

Columbia University Medical Center Consent Form

You are being invited to take part in a study that includes advanced genetic tests.

Please take your time to read the consent form, and to ask questions.

You do not have to participate if you do not want to.

This consent form explains how genetic data, and other clinical data, will be obtained.

Please note that:

- The potential physical risks of participation include the small risks caused by drawing your blood.
- Companies that provide life insurance, disability insurance or long-term care insurance are not prevented from using genetic information.
- We will take all possible steps to protect your privacy, but we cannot completely guarantee that the protection will always work.
- You will not receive any financial compensation for your participation.

When reaching the end of this form, you will be asked to document whether you would like to know the results of your genetic testing, if they may be important for your health or your medical care. This decision is not easy to make, and we are ready to talk about this with you in detail, if you want to.

You will also be asked for permission to store and share your data and whether you would like to designate a person that can represent you for the purposes of this study.

We greatly appreciate your consideration.

Protocol Title: Precision Medicine for Cardiovascular and Metabolic Disorders

Attached to Protocol: IRB- AAAR4378

Consent Form Number: 1

Anticipated Number of Subjects: 10,000

RESEARCHERS' INFORMATION

Principal Investigator: Muredach Reilly, MBBCH, MSCE, on behalf of,

The Cardiovascular and Metabolic Precision Medicine Working Group

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WHAT INFORMATION IS ON THIS FORM?

The purpose of this form is to give you information to help you decide if you want to take part in a research study. This consent form includes information about:

- Why the study is being done;
- The things that you will be asked to do if you are in the study;
- Any known risks involved;
- Any potential benefit; and
- Options, other than taking part in this study that you have.

The study team will discuss the study with you. If at any time you have questions about the study, please ask a member of the study team. Take all the time you need to decide whether you want to take part in this research study. You do not have to participate if you don't want to.

This consent form is written to address a research subject. If, however, you will be providing permission as the parent or legal guardian of a minor or a legally authorized representative, the words 'you' and 'your' should be read as 'your child' or 'the research subject'.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to identify genetic causes for cardiovascular or metabolic disorders and to develop a registry of patients with genetic causes of their cardiovascular and metabolic disorders so that we can better understand, prevent and treat these conditions. You are being asked to take part in this research study because you or your family member has been diagnosed with a cardiovascular or metabolic disorder.

WHAT IS A GENE?

DNA is the material that allows for the inheritance of many human traits, such as hair and eye color or the risk of some diseases. DNA is contained in the cells that make up the body and carries the instructions for your body's development and functions.

A piece of DNA that determines a specific function of a cell is called a "gene." Everyone's DNA is different, and differences in DNA are called "variants." Some variants do not cause any medical problems, but other variants in a gene can lead to disease. Sometimes, we do not have enough information to know whether a specific variant causes disease or not. The goal of genetic research is to identify genetic variants that cause disease.

WHAT GENETIC TESTING COULD BE PERFORMED IN THIS STUDY?

This is a research study, not clinical care. We expect that we will perform a very detailed type of genetic test called whole exome sequencing (WES) and other additional genetic tests such as whole genome sequencing to evaluate your genetic information. WES searches through all the portions of the DNA that make up the genetic code to make proteins ("the exome") for variants that can cause disease. Other testing such as RNA-Seq may also be performed in the future. RNA is the active molecule made from your DNA and it may be useful to see how much and what kinds of it are present.

Our current genetic methods will not be able to identify all types of genetic changes. You should be aware that participation in this research study does not replace a clinical genetics evaluation. **This research study does not replace your clinical care. You may want to discuss with your physician about pursuing clinical genetic testing in addition to or instead of this research study.**

Although one goal of the research study is to generate as much genetic data as is possible, there is no guarantee that your sample or data will be analyzed. If genetic data are generated and analyzed, there may be no findings of relevance to your health at this time. Therefore, it is likely that you will not be provided with any genetic information about yourself in this research study.

WHAT WILL I BE ASKED TO DO IF I CHOOSE TO BE IN THE STUDY?

If you agree to be in this study, you will have a visit with a member of the study team, which typically lasts less than one hour. Most participants only meet with the study team one time.

We will typically perform the following procedures:

- Collect some information about you, including your medical history.
 - If you are a patient at Columbia University Medical Center (CUMC) and/or New York-Presbyterian Hospital (NYPH), we will review CUMC and/or NYPH electronic medical records and collect information, including medical information and certain identifying information about you (your name, date of birth, contact information, and medical record number).
 - If we require medical records from outside institutions, we will ask you to sign a separate authorization form to obtain them.
- Obtain information about your family
- Obtain a blood sample (up to 30 mL or 6 teaspoons)
 - Sometimes, we may use a buccal (cheek) swab or saliva sample instead. Alternatively, if available, we may be able to use leftover blood or DNA sample that was not needed for clinical purposes.
 - A portion of the sample will be banked in the research biobank and clinical laboratory

WHAT RESULTS WILL BE REPORTED TO ME?

For participants diagnosed with a cardiovascular or metabolic disorder:

If the researchers identify genetic variant(s) that they believe is likely or definitely responsible for some or all of your clinical features, these results can be returned to you. In most cases, we do not identify this type of variant, and no results are returned back. We may not identify a genetic cause for your condition for any of the following reasons:

- The disorder is not due to a genetic cause
- A genetic variant exists, but due to limitations in the technology, it was not identified through the testing performed
- A genetic variant is found, but based on current knowledge, it cannot be determined whether it is related to the disorder.

_____ Yes, please notify me of any cardiovascular or metabolic genes identified from this research.

_____ No, please do not notify me of any cardiovascular or metabolic genes identified from this research.

For participants without a diagnosis of cardiovascular or metabolic disorder:

If you are not known to have a cardiovascular or metabolic disorder, you are being asked to participate in the study in order to help with the analysis for your family member. It is therefore very unlikely that you will receive results for yourself. However, you may be found to have the same genetic variant as

your family member who is affected with a disorder. If this is the case, the result will be returned to you, then consult your physician or pursue further genetic counseling.

Incidental Findings:

The nature of exome and genome sequencing and other detailed genetic tests makes it possible that we may identify information about you that was not previously known and is unrelated to the reason why you or your family member were referred to the study. This type of information is called an “incidental finding.” If an incidental finding is found, it could indicate that a person has an increased risk of disease, even if they were not previously diagnosed.

You have the option of whether or not you would like to be informed if the study team identifies certain incidental findings. If you decide that you want to know about incidental findings, we will only report back gene(s) or variant(s) that are specifically recommended to be reported by The American College of Medical Genetics and Genomics (ACMG). Variants in these genes are known to be associated with human disease, like cancer syndromes. These disorders were selected because there may be changes in medical management if a person is known to have a genetic susceptibility to one or more of these disorders. A complete list of diseases/disorders included in the ACMG list is included in the Summary of Informed Consent Form, which you will be given, and could change over time.

Identification of incidental findings is not the primary purpose of this research study, and it is unlikely that incidental findings will be identified in your sample. The absence of a reportable incidental finding does not mean that you have no disease-causing genetic changes, so if you have symptoms or features of a genetic disease in the future, clinical genetic testing should be considered.

Please initial your choice below regarding whether or not you would like to be notified of incidental findings in the ACMG-specified genes identified in this research study:

_____ Yes, please notify me of any incidental findings in any of the ACMG-specified genes identified from this research.

_____ No, please do not notify me of any incidental findings in the ACMG-specified genes identified from this research.

If at any time during or after the study you change your mind about whether or not you would like to be notified, you can contact us at the contact information listed above and change your choice.

Results Confirmation:

If the study team identifies a reportable genetic variant as described above, the variant must be confirmed by a laboratory that is certified by New York State to provide clinical genetic testing (CLIA-certified). Results can only be returned to you after the genetic variant has been clinically confirmed in the CLIA-certified laboratory.

In order to confirm a finding, we may contact you to obtain an additional sample to send to the clinical laboratory for confirmation. If we contact you to obtain an additional sample, we will not be able to give you any information about the research finding until the result has been clinically confirmed. This will be paid for by your health insurance. If your health insurance does not pay for this, this study will pay for this.

Any samples submitted to a clinical laboratory will be labeled with your name and date of birth.

Reporting of Results:

If a finding is clinically confirmed, the results will be provided to you by the physician who referred you to the study, by a member of the referring physician's team, or by a member of the study team. Results may be provided to you in person or over the phone. If you choose, you can designate someone else to receive the results on your behalf. You may be asked by the healthcare provider to attend a clinic visit in order to discuss your results, the cost of which will be charged to you or your insurance. The study will make a genetic counselor available to you, your family members and/or your physician in the event that you have additional questions regarding the results.

If there is a positive test result, you may want to consult with specialist physicians and/or independent genetic counselors. Genetic counseling is provided through the study; however consultation with a medical geneticist or other medical specialists is not.

Please be aware that the research may indirectly reveal unexpected personal information about you or your family (such as ethnic/racial background or an unknown genetic relationship between family members), but that this information will not be returned to you.

WHAT ABOUT PRIVACY AND CONFIDENTIALITY?

The study team may discuss your research analysis with study physicians and the physician who referred you to the study.

If a reportable genetic variant is clinically confirmed and returned to you, the report will become part of your medical record, and can be accessed by CUMC/NYPH healthcare providers. The study team or your CUMC/NYPH physician can provide you with a copy of the report that you can choose to share with other outside healthcare providers.

Every effort will be made to keep your personal information confidential. However, we cannot guarantee total confidentiality. To protect your privacy, your data will be assigned a code number and separated from your name or any other information that could identify you. The file that links your name to the code number will be kept in a password protected database, and only the investigators and study staff will have access to this file.

If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

The following people and/or agencies will be able to look at and copy your research records:

- The researchers, study staff and other professionals who are conducting the study or analyzing study information;
- If necessary for monitoring purposes:
- Authorities from Columbia University, including the Institutional Review Board ('IRB'). An IRB is a committee organized to review, approve and oversee research involving human subjects.
- The U.S. Office for Human Research Protections and the National Institutes of Health.
- a. The investigator, Columbia University Medical Center and NewYork-Presbyterian Hospital study staff and other medical professionals who may be evaluating the study
- b. The United States Food and Drug Administration ('FDA')

You will be asked to sign a separate form to allow the use and disclosure of your protected health information.

WHAT ELSE COULD HAPPEN WITH MY BIOLOGICAL SAMPLES AND/OR DATA?

Use in biorepositories:

Biorepositories hold samples and data to be used for research purposes. This study will include your samples and data in Biorepository here at CUMC, where they may be used for future genetic studies and we may send your deidentified data to the National Institutes of Health's (NIH) database of genotypes and phenotypes (dbGaP) or other public databases. The samples and data in these biorepositories will be used for other research studies that may be related or unrelated to this one. Samples and data that have been deidentified may be shared with other CUMC investigators or with investigators at other institutions, including commercial entities. Samples and data that are stored as a part of these biorepositories will be kept indefinitely.

Development of a cell line:

In some cases, it may be useful to develop a cell line from your sample. A cell line is a continuously growing set of cells that can be used for future research indefinitely.

Use of outside laboratories:

Your sample may be sent to a laboratory for genetic testing outside Columbia.

Storage of samples and data:

Your samples and data will be stored indefinitely. These samples/data will not be available to you for diagnostic or therapeutic purposes.

WHAT ARE THE RISKS OF PARTICIPATING IN THIS STUDY?

There may be slight pain or bruising due to the blood draw. We will use only trained phlebotomists to obtain blood from you.

A risk of taking part in this study is the possibility of a loss of confidentiality, where personal information is shared with someone who should not have access to it. The plans for protecting your confidentiality are described in the "What about privacy and confidentiality?" section. Even without your name and other identifiers, your genetic information is unique to you. There is a potential risk that someone will identify you or learn something about you by looking at your genetic information; this risk may increase in the future as technologies advance and more researchers study your genetic information.

Discrimination based on genetic information is a risk of participating in the study. The Genetic Information Non-discrimination Act (GINA) is a federal law that prevents insurance companies from using your genetic information to deny health insurance coverage. The law also prevents employers from asking for, or using genetic information for employment-related decisions. However, the law does not prevent companies that provide life insurance, disability insurance or long-term care insurance from using genetic information.

You may learn that you or your family member has an increased risk or a diagnosis of a serious, untreatable genetic condition. Such a finding can result in unexpected psychological impact. The detection of such a condition could also affect the health care needs of other family members.

Because we cannot say with certainty how information derived from the genetic research could be used in the future, this study may involve risks that are currently unforeseeable.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in the study, there is a chance that it may be of direct medical benefit to you. If a genetic cause for your medical condition is found, your physician may make changes to your medical management based on this information. It may provide information about what to expect in the future, resolve unanswered questions about why you have your medical condition, and provide information about the chance of having children with similar medical problems.

More likely, there may not be any direct benefit to you. You may not receive any results from the study, or you may receive results that do not affect medical management of your condition. However, we hope that in the future, information learned from this study will benefit other people with similar findings.

WILL I GET PAID OR BE GIVEN ANYTHING TO TAKE PART IN THIS STUDY?

You will not receive any payment or other compensation for taking part in this study.

The research samples and data may allow researchers to make medical tests or treatments that may have commercial value. If this happens, there are no plans to pay you for any products or treatments that are made, or for using your data.

WILL I INCUR COSTS IF I TAKE PART IN THE STUDY?

There will be no costs to you or your insurance company for being in this study.

However, you or your insurance company will be responsible for any additional clinical tests, clinic visits, or medical procedures that may be recommended by your physician as a result of information received from the study.

WHY MIGHT RESEARCHERS WANT TO CONTACT ME IN THE FUTURE?

Regardless of your choice below, we may contact you directly or through your physician for the following reasons.

- Inform you of additional research opportunities for your condition
- We may request that you sign new or updated consent documents
- We may request new or additional biological samples
- If you have previously had or are planning to have surgery to biopsy or resect a portion of the cardiovascular system or metabolic tissues, we may ask you to allow a portion of that tissue sample, and the associated medical records, to be sent to us for further study. In this case, you will be asked to sign a separate consent addendum.
- We may request outside medical records or additional health information

You will always be free to decline to participate in additional research, provide additional information or samples.

You may choose if we can contact you in the future regarding the opportunity to participate in other research studies independent of this one. You will be free to refuse to participate in other research studies without any effect on your participation in this research.

Please initial your choice below:

_____ Yes, I give permission to be contacted in the future for research purposes.

_____ No, I do not give permission to be contacted in the future for research purposes.

HOW LONG WILL I BE IN THE STUDY?

This will be an ongoing research endeavor and so you will be in this research study forever or until the study is closed. Subjects who are under the age of 18 at the time of enrollment will be asked to consent for themselves after their 18th birthday.

You can choose to stop participating at any time without penalty or loss of any benefits to which you are entitled, and you are not required to explain why you would like to withdraw. In order to withdraw from the study before it is finished, you will need to notify in writing the researchers, Dr. Reilly at the following address: New York Presbyterian hospital, Columbia University; 622 West 168th Street Suite 10-305; New York, NY 10032. If you withdraw, your data will continue to be stored and used anonymously. You will need to specify in your written notice if you want your unused biological samples destroyed. Be aware that there are limitations on our ability to exclude your information or remove your biological samples after they have been de-linked from identifying information or deposited in scientific databases.

WHAT OTHER OPTIONS ARE THERE?

You may choose not to take part in this research study.

WHO MAY I CALL IF I HAVE QUESTIONS?

If you have any questions or concerns about the study, you may contact your physician. If you have any questions about your rights as a research subject, you may contact the CUMC IRB by phone at 212-305-5883 or by email at irboffice@columbia.edu. More information about taking part in a research study can be found on the IRB's website at: <http://www.cumc.columbia.edu/dept/irb>.

STATEMENT OF CONSENT: I have read this consent form and the research study has been explained to me. I agree to be in the research study described above.

A copy of this consent form will be provided to me after I sign it.

By signing this consent form, I have not given up any of the legal rights that I would have if I were not a participant in the study.

Signature:

A. Research Participant

_____	_____	_____
Print Name	Signature	Date

B. Parent, Legal Guardian or Legally Authorized Representative

_____	_____	_____
Print Name	Signature	Date

E. Person Obtaining Consent (Study Staff)

_____	_____	_____
Print Name	Signature	Date