NYU Langone MEDICAL CENTER

Research Subject Informed Consent Form

Title of Study: Hirschsprung Disease Research Collaborative
s18-00033

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1. About volunteering for this research study

You are being invited to take part in a research study. Your participation is voluntary which means you can choose whether or not you want to take part in this study.

People who agree to take part in research studies are called “subjects” or “research subjects”. These words are used throughout this consent form. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in this study. You may also decide to discuss this study and this form with your family, friends, or doctor. If you have any questions about the study or about this form, please ask us. If you decide to take part in this study, you must sign this form. We will give you a copy of this form signed by you for you to keep.

Some of the people who may be able to take part in this study may not be able to give consent because of their medical condition. In this case, we will ask the person’s authorized representative, called their Legal Authorized Representative, to give surrogate consent for them. However, throughout the consent form, “you” always refers to the “subject” or person who takes part in the study.

Some of the people who may be able to take part in this study may not be able to give consent because they are under 18 years of age (a minor). Instead, we will ask their parent(s) or legal guardian to give consent. We will also ask the minor to agree (give their assent) to take part in the study if they are between the ages of 7 and 17. They will be given an Assent Form to sign. Throughout the consent form, “you” always refers to the “subject” or person who takes part in the study.

2. What is the purpose of this study?

This research is being done to identify genes that are involved in the development of, or susceptibility (risk) to, the birth defect termed Hirschsprung disease (HSCR). Hirschsprung disease is a disorder

characterized by lack of nerve cells in the gut, which prevents individuals with the disorder from having the muscle contractions necessary to pass stool. Hirschsprung disease is a complex condition caused by many genes in combination with other factors such as lifestyle, diet, and/or environment. We plan to do genetic research on the DNA in blood, saliva samples, and possible other biospecimens provided by individuals with HSCR and their affected and unaffected biological relatives.

DNA is the material that makes up your genes. All living things are made of cells. Genes are the part of cells that contain the instructions which tell our bodies how to grow and work, determine physical characteristics such as hair and eye color, and affect risk for developing certain diseases or having children with the disease. Genes are inherited, meaning they are passed from parent to child.

The samples collected in this study will make up a biorepository to which multiple institutions that are part of the Hirschsprung Disease Research Collaborative contribute. A biorepository is a central facility that manages the collection, processing, storage and sharing of biological specimens (like blood, saliva, and DNA) and related information for research purposes. The information and samples will also be stored for possible use in other research studies about Hirschsprung disease done by other researchers who are part of the Hirschsprung Disease Research Collaborative.

You are being asked to participate in this study because you meet one of the following criteria:

- You have HSCR.
- You have a first, second, or third-degree relative who has HSCR.

3. How long will I be in the study? How many other people will be in the study?

After completing a medical and family history questionnaire, providing permission to access medical records, and donating a blood, cheek swab, or saliva sample, as described in Section 4, you will not need to do anything else to participate in the study.

You may be contacted after that and asked for more information about your medical or family history.

You may be contacted later to ask if you are willing to submit a second sample.

The study will continue using your information and sample(s) indefinitely unless you change your mind about allowing continued use of your information and sample and let the Principal Investigator know in writing. Any future use of your sample will be for research on Hirschsprung disease.

Up to 5,000 people will be in this study. Up to 1,000 people will be enrolled at NYU Langone Health for this study.

4. What will I be asked to do in the study?

- You will be asked to complete a family and medical history questionnaire, which may take up to an hour to complete.

- You will be asked to donate a small sample of blood. In infants (babies under age 1), about a half teaspoon to one teaspoon of blood will be collected. In children 1 to 11 years old, just over a teaspoon will be collected. In adults and children 12 years and older, about 4 teaspoons of blood will be collected. In some cases, such as when a blood draw is difficult to obtain because a doctor, nurse or phlebotomist (person trained to draw blood) is not available to draw the blood, brushing the inside of the cheek with a special swab or giving a saliva sample can be used instead. The blood, cheek swab, or saliva sample will be used to obtain DNA for genetic analysis.

The questionnaire and the blood collection kit will be sent to you with instructions on how to return them.

- You may also be asked to provide some medical records or to sign a records release form to allow the researchers to request your medical records from your doctor(s).

- You may be asked to undergo a brief physical examination performed by a board certified clinical geneticist.

- You may also be asked to provide a photograph of your face in order to aid the assessment of your physical features.

- If you had surgery on your colon, we may ask you for a sample of the colon tissue that was removed during your surgery. We will only do this if you give us your permission on this consent document.

Your medical and demographic information (age, sex, gender) along with results from this research study will be maintained in a password protected database in the Chakravarti laboratory at the NYU School of Medicine indefinitely to allow for continued research on genes involved in HSCR as knowledge, technology, and assays (laboratory tests) improve with time. Your blood sample will be given a coded number once it is received in the laboratory to protect your confidentiality. A key linking the code to your identity will be kept in a separate secure location with access limited to the principal investigator and study team.

You maintain the ability to request withdrawal of your stored information and samples at any point in time, should you change your mind. If you decide you do not want your information and samples to be stored indefinitely for continued research, please send a written request to the principal investigator (his contact information is listed on page 1 of this consent form). Any data that has been generated prior to your request will be used in the study; however, we will destroy the information and samples so that no additional research is conducted with them.

Results from this research study will not be disclosed to you directly, but general and summary results will be published in scientific journals and discussed at scientific meetings, and can be provided to you upon request. Coded samples or data with no directly identifying information may be provided to other legitimate researchers for studies on Hirschsprung disease. These researchers may be from New York University or may be from other institutions. Data shared with other researchers may include medical information and genetic data obtained from our studies. We will never share identifying information, such

as your name, date of birth, or address, with anyone outside of the Chakravarti laboratory without your expressed written consent, except as provided in Section 15 of this form.

You may be contacted in the future and asked to participate in additional studies about Hirschsprung disease or related conditions. You do not have to participate in any of these additional studies. You can decide about each study when you are asked.

Your blood sample may be used to create a living tissue sample (called a "cell line") that can be grown in the laboratory. This allows researchers to have an unlimited supply of your cells in the future without asking you for more samples.

What you should know about the cell lines that will be derived in the course of this study?

- The cell lines created will be similar or identical to you genetically.
- The cell lines may be kept indefinitely.
- The cell lines may be shared with researchers both inside and outside of New York University.

We may also perform a whole genome analysis on your DNA sample. Usually researchers study just a few areas of your genetic code that are linked to a disease or condition. In whole genome studies, researchers analyze all or most of each participant's genes to study links to a particular disease; in this study, the same will be done to study links to Hirschsprung disease.

To do more powerful research, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. Researchers can then study the combined information to learn even more about health and disease.

If you agree to take part in this study, some of your genetic and health information might be placed into one or more scientific databases. For example, the National Institutes of Health (an agency of the federal government) maintains a database called "dbGaP." A researcher who wants to study the information must apply to the database. Different databases may have different ways of reviewing such requests. Researchers with an approved study may be able to see and use your information, along with that from many other people. Your name and other information that could directly identify you (such as address or social security number) will never be placed into a scientific database. However, because your genetic information is unique to you, there is a small chance that someone could trace it back to you. The risk of this happening is very small, but may grow in the future. Researchers will always have a duty to protect your privacy and to keep your information confidential.

5. What are the possible risks or discomforts?

Blood Draw
The risks of a blood draw include brief discomfort, bruising at the site of needle entry, fainting, or in rare cases, infection. If you feel faint, tell a member of the study team immediately.

Saliva Sample/Cheek Swab Collection

In some cases, a swab may be used to collect a saliva sample or cheek swab in children five years of age or under. The swab can be a choking hazard.

Sharing Medical Information

Despite our efforts to the contrary, loss of confidentiality remains a potential risk. Someone could get access to the data we have stored about you. If those data suggested something serious about your health, it could be misused. For example, it could be used to make it harder for you to get or keep a job or insurance. There are laws against this kind of misuse such as the Genetic Information Nondiscrimination Act (GINA, described below), but they may not give full protection.

There may be other unforeseen privacy risks. We believe the chance these things will happen is very small, but we cannot make guarantees. Your privacy and the confidentiality of your data are very important to us and we will make every effort to protect them by labeling data with a unique code that does not readily identify you as a participant, storing the linking key between the code and your identity separately with the principal investigator, securing the databases and locations where data are kept, and limiting access to your information to authorized individuals or entities working on the study.

Genetic Research

Family information such as mistaken paternity and adoption may be discovered in the course of this research study, which could cause anxiety and negatively affect relationships, but this information will not be disclosed to you or any other party.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

All health insurance companies and group health plans must follow this law by May 21, 2010. All employers with 15 or more employees must follow this law as of November 21, 2009.
Be aware that this new Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Group Risks

Although we will not give researchers your name, we will give them basic information such as your race, ethnic group, and sex. This information helps researchers learn whether the factors that lead to health problems are the same in different groups of people. It is possible that such findings could one day help people of the same race, ethnic group, or sex as you. However, they could also be used to support harmful stereotypes.

Questionnaire
You may get tired or bored when we are asking you questions or you are completing questionnaires. You may find some questions upsetting to answer. You do not have to answer any question you do not want to answer.

6. What if new information becomes available?

During the course of this study we may find more information that could be important to you. This includes information that might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

7. What are the possible benefits of the study?

There is no direct benefit to you or your family from being in this study. The information gained from this study will allow researchers to better understand which genes contribute to the development of Hirschsprung disease. This information could lead to better detection, treatment and management of the disease in the future.

Incidental Findings:

In general, the results of the genetic tests done for the purpose of this study are for research purposes and will only yield preliminary results that have not been verified and may not be understood for many years. Therefore, there is no plan to share the research results with you, your family members, or your doctor. However, there is a small chance that in the course of our testing of genes associated with HSCR, the researchers could discover something that might be very important to your health or medical care right now that may or may not be related to HSCR.

If this happens, you may be contacted by a study coordinator with a background in genetic counseling who will explain that the preliminary test results indicate a confirmatory test is in order and ask you if you want to learn more and will discuss options that you have such as:

- Speaking with a genetic counselor before making a decision
- Providing an additional sample for retesting at a special certified laboratory and choosing whether or not to receive the results of this testing. This will be at your expense and may or may not be covered by your insurance.
- Discussing the results of the confirmatory testing with a genetic counselor to understand the meaning of the results and how it impacts you (may result in costs to you that may/may not be covered by your insurance)
- Pursuing additional genetic testing, genetic counseling, and/or follow-up with your physician (may result in costs to you that may/may not be covered by your insurance)

8. What other choices do I have if I do not participate?

You do not have to join this study. If you do not join, your care at NYU Langone Health will not be affected.

9. Will I be paid for being in this study?

You will not be paid for being in this study. If there are charges for the blood draw, we will cover the cost by paying the bill for the blood draw directly or by reimbursing you if you have paid for the blood draw.

10. Will I have to pay for anything?

You will not have to pay for anything to be in this study.

11. What happens if I am injured from being in the study?

For medical emergencies contact 911. If you think you have been injured as a result of taking part in this research study, tell the principal investigator as soon as possible. The principal investigator's name and phone number are listed at the top of page 1 of this consent form.

We will offer you the care needed to treat injuries directly resulting from taking part in this research. We may bill your insurance company or other third parties, if appropriate, for the costs of the care you get for the injury, but you may also be responsible for some of them.

There are no plans for the NYU School of Medicine or Medical Center to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

12. When is the study over? Can I leave the Study before it ends?

This study is expected to end after all participants have completed a blood draw and if appropriate, study questionnaire and medical records request, and all data has been analyzed.

If you decide to participate, you are free to leave the study at any time. Leaving the study will not interfere with your future care, payment for your health care or your eligibility for health care benefits.

13. How will you protect my confidentiality?

Your medical information is protected health information, or "PHI", and is protected by federal and state laws, such as the Health Insurance Portability and Accountability Act, or HIPAA. This includes information in your research record as well as information in your medical record at NYU Langone Health. In compliance with NYU Langone Health policies and procedures and with HIPAA, only those individuals with a job purpose can access this information.

Medical information created by this research study may become part of your medical record. We may include your research information in your medical record for several reasons, including for the billing of services provided in connection with the study, to securely document any medical services you receive, and so that other members of the NYU Langone Health community who may treat you have access to important information about your health.

You have a right to access information in your medical record. In some cases, when necessary to protect the integrity of the research, you will not be allowed to see or copy certain information relating to

the study while the study is in progress, but you will have the right to see and copy the information once the study is over in accordance with NYU Langone Health policies and applicable law.

Certificate of Confidentiality

To help us further protect your confidentiality, this research is covered by a Certificate of Confidentiality from the National Institutes of Health (NIH). The NIH has issued a Certificate of Confidentiality for this research. This adds special protection for the research information (data, documents, or biospecimens) that may identify you.

Research information protected by this Certificate of Confidentiality cannot be disclosed to anyone else who is not connected with the research, without your consent. With this Certificate of Confidentiality, the researchers may not disclose or use research information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, without your consent. However, disclosure, without your consent, is still necessary if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases).

The Certificate of Confidentiality cannot be used to refuse a request for information from appropriate government agencies responsible for project oversight.

The Certificate of Confidentiality does not prevent you from releasing information about yourself and your involvement in this research, including for your medical treatment. Federal regulations may also allow for the use or sharing of information for other scientific research.

By agreeing to be in this research and signing below, you are giving your consent to share research information with others at NYU Langone Health. This means that your research information may be included in your NYU Langone Health electronic medical record.

14. HIPAA Authorization

Federal law requires us, and our affiliated researchers, health care providers, and physician network to protect the privacy of information that identifies you and relates to your past, present, and future physical and mental health conditions. We are asking for your permission (authorization) to use and share your health information with others in connection with this study --- in other words, for purposes of this research, including conducting and overseeing the study.

Your treatment outside of this study, payment for your health care, and your health care benefits will not be affected even if you do not authorize the use and disclosure of your information for this study.

What information may be used or shared with others in connection with this study?
All information in your research record for this study may be used and shared with those individuals listed in this section. Additionally, information in your medical record that the research team believes may be important to the study may be accessed by those listed here. This includes, for example, results from your physical examinations, laboratory tests, procedures, questionnaires, and diaries.

Who may use and share information in connection with this study?
The following individuals may use, share, or receive your information for this research study:

- The research team, including the Principal Investigator, study coordinators, and personnel responsible for the support or oversight of the study
- Governmental agencies responsible for research oversight (e.g., the National Institutes of Health (NIH), Food and Drug Administration or FDA).
- Health care providers, including your doctors and others who provide services to you in connection with this study, and laboratories or other individuals who analyze your health information in connection with this study.
- Other study sites

Your information may be re-disclosed or used for other purposes if the person who receives your information is not required by law to protect the privacy of the information.

What if I do not want to give permission to use and share my information for this study?

Signing this form is voluntary. You do not have to give us permission to use and share your information, but if you do not, you will not be able to participate in this study.

Can I change my mind and withdraw permission to use or share my information?

Yes, you may withdraw or take back your permission to use and share your health information at any time for this research study. If you withdraw your permission, we will not be able to take back information that has already been used or shared with others. To withdraw your permission, send a written notice to the principal investigator for the study noted at the top of page 1 of this form. If you withdraw your permission, you will not be able to stay in this study.

How long may my information be used or shared?

Your permission to use or share your personal health information for this study will never expire unless you withdraw it.

17. Optional permission for future use

NYULMC would also like to store, use, and share your health information from this study in research databases or registries for future research conducted by NYULMC or its research partners. Such health information may include biological samples from the study.

To give this additional permission, check the box below and write your initials where indicated. You may still participate in this study even if you do not give us this additional permission.

NYULMC will continue to protect the confidentiality and privacy of this information as required by law and our institutional polices. If you give this additional permission, you will continue to have the rights described in this form. You have the right to take back this additional permission at any time.

☐ Checking this box indicates my permission to store, use, and share my health information from this study in research databases or registries for future research conducted by NYULMC or its research partners.

_____
Subject/Parent/Guardian Initials

18. Optional permission for collection of surgical sample

If you had surgery on your colon, we may want to collect a sample of the colon tissue that was removed during your surgery. We will only do this if you give us your permission.

☐ Checking this box indicates my permission to collect a sample of tissue from my colon surgery.

_____
Subject/Parent/Guardian Initials

19. Opt out of receiving incidental findings

In the course of testing for genes associated with HSCR through this research study, there is a small chance we may discover something that could be important to your health or medical care. This may or may not be related to HSCR. In this event, we will contact you regarding the preliminary findings to discuss follow-up testing in a clinical genetic testing lab. You do not have to receive this information if you do not wish to.

☐ Checking this box indicates that I do NOT wish to be contacted regarding incidental findings.

_____ Subject/Parent/Guardian Initials

20. Opt out of re-contact

We may contact you regarding future studies about Hirschsprung disease.

☐ Checking this box indicates that I do NOT wish to be re-contacted.

_____
Subject/Parent/Guardian Initials

21. The Institutional Review Board (IRB) and how it protects you

The IRB reviews all human research studies – including this study. The IRB follows Federal Government rules and guidelines designed to protect the rights and welfare of the people taking part in the research studies. The IRB also reviews research to make sure the risks for all studies are as small as possible. The NYU IRB Office number is (212) 263-4110. The NYU School of Medicine's IRB is made up of:

- Doctors, nurses, non-scientists, and people from the Community

22. Who can I call with questions, or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on top of the page 1 of this consent form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Institutional Review Board (IRB) at (212) 263-4110.

A description of this study will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this web site at any time.

When you sign this form, you are agreeing to take part in this research study as described to you. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer.

Name of Subject (Print)	Signature of Subject **(if 18 years or older)**	Date

Name of Person Obtaining Consent (Print)	Signature of Person Obtaining Consent	Date

For adult subjects unable to give consent, the consent for study participation and authorization to collect and use protected health information is given by the following authorized subject representative:

Name of Authorized Subject Representative (Print)	Signature of Authorized Subject Representative	Date

Select the category that best describes the above Authorized Subject Representative:

- ☐ Court-appointed guardian
- ☐ Health care proxy
- ☐ Durable power of attorney
- ☐ Family member/next of kin; for this category describe relationship: _____

Signature of Parent(s)/Guardian for Child

I give my consent for my child to take part in this research study and agree to allow his/her health information to be used and shared as described above.

Name of Parent (Print)	Signature of Parent	Date

Witness to Consent of Non-English Speaking Subjects Using the "Short Form" in Subject's Spoken Language

Statement of Witness
As someone who understands both English and the language spoken by the subject, I represent that the English version of the consent form was presented orally to the subject in the subject's own language, and that the subject was given the opportunity to ask questions.

Name of Witness (Print)	Signature of Witness	Date

Witness to Consent of a Subject Who Cannot Read or Write

Statement of Witness
I represent that the consent form was presented orally to the subject in the subject's own language, that the subject was given the opportunity to ask questions, and that the subject has indicated his/her consent and authorization for participation by (check box that applies).

- ☐ Subject making his/her own "X" above in the subject signature line
- ☐ Subject showed approval for participation in another way; describe:

Name of Witness (Print)	Signature of Witness	Date