

HLA-H Genotyping For Hereditary Hemochromatosis

Hereditary hemochromatosis is an autosomal recessive disorder associated with increased iron absorption and deposition of excessive amounts of iron into the liver, pancreas, and other organs that may lead to liver cirrhosis, hepatocellular carcinoma, diabetes and heart disease.

Two mutations (C282Y and H63D) in the HLA-H gene (also known as the HFE gene) have been described in the majority of patients with hemochromatosis and approximately 1 in 200 Caucasian Americans are homozygous for the C282Y mutation (and at risk for developing the potentially lethal disease). Homozygosity for the C282Y mutation is present in 85-100% of hereditary hemochromatosis patients. Compound heterozygosity (Heterozygosity at both the C282Y and H63D alleles) has a penetrance of less than 4%. Individuals who are homozygous for H63D mutation may develop significant iron overload, however, heterozygosity for either C282Y or H63D has not been significantly associated with hemochromatosis.

Since many of the complications associated with hereditary hemochromatosis cannot be reversed once they have developed, early diagnosis and treatment are essential. Hereditary hemochromatosis is treatable by phlebotomy to remove increased iron stores, however, treatment regimes should be individualized for each patient. Individuals with elevated serum transferrin saturation and/or serum ferritin levels may be candidates for HLA-H Genotyping.

Genotypic analysis for these mutations is performed on chromosomal DNA isolated from whole blood using polymerase chain reaction, restriction fragment length polymorphism (PCR-RFLP) methodology and is performed by Quest Diagnostics Nichols Institute, Chantilly, VA. Test runs are “batched” and results are generally reported within 9 days.

Results are reported for each allele as one of the following: **Not Detected**
Detected; Heterozygous
Detected; Homozygous

SAMPLES

Blood: Draw 4mL blood in a lavender top tube containing potassium EDTA.

References

- Hereditary Hemochromatosis Practice Guidelines Development Task Force of the College of American Pathologists. Hereditary Hemochromatosis. *Clinica Chimica Acta*. 1996;245:139-200.
- Ramrakhiani, S. *et al*. Hemochromatosis: Advances in Molecular Genetics and Clinical Diagnosis. *J Clin Gastroenterol*. 1998;27(2):41-46.
- Brandhagen, DJ, *et al*. Update on Hereditary Hemochromatosis and the HFE Gene. *Mayo Clin Proc*. 1999;74:917-921.