AWMGS
All Wales Medical Genomics Service

Haemochromatosis (HFE) – OMIM 235200

Background

Haemochromatosis is the name given to the condition of iron overload. This can occur through increased iron absorption from food or from blood transfusion. The human body has limited means of getting rid of excess iron which may be deposited over time in tissue and organs, particularly the liver, causing damage and leading to serious illness if untreated. Haemochromatosis resulting from increased iron absorption occurs in some people due to a hereditary condition. The most common form of Hereditary Haemochromatosis (also known as Genetic Haemochromatosis) in people of North European ancestry is caused by a mutation in the *HFE* gene (OMIM 613609), (HFE:c.845G>A, p.Cys282Tyr) and is inherited in an autosomal recessive pattern, which means that both copies of the gene have mutations (inherited one from each parent). People who only carry one copy of the mutated gene are very rarely affected. HFE-related haemochromatosis is an adult-onset disorder with low penetrance (not everyone who is homozygous for p.Cys282Tyr will develop iron-overload) and testing of minors is not recommended. Documented iron-overload-related disease is rare in patients who are compound heterozygotes for p.Cys282Tyr and p.His63Asp (HFE:c.187C>G) mutations in the HFE gene. Where iron-overload is seen, other contributing factors should be considered (e.g. Alcohol consumption, fatty liver or metabolic syndrome).

To request genetic testing for Hereditary Hemochromatosis:

For diagnostic testing please complete a genetics request form* confirming:

- That the patient has raised transferrin saturation and/or serum ferritin[○]
- That the patient is over the age of 18[†]
- Full name and location of the referring clinician

[†]If the patient is under the age of 18 and there is a clear clinical need (elevated iron indices or evidence of liver disease) requests can be accepted from haematology or clinical genetics.

[○] Females with transferrin saturation >45% and serum ferritin >200 micrograms/L and males with transferrin saturation >45% and serum ferritin >300 micrograms/L

For predictive testing (family history) please complete a genetics request form* confirming:

- The relationship to the patient of the family member with confirmed hereditary haemochromatosis (e.g. mother, father, sibling etc)
- That the affected family member is homozygous for the HFE:c.845G>A, p.(Cys282Tyr) variant
- That the patient is over the age of 18
- Name and location of the referring clinician

If it is not possible to confirm the relationship or genotype of the affected family member the patient should be referred to clinical genetics.

Requests for predictive testing in patients who are under the age of 18 will not be accepted.

Any request where the details required above are not clearly stated on the referral form will not be accepted for testing. DNA from these samples will be extracted and stored.

*Request forms are available from: https://medicalgenomicswales.co.uk/images/awmgsdownload/LF-GEN-ReqFormNonAccred1-1--39-.pdf

Molecular Analysis

Common mutation analysis: Real-time allelic discrimination assay for the two common *HFE* mutations – c.845G>A (C282Y) and c.187C>G (H63D)
Family follow-up: Testing for known familial mutations in *HFE* gene in first degree relatives only. Testing in children is not recommended.

Requirements (Price available on request)	TAT(calendar days)
Diagnostic test for two common *HFE* mutations (c.845G>A (C282Y); c.187C>G (H63D))	42
Family follow up testing	42

Contact Details

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Sample Requirements

Blood – 5ml in EDTA (1ml neonates/infants);
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

Links

Orphanet
http://www.orpha.net/
OMIM
http://www.omim.org/
Genetic Test Registry
http://www.ncbi.nlm.nih.gov/gtr/
Support
The Haemochromatosis Society
https://www.haemochromatosis.org.uk/