygous for an APOB variant will develop CAD
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
  - Homozygotes and compound heterozygotes for R3500Q/R3500W are at greater risk for CAD than heterozygotes

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

References


Related Information

Atherosclerotic Cardiovascular Disease Risk Markers