RESEARCH CONSENT FORM

Basic Information

Title of Project: FHS Lifelong Endowment for Genomic and Cellular DiscoverY (**LEGACY**) Program

IRB Number: H-45743

Sponsor: NHLBI

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Study-Related Phone Numbers: Regular business hours: 617-638-8717 24 hours: 617-638-8000, ask pager operator to page Dr. Gopal (#5302)

Overview

We are asking you to be in a research study. A research study is an organized way of collecting information about scientific questions. This form will tell you what you should expect if you agree to be in the study. There are programs in place to make sure that investigators fulfill their obligations listed in this form.

It is your decision whether to join the study. We are doing the research to better understand chronic diseases, specifically heart and lung disease, by studying heart and lung tissue after death, which is call postmortem tissue. We are asking you to be in this study because you are part of a long-standing heart study, the Framingham Heart Study, where you have made generous contributions over the years to participating in research and can donate your heart or lung tissue after death as a final research donation that will provide much scientific discovery. If you agree, you will donate the organ/organs of your choice and the tissues will be processed to be studied in many ways. Your tissues will be stored in a long-standing biobank (tissue repository) indefinitely. You will find more information about what will happen in this study later in this form.

The main risks of being in the study are that there is a minimal risk of loss of confidentiality, however, this risk would not directly affect you as participation in this study is after you have passed away. You will find more information about risks later in this form.

Purpose

Our understanding of heart (cardiovascular diseases, or CVD) and lung disease and has been limited by several factors. First, animal models, or tests done on animals, often don’t fully reflect the wide variety of heart problems seen in humans. Second, it’s difficult to get access to human heart and lung tissue for research. Lastly, we don’t yet fully understand the different ways these diseases show up in people, which makes studying them harder.

To address these issues, we are proposing a new project called the **Framingham Heart Study (FHS) Lifelong Endowment for Genomic and Cellular DiscoverY (LEGACY) Program.** The goal of this program is to collect and organize a large collection of heart, lungs, and blood vessel tissue samples, which we will gather from people who are participants in the Framingham Heart Study. The samples will include tissues taken after death (postmortem) and will be analyzed in detail using advanced technologies like single-nucleus and bulk RNA sequencing, proteomics, metabolomics, genetic sequencing, and other multiomic applications. This method will help us deepen our knowledge about the cells of the heart, blood vessels, and lungs in human tissue.

We will link information that has already been collected about your health and lifestyle over your entire life, including factors like diet, exercise, blood pressure, cholesterol, and any other testing that has been already performed by you being a part of the Framingham Heart Study. This information will be linked to the tissue samples to create a more complete picture of how cardiovascular and lung diseases develop.

This project is unique because it will allow us to study both the structure of the heart, lung, and blood vessels and the molecular details of these tissues in a way that hasn't been done before. By connecting this information with long-term health data from the Framingham Heart Study, we will be able to better understand how different cardiovascular risk factors, such as smoking or high cholesterol, affect the heart and blood vessels over time.

The **FHS Legacy Program** will also help us identify new "biomarkers" for cardiovascular and respiratory diseases. Biomarkers are measurable signs in the body that can indicate whether someone is at risk for heart or lung problems. Finding these biomarkers could lead to better tests for predicting and diagnosing important diseases.

What Will Happen in This Research Study

In this research study, you will decide if you would like to donate your heart and/or lungs to the Framingham Heart Study after you pass away for research. All living participants of the Framingham Heart Study are eligible for participation in this study.

If you give consent for this study, you will be enrolled in the FHS LEGACY program. Your legally authorized representative (**LAR**) will help you participate in this study, and we will make sure they are aware of your consent to participate in the study at the time you provide consent for the study. We will record in our secured database the name of your LAR and the date that the research team confirmed verbally with them directly that they were aware of your consent for the FHS LEGACY program. Once consented to the LEGACY program, we will confirm your ongoing interest in remaining enrolled in the LEGACY program on an annual basis with you, re-confirm the name and contact information for the LAR, and will provide updated communication to the LAR regarding our FHS Biobank line for notification.

After you have passed away, your LAR will call the FHS Biobank Pager line (24/7 available) that will inform the study of the death. Your LAR will confirm with the FHS Biobank operators, who are part of the FHS LEGACY program, the location of your death and also the final location for your memorial service and for your last rites. No further burden or contact will be required of your LAR and the FHS LEGACY program will take care of all next steps.

The FHS LEGACY program will then coordinate with an organ procurement agency, called the National Disease Research Interchange (NDRI), a non-profit that works closely with the National Institutes of Health for tissue obtainment in postmortem settings. NDRI and the FHS LEGACY Program will communicate in a secured, confidential manner your name and date of birth to confirm your consent for organ procurement and to verify your identity at the memorial/funeral home. NDRI has a national presence and can obtain tissue from all 50 states so the organ procurement can occur wherever the FHS participant has passed away. NDRI will then go directly to the hospital or funeral/memorial home to obtain the organs that you have consented to donate after your death.

The organs will be removed quickly, just like if you were in surgery, and the complete process will take under 1 hour even for multiple organs. Your body will be stitched (sutured) back exactly how surgeons would do in a surgery so it a very orderly process. If you plan to have an open casket memorial, the site where the organs are removed would not be able to be detected at all by any friends or family or attendees of the service.

The organs will be immediately placed in preservation solution and immediately transported to Boston University for immediate processing and storage by the FHS LEGACY team. Each participant will be assigned a study ID as part of the FHS LEGACY program when they have consented and once the organs are obtained, all tissue will be only labelled with the study ID and never with any identifying information like your name or date of birth. NDRI will securely store in their password-protected system your name, your date of birth, a copy of this signed consent form, date and time of organ procurement, and location for their records. They will retain NO tissue or any other information related to you or the FHS.

Your organ and issues will be stored indefinitely in the FHS LEGACY organ biobank/repository and will be available to the greater scientific community to perform extensive tissue research. No tissue/sample released to outside researchers will ever have your identifying information – they will be released in groups and always only linked with a Study ID. Only FHS LEGACY committee can approve scientific research and only the FHS LEGACY Directors, Dr. Gopal and Fetterman, will approve and supervise the release of any tissue samples requested.

Genetic testing and/or collecting genetic information

- We may perform a whole examination of your DNA or genome. Usually, researchers study just a few areas of your genetic code that are linked to a disease or condition. In whole genome studies, all or most of your genes are examined and used by researchers to study links to a disease or condition. It is likely we will perform genetic testing on your RNA or DNA in the future from the tissues we have obtained. As this study is done after death, no findings will be returned to subjects.

Communication of pertinent and/or incidental findings to subject's LAR

- At the time of the organ dissection which will be performed by a cardiac/lung pathologist.

- If you or your LAR provide consent, we will mail the pathology report to them.

- Any questions regarding the report and clinical relevance can be directed to the FHS LEGACY PI, Dr. Gopal and her contact information will be made available on the pathology report for the LAR.

- As these are after death findings, these results will have no direct impact on you.

Repositories or other retention of samples or data

- The samples will be obtained as described in the earlier paragraphs of this section **What Will Happen in This Research Study.**

- Research that includes transcriptomics, genetics, metabolism, and epigenomics will be applied to the tissues/organs obtained for this repository

- As we have indicated above, genetic information may be obtained in the research performed

- BMC, BU, and external researchers will be allowed to request release of samples to perform research

- As detailed earlier, an FHS LEGACY Scientific Committee will review all research proposals and will vet all research proposed to be performed on repository samples. This committee, who will be comprised of members of the FHS leadership and outside members, will determine if the science, investigators, and funding proposed for the science is of the highest integrity before approval.

- Once approved, the approval will be reviewed by the FHS Legacy Biobank Directors, Drs. Fetterman and Gopal, who will ultimately make the final arrangements and review of sample release to ensure highest quality for release and return of samples, verify sample integrity, and confirm all samples are released in aggregate and completely de-identified only with assigned Study ID. No demographics, diagnosis, or other information will be released to outside investigators and will be associated with any specific samples.

- There is no direct benefit to participants as this study is postmortem. All participants who agree to this study will mandatorily provide consent to having their tissues/biosamples retained in this FHS LEGACY repository.

Risks and Discomforts

The main risk for participation in this study is a loss of confidentiality of your health information if there was to be an unexpected data breach. The likelihood of such an occurrence is very low as there are multiple steps being taken to protect your information. NDRI will have information that will be password-protected on a secure server and all information and tissue-related information for the FHS LEGACY repository will be stored only linked to a Study ID. Lastly, any loss of confidentiality that could occur would be after death so would not have direct impact on you during your lifetime. The ways we will protect your privacy and confidentiality are described in a separate section later in this form.

The genetic data we may generate from genetic testing on your tissues will have no impact on you as these are after-death specimens and will have little impact on your first-degree relatives as they are performed only for research and not for clinical applications.

If you decide that you want to stop being in the study, we ask that you let us know before you pass away and we will cancel your consent and we will make sure your LAR is aware of your change in decision.

Potential Benefits

You will receive no direct benefit from being in this study. The primary goal of this research is to collect tissues from participants who consent after they pass away to answer scientific questions. Your being in this study may help the investigators learn about chronic heart and lung diseases and facilitate new research discoveries as researchers study the tissue and relate it to all the antemortem (before death) information that has been obtained in you as you being part of the Framingham Heart Study.

Costs

There are no costs to you for being in this research study.

Payment

You will not be paid for being in this study.

Confidentiality

We must use information that shows your identity to do this research. Information already collected about you will remain in the study record even if you later withdraw.

We will store your information in ways we think are secure. The repository has standard operating procedures to protect your confidentiality .We will store biological samples taken from your body (organs/tissue) in small test tubes and freezer-stable containers and stored in a -80°C freezer that is locked and connected to a back-up generator on the BU Medical Campus in Dr. Fettterman/Gopal's research lab as part of the FHS LEGACY biorepository. Your biosample/tissues will be stored by study ID only. The master key that links any identifiers (name, DOB) to this FHS LEGACY ID will be stored in a BMC-BU password protected network drive that can only be accessed by FHS LEGACY research personnel listed on this IRB. Any information about your tissues, storage details, etc will all be organized and stored in a BU-protected, encrypted REDCAP database. We will store paper files in locked filing cabinets. We will store electronic files in computer systems with password protection and encryption. Only the people listed later in this section will be given access to your information. However, we cannot guarantee complete confidentiality.

This study proposes to share data with the National Disease Research Interchange (NDRI). Data that is not stored at Boston Medical Center or Boston University is outside of our control. Your information could get out or be used by NDRI for other purposes that are not related to the study. Please carefully read and think about NDRI's Terms of Service and Privacy Policies before agreeing to give them any of your information. If you do not want to share your data with NDRI that is completely acceptable, but you cannot be in the study.

This study is covered by a Certificate of Confidentiality (CoC) from the National Institutes of Health. All studies funded by the National Institutes of Health that involve identifiable information or biological samples are covered by a CoC. The CoC provides how we can share research information or biological samples. Because we have a CoC, we cannot give out research information or biological samples that may identify you to anyone that is not involved in the research except as we describe below. Even if someone tries to get your information or biological samples in connection with a legal proceeding, we cannot give it to them. The CoC does not prevent you from sharing your own research information.

If you agree to be in the study, we will share information and biological samples that may show your identity with the following groups of people:

- People who do the research or help oversee the research, including safety monitoring.

- People from Federal and state agencies who audit or review the research, as required by law. Such agencies may include the U.S. Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health, and the Massachusetts Department of Public Health.
- People who will get information and biological samples from us. Only approved research that is funded and approved by the FHS Legacy Scientific Committee can be eligible to receive your biologic samples. Drs. Fetterman and Gopal and their team will ultimately release samples and will only release the samples identified only by a study ID. **No identifying information that relates to the samples will ever be released.** These people are expected to protect your information and biological samples in the same way we protect it.

We will share research data where we have removed anything that we think would show your identity. There still may be a small chance that someone could figure out that the information is about you. Such sharing includes:

- Publishing results in a medical book or journal.
- Adding results to a Federal government database.
- Using research data in future studies, done by us or by other scientists.
- Using biological samples in future studies, done by us or by other scientists.

Samples that are collected from you in this study will be analyzed to find out information about your genetics. Your genetics and health information, without your name or other data that could easily identify you, will be put in a database run by the National Institutes of Health (NIH) such as dbGaP or BioLINCC. This may include your whole genome information. Other researchers can ask the NIH to get your information from the database. You should know that it is possible that your genetics information might be used to identify you or your family, though we believe it is not too likely that this will happen. Once your information is given to the NIH database, you can ask to have NIH stop sharing it, but NIH can't take back information that was already shared.

Subject's Rights

By consenting to be in this study you do not waive any of your legal rights. Consenting means that you have been given information about this study and that you agree to participate in the study. You will be given a copy of this form to keep.

If you do not agree to be in this study or if at any time you withdraw from this study you will not suffer any penalty or lose any benefits to which you are entitled. Your participation is completely up to you. Your decision will not affect your ability to get health care or payment for your health care. It will not affect your enrollment in any health plan or benefits you can get.

Questions

The investigator or a member of the research team will try to answer all your questions. If you have questions or concerns at any time, contact Dr. Gopal at 617-638-8717.
You may also call 617-358-5372 or email medirb@bu.edu. You will be talking to someone at the Boston Medical Center and Boston University Medical Campus IRB. The IRB is a group that helps monitor research. You should call or email the IRB if you want to find out about your rights as a research subject.

You should also call or email if you want to talk to someone who is not part of the study about your questions, concerns, or problems.

Subject: ____
Printed name of subject

By signing this consent form, you are indicating that

- you have read this form (or it has been read to you)
- your questions have been answered to your satisfaction
- you voluntarily agree to participate in this research study
- you permit the use and sharing of information that may identify you as described

I give my consent to donate to the FHS LEGACY program after my death the following organ(s). Please check one box:

☐ Heart only

☐ Lungs only

☐ Both heart and lungs

<u>Pathology reporting release to LAR (please check one box):</u>
☐ With my consent to participate in this study, I would like any pathology reports generated by my organ/tissue donation to be released.

☐ With my consent to participate in this study, **I do NOT** want any pathology reports generated by my organ/tissue donation to be released.

<u>To be completed by subject if personally signing</u>

____ ___________
Signature of subject Date

<u>To be completed by LAR if subject does not personally sign</u>

I am providing consent on behalf of the subject.

____ _________________________________
Printed name of Legally Authorized Representative (LAR) Relationship to Subject

____ __________________
Signature of Legally Authorized Representative (LAR) Date

Researcher: ____
Printed name of person conducting consent discussion

To be completed by researcher if subject personally signs

I have personally explained the research to the above-named subject and answered all questions. I believe that the subject understands what is involved in the study and freely agrees to participate.

____ ___________
Signature of person conducting consent discussion Date

To be completed by researcher if subject does not personally sign

I have personally explained the research to the above-named subject's Legally Authorized Representative and answered all questions. I believe that the Legally Authorized Representative understands what is involved in the study and freely agrees to have the subject participate. I consider that the above-named subject (check one):

☐ is capable of understanding what is involved in the study and freely agrees to participate.
☐ is not capable of understanding what is involved in the study.

____ ___________
Signature of person conducting consent discussion Date

NOTE: THE PRINCIPAL INVESTIGATOR MUST KEEP THE ORIGINAL SIGNED, DATED CONSENT FORM AND MUST DOCUMENT THAT A COPY OF THE CONSENT FORM WAS GIVEN OR OFFERED TO THE SUBJECT