

UCLA DIAGNOSTIC MOLECULAR PATHOLOGY LABORATORY
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Hereditary Hemochromatosis

↑CPT

83890; 83898 (x2); 83892 (x2); 83894 (x2); 83912

↑Synonyms

Hemochromatosis; HFE Gene

↑Test Includes

Identification of C282Y and H63D mutations in HFE gene

↑Laboratory

Molecular Pathology

↑Availability

Monday-Friday, 0700-1700

↑Turnaround Time

3-14 days

↑Specimen

Whole blood

↑Volume

4 mL

↑Container

Lavender top (EDTA) tube

↑ Storage Instructions

All specimens should be sent to the Laboratory immediately after collection, preferably by overnight delivery. Specimens should be kept at room temperature or refrigerated but not frozen.

↑ Causes for Rejection

Blood samples frozen and thawed will yield low quality DNA; specimens inadequately identified

↑ Reference Range

No mutations detected

↑ Use

Hereditary hemochromatosis is an autosomal recessive disorder resulting in iron overload. In northern European populations, where the disorder is believed to have originated, as many as 1 in 300 individuals are affected and the carrier frequency is about 10%. Unrecognized, the iron loading results in tissue damage affecting the liver, pancreas, joints, anterior pituitary, and heart. Liver disease is characterized by progressive fibrosis leading to cirrhosis and hepatocellular carcinoma. Morbidity can be completely prevented, and life expectancy can be restored to normal, if the disease is detected early, before the development of cirrhosis, and treated by phlebotomy. The recently discovered HFE gene, previously called HLA-H, is considered to be responsible for familial hemochromatosis. Two major mutations were described, C282Y and H63D. The former results in a cystine to tyrosine substitution at amino acid 282 and was found in homozygous form in up to 80% to 90% of patients with hereditary hemochromatosis. The frequency of the second variant, H63D, is also increased in hemochromatosis patients but its penetrance is probably not complete since it has been observed in affected patients only in the compound heterozygous state (with C282Y) but not in the homozygous state. The molecular genetic test offered will detect either or both these mutations but no others.

↑ Limitations

There remains some controversy over the penetrance of even the C282Y mutation (let alone the H63D mutation) as well as the actual proportion of all hemochromatosis cases that are genetic and due to these mutations. Thus, the DNA test for these two mutations is not a definitive diagnostic test for hemochromatosis or future susceptibility for hemochromatosis. For that purpose standard blood tests such as serum transferrin saturation and ferritin levels should also be considered.

↑Methodology

The HFE gene is amplified using two sets of primers, one set flanking the C282Y mutation and the other set flanking the H63D mutation. The PCR products are subsequently digested with restriction enzyme and the resulting fragments are separated by electrophoresis.
