

# Hereditary Hemochromatosis

## Description:

Hereditary hemochromatosis (HFE) is an autosomal recessive disorder of iron metabolism. Accumulation of excess iron results in damage to multiple organs including the liver, pancreas, heart, joints, and the brain. Individuals may develop cirrhosis of the liver, liver tumors, diabetes, arthritis, and/or heart disease. Two of the most common defects in the gene for HFE are the C282Y and H63D mutations. The carrier frequency of HFE is about 1 in 10 for individuals of Northern European descent.

## Indications:

Diabetes, bronze skin, liver disease, cardiomyopathy, iron storage disease. Family history of HFE.

## Specimen:

2mLs whole blood in lavender top (EDTA) tube is preferred, but whole blood in green top (NaHep) or yellow top (ACD) tubes or four Cytobrushes are also acceptable.

**Note:** Label tube with patient's name, birth date, and date of collection.

## Methodology:

DNA is isolated from peripheral blood and is analyzed for two mutations in the HFE gene, which have been associated with HFE. The analysis is performed by restriction analysis of PCR-amplified segments of the HFE gene: the C282Y mutation is detected by restriction with Rsa1, and the H63D mutation is detected with Mbo1.

## Sensitivity:

The most common mutation, C282Y (Cys282Tyr) is found in the homozygous state in 89-90% of patients with typical HFE. The homozygous C282Y genotype confers an approximately 50% risk of abnormal serum iron binding.

A second mutation, H63D (His63Asp) has been associated with HFE when found in trans with C282Y. Less than 2 percent of compound heterozygotes for C282Y/H63D have signs of HFE and account for approximately 5% of all cases. This mutation also confers a minor increased risk of developing HFE when found in the homozygous state.

## Turn Around Time:

7 days.

## Billing and CPT Codes:

**Hereditary hemochromatosis Mutation Analysis:**  
81256

**Please call 1-866-450-4198 for any pricing or billing questions.**

## Results:

Each test report includes a detailed interpretation of the genetic findings, the clinical significance of the result, and specific recommendations for clinical management and additional testing, if warranted. Results will be reported to the referring physician or health care provider as specified on the test requisition form.

## Shipping Instructions:

Please enclose **test requisition** with sample. **All information must be completed before sample can be processed.** Place samples in Styrofoam mailer and ship at room temperature by overnight Federal Express to arrive Monday through Friday.

## Ship to:

Cytogenetics and Molecular Genetics Laboratories 3333  
Burnet Avenue NRB 1013  
Cincinnati, OH 45229  
513-636-4474



Laboratory of Genetics and Genomics  
CLIA#: 36D0656333  
Phone: (513) 636-4474  
Fax: (513) 636-4373  
Email: LabGeneticCounselors@cchmc.org  
[www.cincinnatichildrens.org/genetics](http://www.cincinnatichildrens.org/genetics)

## References:

Alexander, J. and K.V. Kowdley (2009) "HFE-Associated Hereditary Hemochromatosis." *Genetics in Medicine: Official Journal of the American College of Medical Genetics* 11(5): 307-13.

Allen, K.J., L.C. Gurrin, et al. (2008) "Iron-Overload-Related Disease in HFE Hereditary Hemochromatosis." *The New England Journal of Medicine* 358(3): 221-30.

Babitt, J.L. and H.Y. Lin (2011) "The Molecular Pathogenesis of Hereditary Hemochromatosis." *Seminars in Liver Disease* 31(3): 280-92.

European Association For The Study Of The Liver (2010) *EASL Clinical Practice Guidelines for HFE Hemochromatosis.* *Journal of Hepatology* 53(1): 3-22.

Feder, J.N., A. Gnirke, et al. (1996) "A Novel MHC Class I-like Gene Is Mutated in Patients with Hereditary Haemochromatosis." *Nature Genetics* 13(4): 399-408.

Gan, E.K., L.W. Powell, et al. (2011) "Natural History and Management of HFE-Hemochromatosis." *Seminars in Liver Disease* 31(3): 293-301.

Pedersen, P. and N. Milman (2009) Genetic Screening for HFE Hemochromatosis in 6,020 Danish Men: Penetrance of C282Y, H63D, and S65C Variants. *Annals of Hematology* 88(8): 775-84.

Wu, X.-G., Y. Wang, et al. (2014) "HFE Interacts with the BMP Type I Receptor ALK3 to Regulate Hcpidin Expression." *Blood* 124(8): 1335-43.