Bristol Genetics Laboratory

North Bristol NHS Trust

HFE-related Hereditary Haemochromatosis

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Sample Required:
Adult: 5mls blood in EDTA
Paediatric: at least 1ml EDTA (preferably >2ml)

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 test, family history, address and POSTCODE, NHS number, referring clinician and unit/hospital.

Consent and DNA 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 unless consent for this is specifically denied.

Stored samples may be used for quality assurance purposes and may be used anonymously for the development of new tests for the disorder in question.

Clinical Background and Genetics

- *HFE* related hereditary haemochromatosis (OMIM 235200) is an inherited disorder of iron metabolism. It is one of the most common genetic diseases in individuals of northern European descent, affecting one in every 200-300 individuals.
- It is characterised by inappropriately high absorption of iron, leading to excessive storage in the liver, skin, pancreas, heart, joints and testes.
- Symptoms often begin after the age of 50, although early symptoms are very heterogeneous and may be difficult to detect. Clinical heterogeneity exists even among members of the same family. Symptoms occur more frequently in males than females, with an estimated male-to-female ratio of 3:1.
- While HH can be caused by mutations in a number of genes, the most common form is caused by mutations in *HFE* gene and is known as *HFE*-related hereditary haemochromatosis.
- The condition has an autosomal recessive mode of inheritance and depending on the population, 80-93% of individuals with *HFE*-related hereditary haemochromatosis are homozygous for the pathogenic variant, c.845G>A p.(Cys282Tyr), historically known as C282Y.
- Clinical expression is variable and a significant proportion of individuals with these genotypes do not develop the condition, which demonstrates low penetrance of the mutations and emphasises the need to define genetic modifiers and environmental factors which contribute to iron overload in these individuals.

Service offered

- Real-time PCR is used to detect the common *HFE* mutation c.845G>A p.(Cys282Tyr).

Referrals

- Referrals are usually via the local Haematology department or via Consultant Specialists. Referrals from GPs are accepted provided it is clearly demonstrated on the referral form that they meet the criteria listed below.
- **Confirmatory Diagnostic Testing:** the clinical criteria required for molecular genetic testing to proceed depend on local guidelines. Suggested biochemical criteria include elevated, fasting, serum transferring saturation and persistently raised serum ferritin concentration. Transferrin saturation of 45% would generally be accepted for genetic testing. However, an elevated ferritin is not specific for *HFE*-related hereditary haemochromatosis and therefore should be considered in conjunction with indicators of inflammation and liver disease.
- **Carrier/Predictive testing:** Carrier/predictive testing can be offered for at risk adult relatives of individuals with known *HFE* mutations.

Reporting time and cost

- Guideline reporting time is 28 calendar days
- Please contact the laboratory for up-to-date price.

Clinical Advice

- If clinical discussion is required we would recommend contact with Dr A. Whiteway, Consultant Haematologist, Southmead Hospital, Bristol (Tel: 0117 414 8401).

Quality

- BGL participates in the EMQN *HFE* full scheme (and has UKGTN approval) for this service.

References

- EMQN best practice guidelines for the molecular genetic diagnosis of hereditary hemochromatosis (HH). European Journal of Human Genetics (2016) 24, 479–495.

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