

## Using 23andMe to determine HFE status

This document explains how to read your 23andMe information to determine your HFE status. Please read this entire document, including the disclaimers on the last page, before using the information it contains.

**Note:** 23andMe customers who received health-related results prior to November 22, 2013 should have direct access to their HFE status. You can see what that looks like in Figure 1.

If you purchased the service after that, or buy it today, you will not have the same direct access to the HFE status as shown in Figure 1.

However, you will get access to the uninterpreted raw genetic data and this document shows you how to find your HFE status in that raw data. For more on how the FDA's "DNA embargo" affects the 23andMe service, see this page: <https://www.23andme.com/health>

### Why does HFE matter to me?

HFE is the "iron gene" and it determines your likelihood of developing or transmitting a genetic disorder called hemochromatosis. Our DNA contains two copies of each gene, one inherited from each parent. If both copies of your HFE gene are mutated then your body may not handle iron properly, leading to a condition called *iron overload* in which soft tissue and joints are damaged (possibly leading to liver damage, heart disease, chronic fatigue, depression, diabetes, joint replacement, and other complications).

One in 10 Americans has at least one mutated HFE gene. If you have one mutated HFE gene you could pass it on to your offspring. Parents who both have one HFE gene mutation can produce children with both genes mutated. The double HFE mutation that leads to iron overload exists in about 1 in 200 Americans. Studies disagree as to how many of those people will go on to develop iron overload and experience its unpleasant consequences. Estimates range from 2% to 30% and more research is needed, but it is quite possible that 1 in 800 Americans are affected, a far higher rate than Cystic Fibrosis or ALS, and roughly equal to the incidence of MS.

What we do know for sure is that people who are aware of their genetic predisposition to iron overload can a) exercise vigilance over their iron levels and detect *iron loading* before damage is caused, b) avoid aggravating factors like smoking and heavy drinking, c) avoid iron rich foods and cast iron cookware.

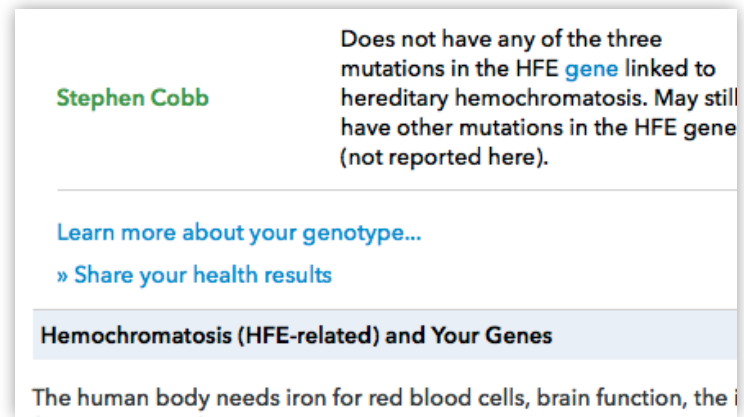


Figure 1: How 23andMe showed HFE status before the FDA ban.

If your body does start to load iron this can be treated by removing blood, as in a blood donation. When you give blood iron is removed from your body. That simple fact gives women a natural defense against iron loading. It also means that a young man who starts giving blood at university or in the military, and continues to do so regularly, has a natural defense against the buildup of iron. However, women who have a hysterectomy or enter menopause are then at risk if they a) have two defective HFE genes and b) do not monitor their iron levels. Likewise a man with genetic hemochromatosis who stops giving blood is also at risk.

Therefore, knowing your HFE status makes a lot of sense for a lot of people. I checked my status even though I had no symptoms. Your HFE gene may be:

- normal,
- mutated or defective,
- partially defective, meaning you won't develop hemochromatosis yourself but your offspring might.

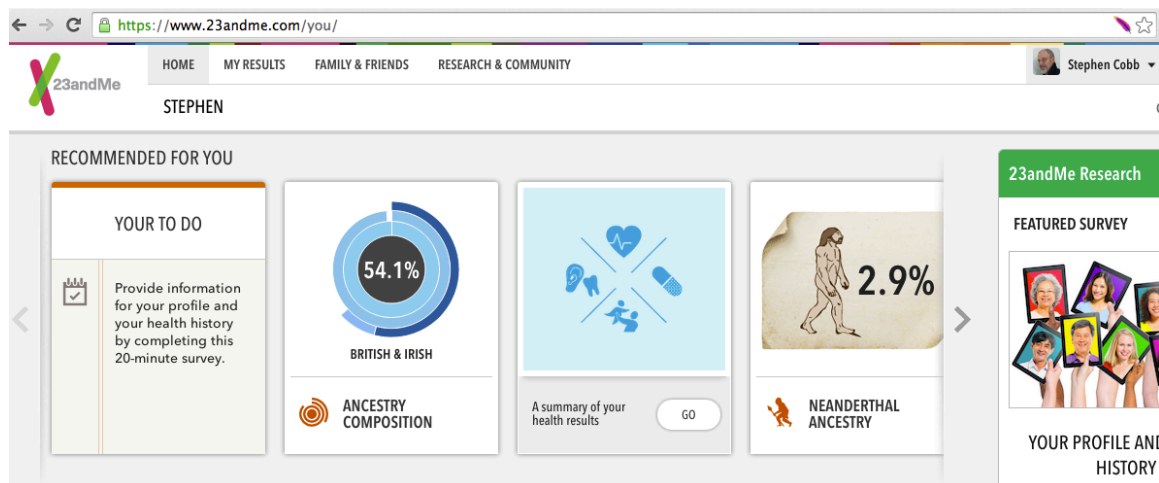
There are several ways to find out your HFE status:

1. Ask your doctor to order HFE gene test (see tips on this later in document).
2. Order the HFE test yourself (see resources at end of this document).
3. Use the 23andMe service that provides a wide range of information derived from your DNA: <http://23andMe>

## Using 23andMe

This document explains how to read your 23andMe raw genetic data to determine your HFE status. I will illustrate with screenshots of my own account.

After you order the service and mail back your sample of saliva in the container provided, you will be given access to results on a website. When you are a registered user of 23andMe your home page looks like this:



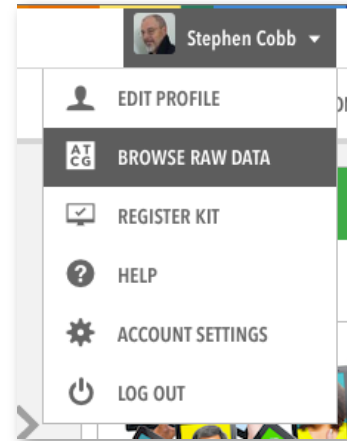
The screenshot shows the 23andMe user interface for a user named Stephen Cobb. The page is titled "RECOMMENDED FOR YOU" and features several interactive cards:

- YOUR TO DO:** A card with a checklist icon and text: "Provide information for your profile and your health history by completing this 20-minute survey."
- ANCESTRY COMPOSITION:** A card showing a circular progress indicator at 54.1% for "BRITISH & IRISH".
- HEALTH RESULTS:** A card with a heart and medical icons, titled "A summary of your health results" with a "GO" button.
- NEANDERTHAL ANCESTRY:** A card showing a 2.9% result with an illustration of a Neanderthal.
- 23andMe Research:** A sidebar section titled "FEATURED SURVEY" showing a collage of photos and the text "YOUR PROFILE ANC HISTORY".

The top navigation bar includes "HOME", "MY RESULTS", "FAMILY & FRIENDS", and "RESEARCH & COMMUNITY". The user's name "STEPHEN" is displayed below the 23andMe logo.

To access your data, pull down the menu below your name on the right and choose BROWSE RAW DATA. You will then see a page with an important warning about that reads as follows (I will explain what SNPs are in a moment):

“This is an advanced view of all the uninterpreted SNP data from your chip. The data from 23andMe's Browse Raw Data feature is for research and informational use only. This data has undergone chip-wide quality review, and a subset of SNPs have been individually validated for accuracy. However, the majority of SNPs have not undergone this rigorous individual validation, and any SNP result obtained from this raw data should be independently verified.”



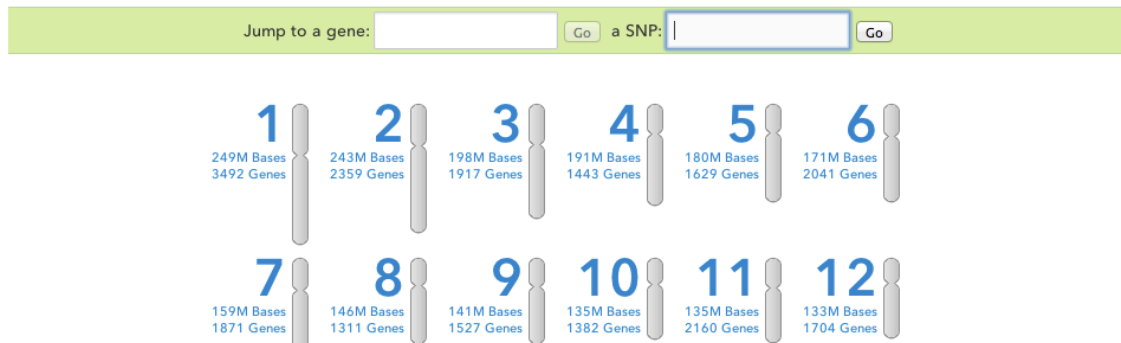
SNP = Single Nucleotide Polymorphism. These are frequently called SNPs (pronounced “snips”) are they are the most common type of genetic variation among people. According to the National Institutes of Health Genetics Home Reference: “Each SNP represents a difference in a single DNA building block, called a nucleotide. For example, a SNP may replace the nucleotide cytosine (C) with the nucleotide thymine (T) in a certain stretch of DNA.”

To the best of my knowledge, the SNPs for HFE have been validated for accuracy. However, you should not rely on this data alone to make any medical decisions. You should consult your doctor and proceed with medical diagnosis (see the Disclaimer at the end of the document).

While many doctors are opposed to patients exploring their own DNA with services like 23andMe, being able to tell your doctor your HFE status should enable him/her to order further tests that should be covered by your insurance.

Most of the DNA inside each of your body's cells is divided into pieces called chromosomes. The remaining DNA is found in tiny loops inside your cells' mitochondria. Click below on any chromosome or the mitochondrial loop to see the genes and SNPs it contains. [Learn more](#) about how to use this feature.

Note: The chromosome display is the same for all customers, regardless of sex. Females will see "no call" results for SNPs on their Y chromosome.



The rest of the 23andMe raw data page looks like this:

Now you need to enter the SNP number for one of the three HFE mutations. These will be explained in a moment, but the locations are as follows:

- rs1800562 for C282Y
- rs1799945 for H63D
- i3002468 for S65C

Below you can see my results for C282Y. Note that it is labeled HFE:

Showing raw data for SNP rs1800562, which is on chromosome 6.



Jump to a gene:  Go a SNP:  Go

or a chromosome:

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y MT

« Return to your whole genome.

Gene	Position	SNP	Versions	Stephen Cobb's Genotype
⊕ HFE	26093141	rs1800562	A or G	GG

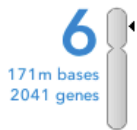
You can see that my genotype at rs1800562 is GG, which is normal. But there are two other possible mutations and I need to check before I can say I am completely clear of hemochromatosis.

If my result for rs1800562 had been AA that would mean both my HFE genes were mutated C282Y, a condition known as homozygous C282Y, the classic form of hereditary hemochromatosis and most likely to cause iron overload.

If your result for rs1800562 is AG or GA that indicates you are carrying one C282Y mutation. And that means you could transfer the mutation to your offspring.

I still need to check the other two locations, SNP rs1799945 for H63D and SNP i3002468 for S65C. Here is my result for rs1799945, where CC = normal.

Showing raw data for SNP rs1799945, which is on chromosome 6.



Jump to a gene:  Go a SNP:  Go

or a chromosome:

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y MT

« Return to your whole genome.

Gene	Position	SNP	Versions	Stephen Cobb's Genotype
⊕ HFE	26091179	rs1799945	C or G	CC

A result of CG or GC on your data at rs1799945 would show that you are carrying one H63D mutation. A result of GG would be homozygous H63D. The C282Y and H63D mutations are the most common, and sometimes they can be mixed together, with one C282Y and one H63D, a condition referred to as heterozygous.

And there are other, less common mutations. 23andMe detects one of these, S65C, which is indicated by T at SNP i3002468 (normal is AA, while AT or TA indicates you are carrying one copy of this mutation).

This table summarizes the possible readings:

Name	SNP	Normal	One Defect (Carrier)	Homozygous
C282Y	rs1800562	GG	AG or GA	AA
H63D	rs1799945	CC	CG or GC	GG
S65C	i3002468	AA	AT or TA	TT
Heterozygous = 1 C282Y defect + 1 H63D defect, or any other combination in which there are two defects.				

### Alternative avenues

The above method is not the only way to determine your HFE status. You can order a [test for HFE alone for \\$195](#). You may even be able to persuade your doctor to order the test for you, but ironically, some doctors are reluctant to approve this test.

Your healthcare insurance will likely cover the cost of a genetic test if your doctor agrees to order the test. Facts that could persuade your doctor to do this include:

- a high ferritin reading,
- Celtic ancestry,
- family history of liver or heart disease,
- fear of being sued for failure to diagnose a potentially fatal condition.

Where some patients run into a brick wall is family testing. For example, suppose you find you are homozygous C282Y and you have siblings and children. They should get tested but their doctors tell them the chances of them having problems are minimal (which is unscientific nonsense). The doctor may go so far as to order an iron panel and say: "See, readings are normal, nothing to worry about." But there is something to worry about! If your siblings are homozygous or heterozygous they will remain at risk of loading iron for the rest of their lives. Knowing their HFE status can reduce worry or raise awareness of iron levels in the future, allowing for preventative measures.

*Reluctance to order HFE tests is ironic because American doctors typically earn revenue for ordering tests, or at least they generate revenue for their clinic/hospital. The possibility of losing revenue to consumer genetic testing services is thought to be one reason that some elements of the medical community oppose direct-to-consumer DNA startup companies like 23andMe.*

## Disclaimer:

This document is not an official publication of 23andMe and 23andMe had no part in preparation or dissemination of this document. This document was prepared by Stephen Cobb who is a customer of 23andMe but otherwise unrelated to 23andMe. This document is for informational use only and should not be used as a basis for medical diagnosis or treatment. Stephen Cobb is not a medical doctor. Consult your doctor for more information about hemochromatosis (and switch to a different doctor if you don't get a satisfactory response).

## Resources:

- The [Iron Disorders Institute](#) is the best source of medically reviewed information about hemochromatosis and has documents to educate yourself and your doctor on this under-diagnosed, widely misunderstood condition (in America the average diagnosis time is nine years from onset, which is long enough for your body to load enough iron to cripple you for life).
- There are numerous blog posts about hemochromatosis at CelticCurse.org:
  - [Hemo-Doc-Stars: doctors who 'get' hemochromatosis](#)
  - [Death by Ignorance: Millions of Americans at risk from hemochromatosis, but few doctors know much about it](#)
- Follow [@CelticCurse on Twitter](#)
- Connect with hemochromatosis patients and caregivers on Facebook via this page: <https://www.facebook.com/Hemochromatosis>

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## Acknowledgements:

Thanks to my wife, Chey Cobb, who is homozygous C282Y, for proofreading this document and for being such a heroic and inspiring survivor of the damage done by undiagnosed hemochromatosis.