

# Human Pangenome Reference Consortium (HPRC): Developing a Research Resource for Studies of Human Genetic Variation

## CONSENT TO PARTICIPATE

**Sponsor:** National Human Genome Research Institute (NHGRI), National Institutes of Health

**Principal Investigator:** Karen Miga, PhD

**Local Contact:** Eimear Kenny, PhD

**Institution:** Icahn School of Medicine at Mount Sinai ("Mount Sinai")

**Address:** One Gustave L Levy Place, Box 1041, New York, NY 10029

**Telephone:** 332-243-7170

**Email:** HPRC\_Study@mssm.edu

---

### 1. Introduction

We invite you to be part of the **Human Pangenome Reference Consortium resource, or HPRC for short**. You may remember that you joined the Mount Sinai BioMe project, took a short survey and gave us a blood sample. Thank you for your generous help in the past! We think the sample you gave to the BioMe project could be helpful for HPRC too. The goal of the HPRC is to make a tool called a "genome reference" that will help doctors more accurately identify and diagnose disease around the world. This genome reference will be made freely available online for anybody to use. HPRC will also carefully store and share your sample with researchers for futures studies. We will collect blood samples and get the living cells from them which can be grown in a laboratory. These are called "cell lines". The cell lines can be sent to researchers around the world.

HPRC is funded by the National Human Genome Research Institute (NHGRI), which is part of the U.S. National Institutes of Health. It is a collaboration among many institutions, including Mount Sinai. You can learn more about it in this video: <https://www.youtube.com/watch?v=swNtGe9QWAQ> and on our web-site <https://hprc-participant.org/> These explain the plans for HPRC and how your help can make a big difference.

**The decision about whether to take part is completely up to you.** You may decide not to take part in this study without any penalty. If you decide not to give your sample, it will not change the medical care you get from Mount Sinai or any other benefits you have.

### DISCLOSURE OF FINANCIAL INTERESTS

NHGRI is the sponsor of this study.

## ***2. What is the purpose of the HPRC?***

Genes are the basic “instruction book” that tells all cells in our bodies how to work. Genes are made of DNA. The DNA of a person is more than 99% the same as the DNA of any other person, but the tiny differences are what make us unique. These differences in DNA are called genetic variations. They can partially explain how people look different or why some people get sick while others do not.

To study genes, researchers read, or “sequence”, DNA, which is like reading the entire set of instructions, or the “genome”. Everyone around the world has genetic variations, but they don’t all have the same number or type of variations. Current databases include mostly data from people of European roots. That needs to change. The word “diversity” for the HPRC means including genomes from people with a wide range of ancestry from different parts of the world. This will help fix the problem. **HPRC wants to make a tool for researchers and doctors that is fair and works well for everyone, everywhere.**

To do so, the HPRC team will study the DNA in blood collected from several hundred people with diverse ancestry. We will then build a more diverse genome reference and share this tool in scientific databases that can be freely found on the Internet so that anybody can use it. We will also store and share your sample with researchers for futures studies.

**This project does not provide medical care. The purpose is to build a tool for researchers and doctors, and to share samples with researchers. You should see your health care provider if you have a health problem or medical question.**

### ***Why was I invited to take part in the HPRC?***

You were selected because the sample you gave to BioMe showed that you are likely to add diversity to HPRC. Researchers looked carefully at everyone’s DNA in BioMe, and found some people are more likely to add new genetic information. You are one of them. This approach is better than just asking where your family comes from, or other ways of describing you or your family.

## ***3. How will you determine if I can take part in the HPRC?***

About 200 volunteers for the HPRC project are expected to participate at Mount Sinai.

To see if you can be one of them, we need to check a few things:

- You speak English or Spanish
- You are at least 18 years old.
- You did not have systemic radiation therapy and have never had a bone marrow transplant.
- You have not had localized radiation, chemotherapy, or immunosuppressant therapy in the last 12 months.
- You have not had a transfusion in the last 8 weeks.
- You understand what this study is about, and you agree to be part of it (this is what we call “informed consent”).
- You are willing to give a blood sample from which researchers will do two things: (1) sequence your DNA to generate genetic information and (2) to make cell lines that provide an unlimited source of your cells that researchers can use for future studies. This means that you are willing

to share your cells and DNA with researchers all around the world.

- You understand that DNA information created through this project will be freely available on the Internet.
- You understand that the cell lines taken from your blood sample **will not** be freely available. HPRC will only share cell lines after making sure that the researcher and their research plans are thoroughly checked and approved. Cell lines can be used for 1) non-profit or government sponsored research and 2) research carried out by for-profit companies such as drug companies. A special cell and DNA bank in New Jersey, called the NHGRI Sample Repository for Human Genetic Research (or NHGRI Repository for short) at the Coriell Institute for Medical Research (or Coriell for short), will hold the samples securely. Coriell is a non-profit research institute that shares biological samples (including cell lines and DNA) with researchers.
- You understand that information that can identify who you are, such as your name, address, birth date, or Social Security number, will **not** be linked to the genetic information or to the cell lines. The only information we will send along with your blood sample will be your **sex when you were born and the fact that it was collected at Mount Sinai. We will not include any of your health information or more detailed personal information about you.**
- If you think you might want to be part of this project, please read the rest of this form, and take as much time as you need to ask questions.

#### ***4. What happens if I agree to take part in HPRC?***

We will draw about 2½ tablespoons of blood (in 3 tubes). We will send the blood samples to the NHGRI Repository at Coriell. Here is what will happen with your blood sample:

##### **DNA**

**We will read all the genetic information from your DNA by “sequencing” it:**

- We plan to share the sequence information freely in public scientific databases, such as the HPRC resource, which will be available online for anyone to access.
- We will analyze the sequence data from all samples to generate a more complete, and representative picture of the human genome which will be called the “pangenome”.

##### **CELL LINES**

**We will make two kinds of “cell lines” from your blood sample:**

- A cell line that is made from white blood cells.
- A stem cell line that can be turned into many cell types, such as muscle cells or brain cells or liver cells.
- This allows researchers to extract an unlimited amount of DNA from the cell lines and make the cell lines available for future research.

**We plan to send the cell lines or DNA from the samples to researchers around the world** from universities, hospitals, non-profit groups, for-profit companies, and government laboratories, among others. The Coriell team will handle sending the cell lines to future researchers who ask for them. Researchers' home institutions are responsible for ensuring they use samples based on the terms of use and the laws and guidelines that apply to biomedical research in their own countries.

Not all the samples sent to the NHGRI Repository will be sequenced or turned into cell lines. Neither you nor the HPRC team will know for sure whether your samples and data are included in the HPRC resource. This is to protect your confidentiality. Any samples that are not sequenced or turned into

cell lines will be destroyed at the end of the project.

Future researchers may use the samples for all sorts of studies. Examples of things researchers might study are:

- How DNA works, what cells do, and how tiny lab-grown mini-organs called “organoids” function.
- How the process of evolution happens over time.
- Comparing your DNA with DNA databases to identify which global groups it resembles.
- Identifying new drugs or drug targets.

The Coriell team does not allow anyone who receives cell lines from the NHGRI Repository to sell them. However, some of the research done with your samples may one day lead to the development of new tests, medicines, or other commercial products. **We want to make sure you understand that you will not get any of the profits from these products, or any discounts on or special access to them.**

It will not cost you anything to participate in this project. We will compensate you **\$80 for your time, travel, and inconvenience** if you complete the explanatory session and sample donation. You will receive this through a gift card after your study visit.

## ***5. How will researchers use my DNA sequence?***

Sequence data that is generated from the blood sample you provided for the HPRC resource will be put in a database that anyone can use through the internet. People who access DNA data from the HPRC resource will not readily know who you are from your data because we will not include your name or other identifying information about you (such as your address, birth date, or Social Security number). HPRC researchers will use the data to do research that improves our understanding of human genetic differences across the world. They will also use it to find ways to make DNA sequencing technology even better. This will benefit genomic applications in medicine and public health.

## ***6. How will researchers use my cell lines?***

The cell lines made from your blood sample will be grown indefinitely in the lab. This lets researchers get an unlimited amount of your cell lines and DNA for a long time, perhaps forever. These cell lines will be stored in New Jersey in the NHGRI Repository. Researchers around the world may then use your cell lines and DNA for their research.

All researchers who ask to use your cell line or DNA must explain why in a form that tells us what they want to study. It is not possible to predict every way the cell lines or DNA might be used. The team at Coriell will review each form to check their reasons to make sure they match what you said was okay when you joined the HPRC study. All researchers must agree in writing to these terms before they get to work with your cell lines or DNA.

To learn more about how different cells in the body work, some research projects may use samples from the HPRC to create a special type of human cell called an “induced pluripotent stem cell” (or iPSC for short). The NHGRI Repository may also use samples from the HPRC to create and distribute iPSCs to researchers around the world. iPSCs are a special stem cell that can become

other types of cells in the body, like those found in the brain or the liver. This is really helpful for learning about how diseases happen. For example, iPSC's from healthy people can be compared with those from people affected with diseases, to help researchers understand diseases better. Making and storing these special cells makes the HPRC resource an even more valuable research tool.

## ***7. Who will decide who uses my samples?***

The Coriell team watches over the cell lines and DNA to make sure they are used in the right way. Before researchers can use these samples, they must sign a special Assurance Form that includes what research they are going to do and a promise to follow the rules of the NHGRI Repository. The Coriell team pays special attention when researchers want to use a type of cell called iPSCs. They will not allow any work that tries to make sperm, eggs, or embryos, or any work that allows researchers to use the cells in actual treatments or surgeries.

To decide what information we should share with you, and to help us think about how this research might affect people taking part, both now and later on, we talked to several groups. We talked with patients, clinicians, and people from local communities served by Mount Sinai. They advised us to tell you more about the BioMe biobank, HPRC, and to be clear about who benefits from this research. We also met with experts around the U.S. who think a lot about how to make sure this type of research is done carefully, ethically, and in ways that honor the people who take part.

## ***8. Are there any benefits to taking part in HPRC?***

If you give your sample to the HPRC project, **you will not get any personal benefits, like health results or reports about your DNA.** Also, finding out important things from the research takes a really long time. But your help is very valuable! It will allow us to make a tool called a genome reference that will help doctors more accurately identify and diagnose disease around the world. This genome reference will be made freely available online for anybody to use.

## ***9. What are the risks of taking part?***

You may have some brief pain and bruising when we draw your blood. There is also a small chance that you may get an infection, have excess bleeding, become dizzy, or faint from the blood draw.

We will generate lots of genetic information about each person who contributes a sample to the HPRC resource. Each sample will be fully sequenced using the most up to date technology. This sequence information will then be put in an **open access database** where anyone can access it online.

Although we will not publish your name or include any medical information, there is a risk that somebody could figure out how to connect you with the genetic data you provided to the project. (see *Section 10. How will you protect my privacy?*). This information could be used to discriminate against you or your family members, though there are laws that protect people in the U.S. from genetic discrimination for reasons related to employment and health insurance.

While very unlikely, there could be risks of loss to privacy if:

- Somebody knew you provided a sample to be studied for this project, got another sample from you, found an expert to test that sample, and then compared the genetic information from that test with the genetic information in the scientific databases.
- Somebody found an expert to compare the genetic information about you in the scientific databases with information known to have come from you (or from a family member) included in some other database developed by someone else for some other purpose.
- Somebody found an expert to look in the scientific databases for a particular known genetic variation known (or someday found) to be associated with a disease or trait that you have or carry, that others know about or can see, and that is very rare.

Any of these things would require that the person trying to link the information to you already knew that you had taken part in this project.

There may also be future risks that we cannot now predict. This is because the sequence of DNA can uniquely identify a person. For example, if publicly available databases that link DNA to individuals become commonplace in the future, someone may be linked, for example, to a disease risk. The use of DNA to identify individuals is still debated worldwide. Strong laws against discrimination provide some protection.

Other risks include linking your sequencing data and cell lines not to your personal information, but to some of your medical information. For example, because you already decided to join the BioMe biobank, Mount Sinai may share or have shared your DNA sequence data and health information (but not your personal details like name or date of birth) with third parties, including companies. There is a chance that those third parties could seek to use the publicly released HPRC data to connect your medical data to cell lines or DNA. Please know that they are not allowed to do that, and it would be breaking their agreement with Mount Sinai if they tried.

If you believe you have been injured because of this research, please contact [hprc\\_study@mssm.edu](mailto:hprc_study@mssm.edu). Mount Sinai will decide if they will pay for medical treatments for any injuries from your research participation.

You are not waiving any legal rights by signing this form.

## ***10. How will you protect my privacy?***

We will protect your privacy in several ways:

- We will store your signed consent form and the information you give us about yourself in a locked file; only the Mount Sinai research team will have access to them.
- We will not give your sample a code number or any key linking you to your data that could point back to you.
- We will collect more samples than we will use so that nobody—not even you or us—will know for sure whether your sample was used or if any of the information in the scientific databases came from your sample. Samples that are not used will be destroyed.

Because of these measures, it is unlikely that anyone who looks at any of the scientific databases to know which information came from you, or even if your DNA is there at all. In the future there may be new ways of linking information back to you that we cannot anticipate now. We believe that the benefits of learning more about human genetic variation and how it relates to health and disease



outweigh the current risks, but this is something you must judge for yourself.

### ***11. Are there any risks to my community or group?***

Mount Sinai researchers will keep information that you tell us about yourself until the end of the project, then we will destroy it. Mount Sinai researchers will also report on race and ethnicity to the National Institutes of Health using the same categories used by the U.S. Census. This will only be reported at a summary level, meaning your individual sample will not be labeled with that information. The only information included with your sample and data will be your sex when you were born, and that the samples were collected in New York City by Mount Sinai. In future studies, researchers may find that certain DNA differences appear more often in people from your group than in people from other groups, or that certain DNA differences are more common in people with a certain disease. This may make some people look down on your group unfairly.

### ***12. Can I change my mind after I decide to participate?***

Because we will not label the samples with any names or identifiers, no one will know who the samples belong to that we send to Coriell. For this reason, we are not able to withdraw your sample from the project. Also, once the sample has been studied, you cannot take the information about the sample out of the scientific databases.

### ***13. How can I find out about the results of research that uses the HPRC resource?***

It will probably take a long time for the data from this project to be used to produce health-related information that is safe and of proven value. For this reason, and because we will not know who the individual sample donors are, we will not be able to give you individual results about your genome. You may, however, check the website at <https://hprc-participant.org/> to read about how researchers have used the samples and data, and what new insights they found.

### ***14. Who do I contact if I have any questions?***

If you have any questions or concerns about this study you may contact Dr. Eimear Kenny at 332-243-7170 or [HPRC\\_Study@mssm.edu](mailto:HPRC_Study@mssm.edu).

If you have any questions or concerns about your rights as a participant in this study, you may contact a person independent of the research team at the Biomedical Research Alliance of New York Institutional Review Board at 516-318-6877. Questions, concerns or complaints can also be registered with the Biomedical Research Alliance of New York Institutional Review Board at [www.branyirb.com/concerns-about-research](http://www.branyirb.com/concerns-about-research).

**Human Pangenome Reference Consortium (HPRC): Developing a Research Resource for Studies of Human Genetic Variation**

## CONSENT TO PARTICIPATE

---

### Consent and Signature

**Please read the information below, think about your choice, and sign if you agree. I agree:**

- to give a blood sample;
- to have cell lines made from the sample that will make it possible for researchers to get an unlimited amount of DNA from it for a long time;
- to have the cell lines and DNA used in both the Human Pangenome Reference Consortium and in future studies as described above;
- to have my entire genetic code from the sample deposited in open access (public) scientific databases on the Internet;
- that the sample, the cell lines, or the data from my sample or cell lines may be studied by companies, and that if any commercially valuable products result from these studies, I will not receive any profits; and
- that once the sample has been placed in the NHGRI Sample Repository (Coriell), I cannot have my DNA sequence data removed from the databases. Also, I cannot have my sample back or the cell lines created from my sample removed.

I have read or listened to the information, I have asked my questions, and all my questions were answered. I know that giving a sample is my choice.

**Name of Participant:** \_\_\_\_\_

**Your Signature** \_\_\_\_\_ **Date** \_\_\_\_\_

**Name of Person Obtaining Consent:** \_\_\_\_\_

**Signature of Person Obtaining Consent** \_\_\_\_\_ **Date** \_\_\_\_\_

**Copy was given to participant: Yes**