Type III hyperlipidaemia
(hyperlipoproteinemia, type III, OMIM #617347)

Apolipoprotein E, *APOE* genotyping

Background

The gene APOE encodes for a major component of specific lipoproteins called very low-density lipoproteins (VLDL); these function to remove excess cholesterol from the blood and carry it to the liver for processing. Maintaining normal levels of cholesterol is essential for the prevention of cardiovascular diseases, including heart attack and stroke.

Type III hyperlipidaemia / hyperlipoproteinemia, type III, also called dysbetalipoproteinemia or remnant hyperlipidaemia, is characterised by raised triglyceride and cholesterol levels due to abnormally high concentration of intermediate density lipoprotein (IDL) and chylomicrons. This condition is inherited as an autosomal recessive trait and demonstrates low penetrance. There are at least three different alleles of the APOE gene. The major alleles are called E2, E3, and E4. The most common allele is E3, which is found in more than half of the population. Individuals that carry two copies of the APOE E2 allele are at risk for the condition of type III hyperlipidaemia. The E2 isoform shows defective binding of remnants to hepatic lipoprotein receptors and delayed clearance from plasma. Additional genetic and/or environmental factors must be required for development of the disorder, however, because only 1-4% of E2/E2 homozygotes develop this condition. The condition predisposes people to coronary artery disease and peripheral vascular disease.

Please note that the E4 allele has been found to be associated with some cases of Alzheimer's disease. APOE E4/E4 analysis is not recommended for clinical diagnosis or predictive testing of Alzheimer's disease (see OMIM 104310) as there is only a statistical association with the disease. APOE E4/E4 is not causative or predictive of the disorder. **This laboratory does not offer testing for the E4 allele**. Referrals for individuals with dementia, cognitive impairment, memory loss, Alzheimer's or similar, will not be tested.

Inheritance: Autosomal recessive

Molecular Analyses

APOE Genotyping:
TaqManAD single nucleotide polymorphism (SNP) genotyping assays to detect homozygosity for the common APOE gene allelic variants APOE:c.388T=, p.(Cys130=) and APOE:c.526C>T, p.(Arg176Cys), for determination of the APOE E2/E2 genotype. (Genbank accession number (APOE) NM_000041.3)

Reporting policy:
Patient results are reported as evidence for or absence of the *APOE* E2/E2 genotype only.

No detail of E3 or E4 alleles shall be reported.

Test (Price available on request)	TAT (calendar days)
Targeted, diagnostic testing for APOE variants	42

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Accredited to ISO 15189:2012
(8988)

Links
Orphanet
http://www.orpha.net/
OMIM
http://www.omim.org/
Genetic Test Registry
http://www.ncbi.nlm.nih.gov/gtr/

Support
https://www.heartuk.org.uk/genetic-conditions/type-3-hyperlipidaemia

Sample Requirements
Blood – 5ml in EDTA (1ml neonates/infants);
Mouthwash/buccal cells; other tissue
Please contact lab prior to sending a prenatal sample.
Please label samples with three identifiers and date of collection.
All samples must be accompanied by request form
Consent for testing & DNA storage is assumed when request for test received