

Hemochromatosis DNA Screen

Background

Hereditary hemochromatosis is an autosomal recessive disease that is very common among people of European ethnicity. The *HFE* gene was identified as the cause of this disease. In Northern European patients with a diagnosis of hereditary hemochromatosis, about 80-90% have two copies of a mutation in this gene referred to as Cys282Tyr or C282Y. A second mutation, His63Asp or H63D, occurs in a smaller percentage of these patients and is associated with a lower penetrance (likelihood of developing clinical disease). The Cys282Tyr mutation is very uncommon in Asian and African populations, so this test is less useful in people from those ethnic backgrounds.

Indications for Testing

- Evaluate suspected hemochromatosis
- Differential diagnosis of liver diseases with increased iron loading
- Testing relatives in families already known to carry *HFE* mutant alleles
- Distinguish homozygotes from heterozygotes in hereditary hemochromatosis families

Ordering

1. Obtain blood sample - (see Sample Requirements below).
2. Fill out a Clinical Lab Request - Genetics for each patient.
(available at <http://depts.washington.edu/labweb/Divisions/MolDiag/MolDiagGen/index.htm>).
 - Request: "Hemochromatosis"
3. Provide items needed for test interpretation:
 - Clinical diagnosis/reason for ordering test
 - Ethnic background (Caucasian, Asian, African, etc.)
 - Lab values: % saturation transferrin, serum ferritin; liver iron (if available)
 - Family history of hemochromatosis (Y or N)
 - History of therapeutic phlebotomy (Y or N)
4. Call Laboratory Medicine Community Services at (206)598-6066 to arrange the best method of shipment.

Sample Requirements and Specimen Handling

Whole blood - EDTA (purple top) - 5 mL.
Samples should be received within 72 hours of collection.
Samples may be refrigerated until shipped.
For prenatal diagnosis specimens, consult laboratory.
Heparin (green top) tubes are not acceptable.

Test Frequency and Reporting

Test results usually within 1-2 weeks of specimen receipt.

References

- Feder JN et al. A novel MHC class I-like gene is mutated in patients with hereditary haemochromatosis. *Nature Genetics* 13:399-408, 1996.
- Kowdley KV et al. Hereditary hemochromatosis. In: *GeneReviews at GeneTests: Medical Genetics Information Resource (database online)*. Copyright, University of Washington, Seattle. 1997-2003. Available at <http://www.genetests.org>

Beutler E. The HFE Cys282Tyr mutation as a necessary but not sufficient cause of clinical hereditary hemochromatosis. *Blood* 101:3347- 3350, 2003.
Pietrangelo A. Hereditary hemochromatosis – A new look at an old disease. *N Engl J Med* 350:2383-2397, 2004.