Study Title: Functional Studies of Novel Genes Mutated in Primary Ciliary Dyskinesia II: Genotype to Phenotype

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University of North Carolina at Chapel Hill
Consent to Participate in a Research Study
Adult Participants

Consent Form Version Date: 02/27/2023
IRB Study # 20-3465
Title of Study: Functional Studies of Novel Genes Mutated in Primary Ciliary Dyskinesia II: Genotype to Phenotype
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Funding Source and/or Sponsor: NIH

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This is a consent form. It provides a summary of the information the research team will discuss with you. If you decide that you would like to take part in this research study, you would sign and date this form to confirm your decision. If you sign and date this form, you will receive a signed and dated copy of this form for your records.

CONCISE SUMMARY

The purpose of this study is to determine how patients with primary ciliary dyskinesia (PCD) clear mucus differently based on their genetic mutation, and to determine if albuterol can help them clear mucus from their airways better.

Participants will undergo screening with basic physical exam and lung function testing. Participants will then inhale a radiolabeled substance and undergo medical imaging to measure the clearance of mucus in the airways. Albuterol will be administered after lung function testing will be repeated. Finally, imaging will be repeated two more times. The study will be completed in one day and will last about 6 hours.

The major risk of the study is radiation exposure from the inhaled radiolabel substance. The radiation exposure is very small, but radiation history will be collected and if it is more than the safety limits, then you will not be able to participate in the study. The major benefit of the study is to try to understand how patients with PCD clear mucus and if albuterol treatment will help.

You should not join this research study until all of your questions are answered.

If you are interested in learning more about the study, please continue reading below.

What are some general things you should know about research studies?
You are being asked to take part in a research study. To join the study is voluntary.

You may choose not to participate, or you may withdraw your consent to be in the study, for any reason, without penalty.

Things to know before deciding to take part in a research study:

- The main goal of a research study is to learn things to help patients in the future.
- The main goal of regular medical care is to help each patient.
- The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.
- Your medical records may become part of the research record. If that happens, your medical records may be looked at and/or copied by the sponsor of this study and government agencies or other groups associated with the study.

Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill. If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study.

You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?
The purpose of this research study is to compare how patients with primary ciliary dyskinesia with different genetic mutations clear mucus from your lungs differently. It will also test whether albuterol, an inhaled medication, can help clear mucus better.

Are there any reasons you should not be in this study?
You should not be in this study if you:

1. Are pregnant or nursing a child.
2. Take medications in the beta blocker family (labetalol, propranolol, etc.)
3. Smoke or vape tobacco products

How many people will take part in this study?
Approximately 32 people who are 12 years of age or older at this institution will take part in this study.

How long will your part in this study last?
The study visit will last approximately 8 hours. However, you will receive screening and reminder phone calls in the days leading up to the study, and one additional contact after the visit.

How will you be contacted during the study?

In addition to phone calls, the study team would like to communicate with you by text message and e-mail, however, you may say "no" to receiving these messages and still participate in this study. If you say "yes", messages may contain personal information about you and may be sent or received by the study team's personal electronic devices or in a method that is not be able to be encrypted (protected) and there is the risk your information could be shared beyond you and the study team. This information may include study visit reminders and notifications to contact the study team. Communication via text message or e-mail will only be used with adult participants or parent/legal guardian(s) of minors.

If you wish to stop receiving unprotected communication from the study team or have lost access to your device, please notify the study team using the study contact information on the first page of this consent form. After the study is complete and all research activities finished, or you withdraw from the study or request to stop receiving unprotected communication, you will no longer receive un-encrypted (un-protected) messages specific to this study.

_____ **Yes**, I consent to the study team utilizing the following email to send communication.

List Email: _____

_____ **Yes**, I consent to the study team utilizing the following cell phone to send text message communication. List Cell Phone: _____

_____ **No**, I do not consent to receive un-protected communication from the study team.

What will happen if you take part in the study?

Informed Consent: We will explain the study to you. If you decide to participate you will be asked to review, sign, and date the consent and HIPAA authorization forms.

Medical History: Your medical chart will be reviewed and you will be asked questions about your health and Primary Ciliary Dyskinesia including current and past illnesses, and use of medications.

Demographic Information: We will collect information about you including, sex, birthdate and race.

Physical Examination: Your study doctor will listen to your lungs and heart. They will briefly examine nose, mouth and neck for any abnormal signs.

Pregnancy Test: Pregnancy testing is required for participation in this study; all girls and women age 12 and older will be tested for pregnancy. Only those testing negative will be allowed to participate.

Spirometry: This test measures how much air your lungs can hold and how fast you can breathe out. You will take a deep breath and then blow into a mouthpiece as hard as you can and for as long as you can. You might have to wear soft nose clips during the test to stop air from escaping through your nose. You will be asked to repeat this test at least 3 times.

Mucociliary Clearance Scan: This procedure is a scan or image of your lungs to see how mucus is being cleared. We will first place a source of Cobalt 57 in front of your chest for up to 5 minutes to obtain a transmission scan (picture) of your lungs. This scan will identify various regions of your lungs to help the researchers analyze data from all the gamma camera scans. You will then have a background scan of your lungs that lasts 15 minutes. Immediately after this scan you will inhale aerosolized radiolabeled solution that will help us see where mucus goes and how it moves in the lungs and airways. This procedure lasts about 5 minutes. You will then have scans of your lungs during the next 6 hours. You will inhale 4 puffs of albuterol using an inhaler and take another scan (picture) of your lungs to see how it affect mucus moving in lungs and airways. After the 2 hour scan you will perform spirometry (lung function test) and 30 voluntary coughs over the next 30 minutes of scanning.

Pre-Visit Reminders: We will provide reminders before your study visits. We will also remind you about stopping certain medications 12 hours before the study if applicable.

Current Medications: You will be asked about all medications and non-drug therapies you are currently taking.

Medication Restrictions: Please inform your study doctor of any medications and non-drug therapies that you are currently taking. Your study doctor will tell you whether you can continue using a particular medication or non-drug therapy while you are participating in this study. You will be asked not to take the following medications while you are participating in the study:

- Albuterol Inhaler/MDI to be stopped 12 hours before study
- Inhalers which have salmeterol, formoterol or other medicines in the same family to be stopped 12 hours before the study
- Airway Clearance Medications such as Hypertonic Saline or Pulmozyme to be stopped 24 hours before the study.

Explanation of Study Visit			
Procedures		General Screen (phone)	Study Visit
Informed Consent		X	X
Medical History, med review		X	X
Medications		X	X
COVID-19 Screen		X	X
Physical Exam	Complete		X
	Symptom-Directed		X
	Vital Signs		X
Urine Pregnancy Test			x

Spirometry			x
Mucociliary Clearance Measurement			x
Approximate Length of Time		~1 hour	~6 hours

What are the possible benefits from being in this study?

Research is designed to benefit society by gaining new knowledge. You will not benefit personally from being in this research study.

What are the possible risks or discomforts involved from being in this study?

There are some minimal risks related to the procedures used in the study. Some of these procedures you may have had at your regular clinic visits. There may be uncommon or previously unknown risks. You should report any problems to the researcher.

Procedure	Possible Risk Associated with Procedure
Spirometry	There is a small risk of wheezing, shortness of breath and lightheadedness.
Mucociliary Clearance Measurement (Gamma scintigraphy and radiolabeled compound)	The mucociliary clearance scan has radiation exposure risks and is estimated to be 44 mRems. For context, adults in Chapel Hill area receive about 300 mRems per year in natural radiation exposure. More information on radiation risks are below.
Albuterol	Common risks are headache, dizziness, fast heartbeat, sore throat, runny nose Less common risks are change in blood pressure and other cardiovascular changes. There is a rare risk of paradoxical bronchospasm (airway spasms) and anaphylaxis (allergic reaction) that may be life threatening.

Confidentiality:

Being in any research study has the risk of loss of privacy or confidentiality. Below tells you how your information will be protected.

Risks associated with radiation exposure:

This research study involves exposure to radiation from inhaled radiolabeled sulfur colloid for gamma scintigraphy scans. While radiolabeled sulfur colloid is FDA approved for oral and IV administration, its use by inhalation is experimental. There is, however, no significant increased radiation risk for our experimental vs. FDA-approved use. Please note that this radiation exposure is not necessary for your medical care and is for research purposes only. Since radiation can be especially harmful to a developing fetus, it is important that pregnancy be avoided during this study by using effective birth control measures (either hormonal contraceptives, like birth control pills; or a barrier method, like condoms.

The radiation dose you receive will be 44mRems. The risk from the radiation dose received from this procedure is too small to be detected. The radiation exposure described here is what you will get from this research study only. It does not include any exposure you may have received or will receive from other tests outside this study that are a part of your medical care.

The average person in the United States receives a radiation exposure of 0.3 rem (or 300 mRem) per year from natural background sources, such as the sun, and from radioactive materials that are found naturally in the earth's air and soil. The dose that you will receive from participation in this research study (44 mRem) is less than amount you receive from these natural sources in one year (equivalent to 15% of exposure from background radiation in one year).

The amount of radiation you will receive in this study has a minimal risk and is below the dose guideline established by The University of North Carolina Radiation Safety Committee for research subjects. You must inform one of the investigators if you have had any x-rays or other radiation exposure within the past year so that we do not exceed the yearly dose limits. If you wish, Dr. Bennett will provide you with additional information and answer any questions you may have. If desired, additional information can be obtained from Marija Ivanovic, Ph.D, Chairman of the Radiation Safety Subcommittee of UNC Hospitals at 984-974-7779.

What are the risks to a pregnancy or to a nursing child.
The risks to pregnancy or a nursing child are unknown. If you are a woman and are pregnant or nursing a child, you should not be in the study.

If you choose not to be in the study, what other treatment options do you have?
There is no treatment in this study. Your alternative is not to be in this study and continue your normal care.

What if we learn about new findings or information during the study?
You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

The imaging we are using in this research study is not the same quality as imaging that you may have as part of your health care. The images will not be reviewed by a doctor who normally reads such images (such as a radiologist). As a result, you may not be informed of any unexpected findings. The results will not be placed in your medical record. Occasionally the technologist or principal investigator may notice something abnormal on the imaging. If this does occur, the images will be reviewed by a qualified doctor to determine if there is anything of clinical importance. If something is found to be important then you, and/or your primary care provider will be notified. Any further follow up and costs associated with the incidental finding will be your responsibility. There may be benefits to learning such results (such as early detection and treatment of a medical condition), but there are risks as well (such as problems with getting insurance or a job, or feeling worried about a finding for which no treatment is required or appropriate).

Do you wish to be informed in case of clinical/relevant unexpected findings? Please initial in the box below if you do not wish to be notified of clinical/relevant unexpected findings. If you do not initial in

the box, you will be notified of any findings.

_____ I do not wish to be notified.

Will I receive any other clinical results?

Other clinically relevant results of this research will be communicated with you:

- Lung Function testing

How will information about you be protected?

If you take part in this study, we will make every effort to keep your information confidential.

We will store all of your research records in locked cabinets and secure computer files. We will not put your name on any research data. Instead, we will label your information or samples with a study number. The master list that links a person's name to their study number is stored in a locked cabinet or on a secure computer file.

Absolute confidentiality cannot be guaranteed because of the need to give information to these parties. If results of this research are published, we would not use information that identifies you. We would only use your information for research.

These are some reasons that we may need to share the information you give us with others:

- If it's required by law.
- If we think you or someone else could be harmed.
- Sponsors, government agencies or research staffs sometimes look at forms like this and other study records. They do this to make sure the research is done safely and legally. Anyone who reviews study records would keep your information confidential. Agencies or sponsors that may look at study records include:
    - National Institute of Health (NIH)
    - Institutional Review Board (IRB) and others responsible for watching over the safety, effectiveness, and conduct of the research.

Participants will not be identified in any report or publication about this study. We may use de-identified data and/or specimens from this study in future research without additional consent.

What is a Certificate of Confidentiality?

This research is covered by a Certificate of Confidentiality. With this Certificate, the researchers may not disclose or use information, documents or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings in the United States, for example, if there is a court subpoena, unless you have consented for this use.

The Certificate cannot be used to refuse a request for information from personnel of a federal or state agency that is sponsoring the study for auditing or evaluation purposes or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law, such as mandatory reporting requirements for child abuse or neglect, disabled adult abuse or neglect, communicable diseases, injuries caused by suspected criminal violence, cancer diagnosis or

benign brain or central nervous system tumors or other mandatory reporting requirement under applicable law. The Certificate of Confidentiality will not be used if disclosure is for other scientific research, as allowed by federal regulations protecting research subjects or for any purpose you have consented to in this informed consent document.

You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.
You will be asked to sign a separate form ("HIPAA Authorization") to allow researchers to review your medical records.

What will happen if you are injured by this research?
All research involves a chance that something bad might happen to you. If you are hurt, become sick, or develop a reaction from something that was done as part of this study, the researcher will help you get medical care, but the University of North Carolina at Chapel Hill has not set aside funds to pay you for any such injuries, illnesses or reactions, or for the related medical care. Any costs for medical expenses will be billed to you or your insurance company. You may be responsible for any co-payments and your insurance may not cover the costs of study related injuries.

If you think you have been injured from taking part in this study, call the study physician at the phone number provided on this consent form. They will let you know what you should do.

By signing this form, you do not give up your right to seek payment or other rights if you are harmed as a result of being in this study.

What if you want to stop before your part in the study is complete?
You can stop being part of the study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

If you withdraw or are withdrawn from this study all data collected up until the point of withdrawal will be retained, however no additional information will be collected unless you provide additional written permission for further data collection at the time of your withdrawal.

Will you receive anything for being in this study?
You will be receiving $150.00 for taking part in this study. Any payment provided for participation in this study may be subject to applicable tax withholding obligations.

All study payments will be paid through the University of North Carolina Disbursement Services office. Receipt of payment can take up to 4 weeks or longer. Your name, address, and U.S. tax payer identification number (SSN or ITIN) are required to process payments and/or to report taxable income to the IRS. You must complete a W-9 (for U.S. persons) or W-8BEN and the Foreign Vendor Withholding Assessment with supporting documents (for non-resident aliens) in order to receive payment for participation.

U.S. person participants must complete Form W-9 in order to receive payment for participation. If payment by UNC equals or exceeds $600 per calendar year for U.S. persons, UNC will report the amount to the Internal Revenue Service on Form 1099. Nonresident alien participants must complete Form W-8BEN and the Foreign Vendor Withholding Assessment with supporting documents in order to receive payment for participation. Payments to nonresident alien participants may be subject to tax withholding and are generally reported to the Internal Revenue Service on Form 1042-S. This information will not be linked to any of the study data and will only be used for payment purposes.

If you do not provide your SSN or ITIN, or complete the appropriate documentation noted above, we cannot issue you a payment for participation. However, you may still choose to participate in this study.

We will also reimburse you for any travel costs needed for the study such as parking, transportation, and hotel if applicable.

Will it cost you anything to be in this study?
It will not cost you anything to be in this study.

What if you are a UNC student?
You may choose not to be in the study or to stop being in the study before it is over at any time. This will not affect your class standing or grades at UNC-Chapel Hill. You will not be offered or receive any special consideration if you take part in this research.

What if you are a UNC employee?
Taking part in this research is not a part of your University duties and refusing will not affect your job. You will not be offered or receive any special job-related consideration if you take part in this research.

Who is sponsoring this study?
This research is funded by National Institutes of Health (NIH). This means that the research team is being paid by the sponsor for doing the study. The researchers do not, however, have a direct financial interest with the sponsor or in the final results of the study.

What if you have questions about this study?
You have the right to ask, and have answered, any questions you may have about this research. If you have questions about the study (including payments), complaints, concerns, or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.
A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

What if you have questions about your rights as a research participant?
All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

Participant's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

_____
Signature of Research Participant

____/____/____
Date

_____
Printed Name of Research Participant

Researcher's Signature

I have fully explained the research study described by this form. I have answered the participant and/or parents'/guardians' questions and will answer any future questions to the best of my ability. I will tell the family and/or the person taking part in this research of any changes in the procedures or in the possible harms/possible benefits of the study that may affect their health or their willingness to stay in the study.

_____ _____
Printed Name of Person Conducting the Informed Consent Discussion — Position

_____ ____/____/____
Signature of Person Conducting the Informed Consent Discussion — Date