

### **Report Contents**

- 1. Coriell Personalized Medicine Collaborative Research Study Report. This report includes all data included in the clinical report as well as supplemental interpretations and educational material. This research report is based on Questionnaires Finalized on 08/01/2010**
- 2. Clinical Report. This report was generated and approved by Coriell's CLIA certified genotyping laboratory.**



## Sample Results

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### CPMC Research Study Report

|                                 |                  |                        |            |
|---------------------------------|------------------|------------------------|------------|
| <b>Name:</b>                    | NATALIE DEMO     | <b>Gender:</b>         | Female     |
| <b>Date of Birth:</b>           |                  | <b>Date Collected:</b> | 11-30-2016 |
| <b>Coriell ID:</b>              | DEMONAT          | <b>Date Received:</b>  | 11-30-2016 |
| <b>Lab Accessioning Number:</b> | DEMONAT          | <b>Date of Report:</b> | 12-01-2009 |
| <b>Ordering Physician:</b>      | Dr. Edward Viner |                        |            |

#### Risk of Developing Iron Overload/Hemochromatosis Based on:

- CPMC Iron Overload/Hemochromatosis Variant 1 (rs1800562)

The CPMC is a research study investigating the utility of personalized genomic information on health and health behavior. Most common health conditions are caused by an interaction between multiple genetic variants and non-genetic risk factors such as lifestyle and environment. The genetic variant risk in this report is based on one genetic variant, but does not represent your complete genetic risk for iron overload/hemochromatosis. These results were generated as part of this research study in a CLIA-approved laboratory.

More information about the study, how to interpret CPMC results, and how we calculate risk is available on our website <http://cpmc.coriell.org> or by contacting our genetic counselor. Participants may schedule an appointment with our board-certified genetic counselor through the web portal by clicking on "request an appointment". Our genetic counselor also can be reached by email at [cpmcgc@coriell.org](mailto:cpmcgc@coriell.org) or by phone at 888-580-8028.

This research report includes all data included in the clinical report as well as supplemental interpretations and educational material. Please see the report that follows for the official clinical report.

## Genetic Variant Result

### Iron Overload/Hemochromatosis

Relative risk cannot be estimated due to the small number of women with iron overload. When relative risk cannot be estimated, no graph will be provided.

## Iron Overload/Hemochromatosis

### Risk Due To Genetic Variant #1 (rs1800562)

Your Result: 2 copies of the non-risk variant were detected (GG).

Non-Risk Variant = G Risk Variant = A

**Relative risk cannot be estimated due to the small number of women with iron overload.**

**When relative risk cannot be estimated, no graph will be provided.**

You have 2 copies of the non-risk variant. Based on this result, you are less likely to develop iron overload than a woman with two copies of the risk variant.

Over a lifetime, this result gives you up to a 1% risk of having iron overload.

**These results are based on a single study**

## Iron Overload/Hemochromatosis - Variant #1 (rs1800562)

We all have 2 copies of every gene, one from each of our parents.  
Each copy may have small changes called genetic variants.  
Some genetic variants are associated with an increased risk of disease.  
Some genetic variants are associated with a decreased risk of disease.

Having one or two copies of this variant **increases** your risk for iron overload/hemochromatosis.

**This variant accounts for 85% of cases of iron overload / hemochromatosis in Caucasians.**

### How Common Is This Variant?

Non-Risk Variant = G    Risk Variant = A

**GG - 97 in 100 people have 2 copies of the non-risk variant**

**GA - 3 in 100 people have 1 copy of the non-risk variant and 1 copy of the risk variant**

**AA - 0 in 100 people have 2 copies of the risk variant**

**This frequency is based on data from an African American population.**



Gene: HFE

Chromosome: 6p22.1

## Causes

### Genetic vs. Non-Genetic Risk Factors

Iron overload/hemochromatosis can be caused by both genetic factors and non-genetic (or environmental) risk factors.

**Although there are multiple genetic variants that can contribute to hereditary iron overload, the CPMC has tested you for the one genetic variant associated with about 85% of cases of hereditary iron overload/hemochromatosis in the Caucasian population.**

Most cases of iron overload in non-Caucasian individuals are not caused by this variant.

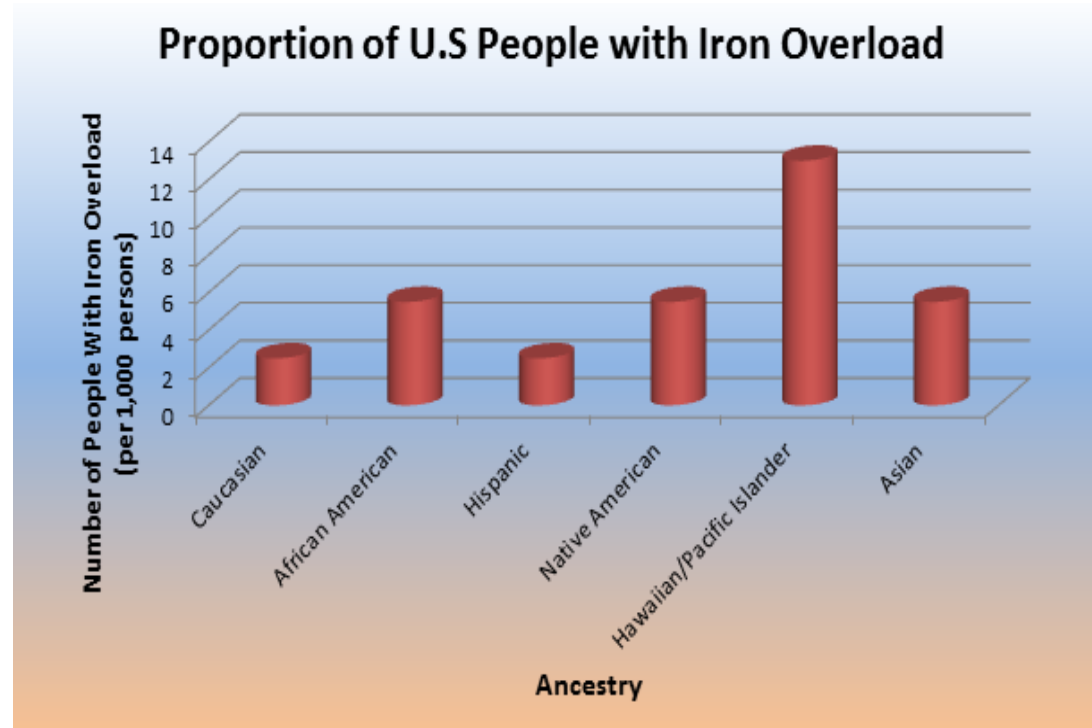
Non-genetic causes of iron overload include liver damage which can be caused by chronic alcohol use and hepatitis.

## How Common

Ancestry contributes to your risk of iron overload/hemochromatosis.

**You reported you are African American; an estimated 5 to 6 in 1,000 African Americans have iron overload.**

Note: Not all cases of iron overload are caused by the HFE variant included in this report.



## Limitations

### Iron Overload/Hemochromatosis

- This result alone does NOT diagnose iron overload/hemochromatosis. Iron overload/hemochromatosis must be diagnosed by your health care provider.
- This result does NOT mean that you have or will absolutely develop iron overload/hemochromatosis.
- This result does NOT mean that you will not develop iron overload/hemochromatosis in the future.
- This result ONLY assesses your risk for developing iron overload/hemochromatosis due to the factors presented in this report and does not mean that other genetic variants or risk factors for iron overload/hemochromatosis are present or absent.
- Personal risk factors, such as age, family history or lifestyle, may have a greater impact on your risk to develop iron overload/hemochromatosis than any individual genetic variant.
- Risk estimates are based on current available literature.
- Although rare, it is possible that you may receive an incorrect result; 100% accuracy of reported results cannot be guaranteed.
- Occasionally there may be a specific variant on a gene chip that is not able to be read or interpreted. In this case you will not receive a result for that variant. It is expected that you will receive results for about 95% of variants approved by the ICOB.
- Relative risks used to estimate risk of disease for CPMC participants are based on groups of people with the same risk or protective factor as the individual CPMC participant. In some cases, the relative risk is estimated based upon an odds ratio and known or assumed disease prevalence.
- Separate risk estimates for each risk or protective factor have been given. Risk or protective factors may be related to each other and risk estimates cannot be combined.
- Risk information for non-genetic factors is based on information you provided in your medical, family, lifestyle questionnaire. If you did not provide answers or if you answered "do not know", risk estimates for some factors may not be available.
- Risk information for non-genetic factors is based on information you provided in your medical, family, lifestyle questionnaire and may not be reflective of your current risk if any of these factors have changed. You will be given the opportunity to update your medical, family and lifestyle questionnaire responses periodically.
- Every effort will be made to provide you with risk information based on your reported race/ethnicity. However, data may not be available for all races/ethnicities for all risk factors. Please see your individual results to determine which race/ethnicity the data given is based on.
- For some risk factors data may be provided by gender. Every effort will be made to provide you with risk information based on your reported gender. However, when risk data is not available for both genders, risk results for the available gender will be provided.



## Methods

### Iron Overload/Hemochromatosis

**This condition and genetic variant(s) were approved by the Informed Cohort Oversight Board (ICOB)**

#### **Test Methodology**

Saliva samples were collected using Oragene DNA Collection Kits (DNA Genotek) and DNA was extracted manually according to the manufacturer's instructions. Purified DNA was quantified using UV absorbance at 260 nm. Five hundred nanograms of the resulting DNA from each sample were used as template in the Affymetrix Genome-Wide Human SNP Nsp/Sty 6.0 GeneChip assay. Data analysis was performed using Affymetrix Genotyping Console software.

**See [CPMC Technical Paper](#) for genetic variant selection and reporting methodology.**

[Risk interpretation based on Coriell's Iron Overload/Hemochromatosis Risk Algorithm Version 1 (June 1, 2009)]

1. Stack, C. et al (2011). Genetic risk estimation in the Coriell Personalized Medicine Collaborative. *Genet Med.* 13(2):131-139.
2. Brandhagen, D.J. et al (2000). Prevalence and Clinical Significance of HFE Gene Mutations in Patients With Iron Overload. *American Journal of Gastroenterology.* 95(10):2910-2914.
3. Adams, P.C. et al (2005). Hemochromatosis and Iron-Overload Screening in a Racially Diverse Population. *New England Journal of Medicine* 352:1769-78
4. Allen, K.J. et al (2008). Iron-Overload-Related Disease in HFE Hereditary Hemochromatosis. *New England Journal of Medicine* 358:221-30.
5. McVean G.A. et al (2012). An integrated map of genetic variation from 1,092 human genomes. *Nature.* 491; 56-65.

## Sample Results



### Coriell Institute for Medical Research

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#### Clinical Report for Iron Overload/Hemochromatosis Genetic Variant 1 (rs1800562)

|                                 |                           |                        |            |
|---------------------------------|---------------------------|------------------------|------------|
| <b>Name:</b>                    | NATALIE DEMO              | <b>Sample Type:</b>    | Saliva     |
| <b>Race/Ethnicity:</b>          | Black or African-American | <b>Gender:</b>         | Female     |
| <b>Date of Birth:</b>           |                           | <b>Date Collected:</b> | 11-30-2016 |
| <b>Coriell ID:</b>              | DEMONAT                   | <b>Date Received:</b>  | 11-30-2016 |
| <b>Lab Accessioning Number:</b> | DEMONAT                   | <b>Date of Report:</b> | 12-01-2009 |
| <b>Ordering Physician:</b>      | Dr. Edward Viner          |                        |            |

| Name of Gene/Region: HFE |  | Chromosomal Location: 6p22.1 |
|--------------------------|--|------------------------------|
| Variants tested          | Result   | Reference Genotype           |
| rs1800562                | GG   | GG                           |
| <b>Interpretation</b>    | <b>Individuals with this result are at a lower risk to develop iron overload/hemochromatosis compared to someone with two copies of this genetic risk variant.</b><br>These risk estimates are based on studies in a European population. When race/ethnicity specific risk estimates are not available, risk estimates based on Caucasian populations are provided. |                              |
| <b>Other Risks</b>       | Other genetic variants and other risk factors including co-morbidities, lifestyle and family history may contribute to the risk of iron overload/hemochromatosis. For additional information on other risk factors please see the accompanying CPMC research report.   |                              |

Risk interpretation based on Coriell's Iron Overload/Hemochromatosis Risk Algorithm Version 2 (June 1, 2014)

#### **Test Limitations**

DNA-based testing is highly accurate, however there are many sources of potential error including: mis-identification of samples, rare technical errors, trace contamination of PCR reactions, and rare genetic variants that interfere with analysis. There may be other variants, not included in this test, that influence the risk to develop iron overload/hemochromatosis. This test is not diagnostic for iron overload/hemochromatosis and cannot rule out the risk of developing iron overload/hemochromatosis in the future. Risk estimates are based on current available literature (see reference). This test or one or more of its components was developed and its performance characteristics determined by the Coriell Institute for Medical Research. It has not been approved by the Food and Drug Administration (FDA). The FDA has determined that such approval is not necessary. The Coriell Institute is regulated under the Clinical Laboratory Improvement Amendments (CLIA) of 1988 as qualified to perform high-complexity testing.

#### **Test Methodology**

Saliva samples were collected using Oragene DNA Collection Kits (DNA Genotek) and DNA was extracted manually according to the manufacturer's instructions or automatically using a DNAadvance Kit (Agencourt). Purified DNA was quantified using UV absorbance at 260 nm. Five hundred nanograms of the resulting DNA from each sample were used as template in the Affymetrix Genome-Wide Human SNP Nsp/Sty 6.0 GeneChip assay. Data analysis was performed using Affymetrix Genotyping Console software.

#### electronically signed by

Marie Hoover, PhD, Laboratory Director

This clinical report only includes data generated in the CLIA approved genotyping laboratory, for additional information please see the CPMC research report.

#### **References**

1. Allen, K.J. et al (2008). Iron-Overload-Related Disease in HFE Hereditary Hemochromatosis. New England Journal of Medicine 358:221-30