BLOODCENTER of WISCONSIN™

HEMOCHROMATOSIS

BloodCenter of Wisconsin Molecular Diagnostics Laboratory offers a DNA test for 3 mutations associated with hereditary hemochromatosis.

BACKGROUND:

Hereditary hemochromatosis (HHC) is a common genetic disorder in individuals of Northern European descent with a frequency of affected individuals between 1/200-1/400. It is an autosomal recessive disorder that results in the excess accumulation of iron leading to organ damage. Three mutations in the HFE gene (C282Y, H63D, S65C) have been described in the majority of patients with HHC.

Molecular testing for these mutations can be used to confirm a diagnosis of HFE-associated hemochromatosis (HFE-HHC) in patients with clinical symptoms consistent with HFE-HHC. Most individuals with HFE-associated hemochromatosis are either homozygous for the C282Y mutation (~85%) or compound heterozygotes for the C282Y and H63D mutations (<10%). A smaller number of HFE-HHC patients are homozygous for H63D or compound heterozygous for C282Y and S65C. The clinical significance of the S65C mutation is unclear.

Population studies indicate that the penetrance of clinical symptoms of HHC in individuals homozygous for the C282Y mutation is quite low; a significant number of homozygous individuals do not develop iron overload. The C282Y/H63D genotype has a very low penetrance; about 0.5%-2% of these individuals develop clinical evidence of iron overload. The H63D/H63D genotype has even a lower penetrance than the C282Y/H63D genotype.

REASONS FOR REFERRAL:

- Confirmation of diagnosis in affected individuals
- Carrier detection
- Testing of individuals with a family history of hemochromatosis
- Early detection allows treatment to prevent organ damage

METHOD:

Gene amplification followed by detection of C282Y (845G>A), H63D (187C>G) and S65C (193A>T) with sequence-specific FRET probes. As this is a genetic test, genetic counseling may be appropriate. Informed consent is recommended, and is required in New York. Consent forms are available upon request.

LIMITATIONS:

The assay sensitivity and specificity for these alleles is >99%. This assay only detects the C282Y, H63D and S65C mutations in the HFE gene. The presence of other mutations in HFE or other genes that cause hemochromatosis cannot be ruled out.

PO Box 2178
Milwaukee, WI 53201-2178
Location/Sample Deliveries:
638 N. 18th St. Milwaukee, WI 53233-2121
p800-245-3117 | f414-937-6202 | www.bcw.edu

SPECIMEN REQUIREMENTS:

5 ml EDTA (lavender top) whole blood. Samples must be received within one week of collection. Presence of the mutation should be confirmed in an affected family member for carrier or presymptomatic testing.

SHIPPING REQUIREMENTS:

Blood samples should be shipped at room temperature by overnight carrier. Ship the package in compliance with carrier's guidelines. Please contact your carrier for current biohazardous shipping regulations. Packages should be addressed to:

Client Services/Molecular Diagnostics Laboratory
BloodCenter of Wisconsin
638 North 18th Street
Milwaukee, WI 53233
800-245-3117, ext. 6250

TURNAROUND TIME: 3-6 days

CPT CODES: 81256

REFERENCES:

- Beutler, E, Gelbart T, West C, Lee P, Adams M, Blackstone R, Pockros P, et al (1996) Mutation analysis in hereditary hemochromatosis. Blood Cells Mol Dis 22:187-194.
- Carella M, D'Ambrosio L, Totaro A, Grifa A, Valentino MA, Piperno A, Girelli D et al (1997) Mutation analysis of the HLA-H gene in Italian hemochromatosis patients. Am J Hum Genet 60:828-832
- Feder JN, Gnirke A, Thomas W, Tsuchihashi Z, Ruddy DA, Basava A, Dormishian F et al (1996) A novel MHC class I-like gene is mutated in patients with hereditary haemochromatosis. Nat Genet 13:399-408.
- Jouanolle AM, Gandon G, Jezequel P, Blayau M, Campion ML, Yaouanq J, Mosser J, et al (1996) Haemochromatosis and HLA-H. Nat Genet 14:251-252.
- The GeneClinics Medical Genetics Knowledge Base at www.genetests.org contains descriptions of inherited diseases and relates genetic testing information to diagnosis, management and counseling. The entries are expert-authored, peer reviewed and updated regularly. This site contains an excellent review of hereditary hemochromatosis in its GeneReviews section. Accessed on 12/30/2005.
- Mura C, Raguenes O, Ferec C. (1999) HFE mutations analysis in 711 hemochromatosis probands: evidence for S65C implication in mild form of hemochromatosis. Blood 93: 2502-5
- Beutler E, Felitti VJ, Koziol JA, Ho NJ, Gelbart T (2002) Penetrance of 845G--> A (C282Y) HFE hereditary haemochromatosis mutation in the USA. Lancet. 359:211-8.
- Kowdley KV,Tait JF, Bennett RL, Motulsky AG (2004) HFE-Associated Hereditary Hemochromatosis.

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