Bristol Genetics Laboratory is a UKAS accredited medical laboratory No.9307.

North Bristol NHS Trust

R324 Familial Chylomicronaemia Syndrome (FCS)

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Sample Required:
See Sample requirements page at www.nbt.nhs.uk/genetics **for full details**

Samples should be accompanied by a FULLY completed request form (available as download at www.nbt.nhs.uk/genetics or from the laboratory).

Please include details of the test required, family history, address and POSTCODE, NHS number, referring clinician and centre.

Consent and Storage:
All genetic testing requires consent. **It is the responsibility of the referring clinician to ensure that appropriate consent has been obtained.**

DNA is stored from **ALL** patients undergoing DNA testing, unless consent for this is specifically denied.

Stored material from all referrals may be retained for quality assurance purposes and may be used anonymously for the development of new tests for the disorder in question.

Clinical Background and Genetics

The Familial Chylomicronaemia Syndrome (FCS) gene panel has been designed for the analysis of genes associated with regulation and metabolism of triglyceride rich lipoproteins. Pathogenic variants are associated with FCS.

- Severe hypertriglyceridaemia is defined as triglyceride concentration > 10mmol/L.
- Hypertriglyceridaemia is seen in lipid phenotypes (Frederickson classification) 1, 2B, 3, 4 and 5.
- Clinical features can include eruptive xanthomas, palmar creases, xanthomas and pancreatitis.
- Hypertriglyceridaemia especially post-prandially appears to increase cardiovascular disease (CVD) risk.

Service offered

- 8 gene panel targeting genes associated with familial chylomicronaemia syndrome (R324, PanelApp version 1.3). Panel tested using a bespoke design Twist BioSciences probeset with Illumina Nextera DNA flex library preparation.
- The following genes are included: *LPL*, *GPIHBP1, APOA5, GPD1, LMF1, CREB3L3, APOE* (E2 allele only), *APOC2.*
- Familial tests for known pathogenic variants using Sanger sequencing.

Quality

- BGL participates in the EMQN scheme for DNA sequencing and GenQA scheme for variant pathogenicity interpretation.

Referrals

- Referrals are accepted nationally from Cardiology, Chemical Pathology, Clinical Genetics and Metabolic Medicine.
- Testing criteria: fasting triglycerides >20mmol/L, AND exclusion of secondary causes of hypertriglyceridaemia e.g. excess alcohol, uncontrolled diabetes
- See the National Genomic Test Directory for further details

Target Reporting Times

Diagnostic screen of 8 genes: *42 days (6 weeks) routine service*
Clinically urgent samples: *4-6 weeks typical reporting time*
Please indicate urgent samples
Targeted test for a known variant: *42 days (6 weeks) (Sanger sequencing)*

Clinical Advice

If clinical discussion is required we would recommend contact with: Dr Paul Downie, Consultant Chemical Pathologist, Salisbury NHS Foundation Trust
Email: paul.downie1@nhs.net

References

Dron JS and Hegele RA (2020) Genetics of Hypertriglyceridemia. *Front. Endocrinol*. 11:455.