Alpha-1 Carrier Genomics Study

Informed Consent

Date of Document: 5/12/2016

NCT02810327

Medical University of South Carolina
Consent to Be A Research Subject
Alpha-1 Carrier Genomics Study

A. PURPOSE AND BACKGROUND

You are being asked to volunteer for a research study. You have been identified because you previously tested for Alpha-1 antitrypsin deficiency (Alpha-1) in the Alpha-1 Coded Testing (ACT) study and your Alpha-1 genotype was found to be MZ.

The goal of this study is to better understand why some MZ individuals develop chronic obstructive pulmonary disease (COPD) while others do not. This document explains a way that you may choose to participate in a study that will examine portions of the Alpha-1 gene that were not previously tested to determine whether other changes in this gene correlate with development and progression of COPD. Participation is optional and involves responding to questionnaires and performing a finger stick to obtain blood spots using a test kit that is mailed to you. The blood you provide will be used for genetic testing and correlation of results with your COPD history.

This study is being sponsored by the Medical University of South Carolina (MUSC). The investigator in charge of this study is Dr. Charlie Strange at MUSC. This study will enroll 150 individuals. MUSC has received funding from CSL Behring, who makes an augmentation therapy for Alpha-1, to perform this research study. In addition, Dr. Strange has received money in consultation from CSL Behring.

You are additionally invited to donate a blood sample to the MUSC Alpha-1 Biorepository to be used in future research on Alpha-1. This is optional. If you wish to do this a separate consent for you to sign will follow and you will be mailed a blood tube to take to your physician's office and fill.

B. PROCEDURES

If you agree to participate, the following procedures will occur:

1. Consent.

You must sign this consent form in order to participate in the MUSC Alpha-1 Carrier Genomics Study. Once this paper consent form is signed, dated and returned it will be scanned and submitted to the electronic database established for this study. This consent will reside on the computer servers at MUSC. You will be given a signed copy of this consent form to keep. You may withdraw your consent at any time by calling the study coordinator toll free at 1-877-886-2382.

2. Read and fill in the enclosed questionnaires. These questions will ask you about demographic information and your respiratory health. Completing the questionnaires will take approximately

30 minutes.

3. Upon receipt of your consent and completed questionnaires you will be mailed a test kit for the purpose of sticking your finger to provide blood spots that will be used for genetic testing.

4. Obtain your blood sample by following the instructions provided in your test kit. Your kit will contain the instructions and supplies for obtaining drops of blood from your finger, which will be collected on a piece of filter paper.

5. Mail the blood sample in the provided postage paid mailer. The blood will be mailed directly to the Biocerna laboratory that will perform testing for variants in the Alpha-1 gene. Your sample will be associated with a unique barcode and your identity will not be known to the lab. Your barcode will be linked to a study identification number in secure databases at MUSC. Only researchers at MUSC will have access to the personal health information you provide on questionnaires. By submitting this test, you agree to your deidentified blood sample being used for Alpha-1 gene sequencing.

6. Mail results of your recent pulmonary function tests, if these have been performed. These may be sent to:

Dr. Charlie Strange
96 Jonathan Lucas St., 812CSB MSC630
Charleston, SC 29425

C. DURATION

Your participation in the MZ Carrier Genomics Study will conclude when your blood sample results are returned to you, usually within 6 months from the time of sending your blood sample. Data regarding the responses you provide and your genomic findings may be stored in a secured and HIPAA-compliant database indefinitely unless you withdraw your participation. Your right to withdraw your participation in this study is detailed in section J below.

D. RISKS AND DISCOMFORTS

Blood obtained by finger stick involves puncture of the skin with a needle that can cause pain. Very rarely, infections can occur at the site of puncture. Blood obtained by needle stick involves puncture of a vein with a needle. Pain and bruising may occur at the needle site; rarely, infections can occur at the site of puncture.

The risks associated with obtaining a genetic sequencing of the Alpha-1 gene (called *SERPINA1*) include the possibility of identifying previously unknown genetic risks for COPD and the possibility of identifying genetic changes for which the significance is unknown. There is also the possibility that no previously untested genetic variants in your Alpha-1 genes will be detected.

Genetic testing may or may not suggest risk for disease. Testing and results of testing may be

associated with feelings anxiety and uncertainty. Abnormal or uncertain results from genetic tests can cause stress on relationships with family and friends.

Although privacy protection procedures are in place, there is a chance of loss of confidentiality surrounding the test results and/or information you provide. Additionally there is the small risk of loss or unintended receipt of samples and information transmitted by mail. Preaddressed mailing labels are provided and mail is carried by first class US Postal Service Mail only. MUSC cannot guarantee protection of your mailed information; however, it is a federal offense to open someone else's mail.

Because genetic variants are often shared by family members, testing may reveal risks to relatives. Less likely, non-paternity may be discovered should parents or children choose to test for your findings. Non-paternity means that the biological father of an individual is not the person believed to be the father. Your results will be mailed to you only. It is your choice to keep your Alpha-1 results private or to disclose them to family members or medical professionals.

Genetic Research.
Research to identify genes that cause or contribute to a disease or trait is an increasingly important way to try to understand the role of genes in human disease. You have been given this consent form because the Medical University of South Carolina investigators want to include your tissue, cell or blood sample in a research project, or because they want to save such biological samples for future research. There are several things you should know before allowing your tissues, cells or blood to be studied or to be stored.

1. Your tissue, cell or blood sample will be stored under an identifier which could be linked to you. Sometimes these samples are shared for research purposes with other investigators at other research sites. If this is done, the other investigators would not know your name.

2. In addition to your name, other information about you might be connected to your blood or tissue sample. For instance, information about race, ethnicity, sex, your medical history, and so forth might be available to investigators studying your tissue or blood. Such information is important for scientific reasons and sometimes for public health. It is possible that genetic information might come to be associated with your racial or ethnic group.

3. Genetic information about you will often apply (in one degree or another) to family members. It is not generally the University's policy to provide genetic information about you to your family members. However, certain studies, called "pedigree studies", share such information among family members. For this and related research, you will be asked if you are willing to share your genetic information with your family members.

4. You have the right to refuse to allow your tissue or blood to be studied or saved for future research studies. You may withdraw from this study at any time and remove any samples that contain identifiers from research use after the date of your withdrawal. This means that while the CSL Behring Biocerna Lab might retain the deidentified samples-the law often requires this-they

would not be used for research.

5. South Carolina law mandates that your genetic information obtained from any tests or from this research be kept confidential. Our state law prohibits any insurer from using this information in a discriminatory manner against you or any member of your family in issuing or renewing insurance coverage for you or your family. Our state law further prohibits our sharing your genetic information with anyone except in a few narrow circumstances, one of these being a research project of this type, approved by the Institutional Review Board and then we must take all steps to protect your identity. You will still be responsible for paying for health care, however. The Medical University of South Carolina will not be responsible for such costs, even if care is needed for a condition revealed during research or clinical testing.

6. Genetic research raises difficult questions about informing you and other subjects of any results, or of future results. Some people feel anxious about the possibility of having a defective gene that would place them or their children at risk. Some people want to know what is found out about them; others do not. The risks of knowing include anxiety and other psychological distress. The risks of not knowing what is found include not being aware if there is treatment for the problem being studied. But these risks can change depending on whether there is a treatment or cure for a particular disease, and on how clear the results are. If there is a medical reason to seek specific information from you, your doctor will tell you this. A process called "genetic counseling" is often appropriate in such cases; you should ask your doctor or nurse about this if you have any questions.

Investigators in this study may try to recontact you in the future to find out about your health. If you are recontacted and want to know what the investigators have learned about your samples, you should understand that the following are the kinds of things the investigators or your health team might tell you:

a) Information is too sketchy to give you particular details, but you may access overall results of this study as they are published.
b) You carry a gene for a particular disease that can be treated.
c) You can carry a gene for a particular disease for which there is no current treatment. This news might cause severe anxiety or other psychological distress, depending on the severity of the disease.
d) You carry a gene for a disease and might consider informing relatives that they, too, might carry the gene. It can be very difficult to decide whether to share such information with relatives. Genetic counselors can help sort out the various options in such a case.
e) You carry a gene variant called a variant of uncertain significance (VUS). This means that it is not known whether your variant is related to disease or not. This type of uncertain information might cause anxiety over not knowing whether your finding is problematic or actionable. This may complicate family discussions, as other relatives may carry the same VUS.

Also, for any future research, we may contact you with a new consent form giving you additional information.

7. If you are concerned about a potential genetic disorder, you and your doctor might choose to test specifically for it. This would require additional blood or tissue samples and would not be part of this research project. You should discuss this option with your doctor or genetic counselor.

8. The presence of a genetic marker does not necessarily mean that an individual will develop a disease. Informing people of all such markers independently of medical need can cause unnecessary anxiety. On the other hand, the absence of a marker does not mean that someone will not get the disease. Genetic diseases appear as a result of a complex mixture of hereditary, environmental, behavioral and other factors. 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.

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, nor does it protect you against genetic discrimination by all employers.

These are the best-known risks and challenges of genetic research. There might be other risks we do not know about yet. It is important that you talk to your doctor, nurse or genetic counselor if you have questions or concerns about the research study.

E. POSSIBLE BENEFITS

You will obtain a detailed Alpha-1 gene sequencing blood test that is able to detect subtle Alpha-1 variants not detected by routine testing. Your results may provide more insight about your genetic risk for COPD.

The test results will be returned only to you. Since you will be the only person that knows the result of your test, you can decide if you wish others to know this information.

The results of this study will support future understanding of the role of genomic variants in Alpha-1 and COPD susceptibility. Such results will help improve testing recommendations, risk reduction strategies and treatment options for people at risk for Alpha-1 related COPD. Your participation may indirectly improve the care and support of Alpha-1 patients. You may obtain further information about Alpha-1 through this trial.

F. COSTS
There are no costs associated with this study; the test kit and results are free.

G. PAYMENT TO PARTICIPANTS
You will receive no compensation for participating in this trial.

H. ALTERNATIVES
You may have your physician send your blood to the laboratory used in this study or to a different laboratory for Alpha-1 gene sequencing or elect to not to have further genetic testing related to Alpha-1.

I. CONFIDENTIALITY
There is a risk of loss of confidentiality in this study. Although many steps are taken to protect confidentiality we cannot guarantee that your identity will not become known to others. You will be assigned a study number and your personally identifying information will not be disclosed. You will not be personally identified in results of research conducted on your sample.

Potential breaches in the computer system will be reported to all participants. Although every reasonable effort will be made to keep your identifying information confidential, there can be no guarantees that errors in protecting this information will not be made. If it became known that you have Alpha-1 or other disease, there may be risks to you related to your employment, health, or life insurance. Contact the Alpha-1 Research team with questions. Finally, you should understand that the investigator is not prevented from taking steps, including reporting to authorities, to prevent serious harm to yourself or others.

J. RIGHT OF WITHDRAWAL
You have the option to withdraw your consent and cease participation at any time for any reason. Should you change your mind and wish to withdraw from the study, you will be free to do so without having to provide any explanation. If you choose to withdraw from the study, data you provided will be removed from the secure study database and any remaining sample destroyed. Any research that may have already occurred using your sample and/or data determined by testing or analysis prior to your withdrawal cannot be undone. While your study data will be deleted upon withdrawal, the CSL Behring Biocerna Lab might retain deidentified genomic findings from your sample if testing was already performed, as this is often required by law. While such findings cannot be unknown, they will not be used for research.

You may withdraw by written request mailed to the Alpha-1 Carrier Genomics Study at 96 Jonathan Lucas St. CSB 812 MSC 630 Charleston, SC 296425.

K. MUSC STATEMENTS
Results of this research will be used for the purposes described in this study. This information may be published, but you will not be identified. Information that is obtained concerning this research that can be identified with you will remain confidential to the extent possible within State and Federal law. The investigators associated with this study, the sponsor, and the MUSC

Institutional Review Board for Human Research will have access to identifying information. All records in South Carolina are subject to subpoena by a court of law.

In the event that you are injured as a result of participation in this study, you should immediately go to the emergency room of the Medical University Hospital, or in case of an emergency go to the nearest hospital, and tell the physician on call that you are in a research study. They will call your study doctor who will make arrangements for your treatment. If the study sponsor does not pay for your treatment, the Medical University Hospital and the physicians who render treatment to you will bill your insurance company. If your insurance company denies coverage or insurance is not available, you will be responsible for payment for all services rendered to you.

Your participation in this study is voluntary. You may refuse to take part in or stop taking part in this study at any time. You should call the investigator in charge of this study if you decide to do this. Your decision not to take part in the study will not affect your current or future medical care or any benefits to which you are entitled.

The investigators and/or the sponsor may stop your participation in this study at any time if they decide it is in your best interest. They may also do this if you do not follow the investigator's instructions.

Volunteers Statement

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. If I have any more questions about my participation in this study or study related injury, I may contact Charlie Strange, MD at 843-792-3174. I may contact the Medical University of SC Hospital Medical Director (843) 792-9537 concerning medical treatment.

If I have any questions, problems, or concerns, desire further information or wish to offer input, I may contact the Medical University of SC Institutional Review Board for Human Research IRB Manager or the Office of Research Integrity Director at (843) 792-4148. This includes any questions about my rights as a research subject in this study.

I agree to participate in this study. I have been given a copy of this form for my own records.
If you wish to participate, you should sign below.

_____	_____	_____	_____
Signature of Person Obtaining Consent	Date	Signature of Participant	Date

I am interested in donating a tube of my blood to MUSC Alpha-1 Biorepository to be stored for use in future Alpha-1 related research. If yes, a separate consent with additional information and instructions will follow.

____Yes ____ No