Title: A Prospective Natural History Study of Smoking, Immune Cell Profiles, Epigenetics and COVID-19

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PRINCIPAL INVESTIGATOR: Stavros Garantziotis, MD

STUDY TITLE: (20-E-0108) A Prospective Natural History Study of Smoking, Immune Cell Profiles, Epigenetics and COVID-19

STUDY SITE: National Institute of Environmental Health Sciences

Cohort: Healthy Adult Volunteer

Consent Version: *07/15/2022*

WHO DO YOU CONTACT ABOUT THIS STUDY?

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KEY INFORMATION ABOUT THIS RESEARCH

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). This section provides the information we believe is most helpful and important to you in making your decision about participating in this study. Additional information that may help you decide can be found in other sections of the document. Taking part in research at the NIH is your choice.

We are asking smokers and non-smokers to participate in this research study. We are studying the effect of COVID-19 on the body's immune system, specifically T-Cells found in human blood. This will help us to better understand how COVID-19 affects smokers' and non-smokers' immune systems before and after being infected with the virus.

You may be eligible to participate if you are a healthy, adult volunteer who is currently a smoker or non-smoker. We will call you and ask you questions about your medical history including COVID-19 vaccination status and dates, smoking status and if you have any COVID-19 symptoms.

You will come to the Clinical Research Unit (CRU) to be tested for COVID-19. If you test positive for COVID-19 antibodies or virus during your first visit, then you no longer qualify for the study. If you test negative for COVID-19 antibodies and virus during your first visit, you will be asked to return for follow-up visits to the CRU to be tested for COVID-19 monthly, for up to 6 months or until you test positively for COVID-19. Once you test positively you will be asked to complete a final visit before you complete the study. Even if you never test positive for COVID-19 you will be able to complete a final visit and therefore complete the study if you

follow all required visits. You will be asked to provide blood, nasal swabs, cheek swabs, saliva, and answer questions about your medical history and smoking status.

If you receive the COVID-19 vaccine prior to screening you will still be eligible to enroll, but you will only need to complete one COVID-19 Antibody Screening Visit before being scheduled for the final visit. If you inform us that you were vaccinated during one of your COVID-19 Antibody Screening Visits, then your next visit will be a final visit. The tests used in this study will detect COVID-19 infection antibodies and antibodies produced from SARS-CoV-2 vaccination(s).If you have not completed vaccination by your final visit, we will follow up with you on your vaccination status. Once you are vaccinated, we will ask to schedule you for a repeat final visit.

You will be compensated for your time and effort. Compensation will be based on the number of completed visits and provided samples.

Risks associated with participation in this study are minimal and may include:

- Blood Draw: Mild discomfort when we draw a blood sample.
- Saliva: No known risks.
- Nasal Swab: discomfort and minor nosebleed
- Cheek Swab: No known risks
- Questionnaires: minor risk of breach of confidentiality

You will not benefit from being in this study.

The remaining document will now describe the research study in more detail. This information should be considered before you make your choice. Members of the study team will talk with you about the information in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take all the time you need to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

This is a research study. The purpose of this research study is an immediate response to the newly emerged corona virus disease 2019 (COVID-19) as it is critical to gain a rapid understanding of

the disease. This study will explore the effects of COVID-19 on the body's immune system in relationship to smoking status.

We are asking you to join this research study because you are a healthy, adult volunteer who is a smoker or non-smoker who may potentially contract COVID-19.

WHAT WILL HAPPEN DURING THE STUDY?

If you decide to take part in this study, you will be asked to schedule several visits to take place at the Clinical Research Unit (CRU) for blood draws, nasal and cheek swabs, saliva collection, and you will be asked questions about your medical history and smoking status.

Screening Pre COVID-19 Visit: The first visit is the Screening Pre COVID-19 visit. This visit will last approximately 2 hours and consists of a **blood draw** of up to 120 milliliters (mL), this is about 8 tablespoons. The blood will be collected by putting a needle into a vein in your arm. The blood samples will be used for scientific testing, clinical labs and to determine study eligibility. Some of the clinical labs done on your blood will include nicotine/cotinine to screen for current smoking or exposure to second-hand smoke. We will also test for presence of antibodies for COVID-19, cytomegalovirus, and herpes virus. In addition, we will collect **nasal and cheek** swabs, and have you produce a **saliva sample** in a provided container. We will also ask you about your medical history, including vaccination status and dates, medications you are currently taking, and about your smoking status as part of a **medical screening.** If you have already received the COVID-19 vaccination at entry into the study, then you will only be required to complete a Screening Pre-COVID-19 Visit, one COVID-19 Antibody Screening Visit and the Final visit.

COVID-19 Antibody Screening Visit(s): After completing your Screening Pre COVID-19 Visit, you will be asked to return to the CRU monthly for a COVID-19 Antibody Screening Visit. The COVID-19 Antibody Screening Visits will be scheduled monthly up to 4 times or until you have a positive COVID-19 antibody, other test result or receive a COVID-19 vaccination, whichever occurs first, then you will be scheduled for your final visit. Each COVID-19 Antibody Screening Visit is approximately 45 minutes and consists of a **blood draw** of up to 15 milliliters (mL) of blood, this is about 3 teaspoons, **a nasal swab, a cheek swab and a saliva sample**. The samples will be used for clinical labs to test for COVID-19.

Final Visit: The last visit we will schedule you for is the Final Visit. This visit will last approximately 1 hour and 15 minutes and consists of a **blood draw** of up to 120 milliliters (mL), this is about 8 tablespoons. The blood samples will be used to repeat the same scientific testing and clinical labs as the Screening Pre-COVID-19 Visit. Some of the clinical labs done on your blood will include nicotine/cotinine to screen for current smoking or exposure to second-hand smoke. We will also test for presence of antibodies for COVID-19, cytomegalovirus, and herpes virus. In addition, we will collect **nasal and cheek swabs**, and have you produce a **saliva sample** in a provided container. We will also ask you about your medical history including COVID-19 vaccination status, medications you are currently taking, and about your smoking status as part of a **medical screening.** If you complete the study before you receive a COVID-19 vaccination, we may ask if you are willing to repeat the Final visit once you are vaccinated.

For the safety of you and our staff, if at any time you are sick and test positive for a COVID-19 infection prior to your **COVID-19 Antibody Screening visit** or **Final visit**, you will be rescheduled 14 days or more after you no longer have symptoms. If you become sick and test

positive for a COVID-19 infection prior to your **Screening Pre COVID-19 Visit** you will no longer be eligible to participate.

HOW LONG WILL THE STUDY TAKE?

If you agree to take part in this study, your involvement is expected to last up to 6 months. The study will involve up to 7 monthly visits: The Screening Pre-COVID-19 visit will take up to 2 hours, each Antibody screening visit will last approximately 45 minutes and the Final Visit with take approximately an hour and 15 minutes.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

We plan to have approximately 200 people participate in this study at the CRU. We expect that some people may not qualify, and some may drop out early. We are hoping that at least 90 people will complete the entire study.

WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN THE STUDY?

You may experience a small amount of discomfort or slight pain, like a pinch, upon needle insertion during the blood draw. After blood is collected, you may develop a small bruise at the site where the needle was inserted. There is minimal risk of infection, fainting, or vomiting.

There are no known risks associated with saliva collection. The risks and discomforts of nasal swab collection include slight discomfort and a possibility of minor nosebleed.

There are no known risks for cheek swab collection

There is a risk of potential breach of confidentiality of data collected on this study such as questionnaires, medical and health-related information. To minimize this risk, the electronic data is entered into a password protected database and any paper documents are kept in a locked room that only authorized study staff have access to.

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

You will not benefit from being in this study.

Are there any potential benefits to others that might result from the study?

In the future, other people might benefit from the knowledge gained during this study. This information may help to better understand COVID-19 and what makes certain people more susceptible to it.

WHAT OTHER OPTIONS ARE THERE FOR YOU?

We want you to understand that you can choose not to participate in the study instead of being in this study.

DISCUSSION OF FINDINGS

New information about the study

If we find out any new information that may affect your choice to participate in this study, we will get in touch with you to explain what we have learned. This may be information we have learned while doing this study here at the NIH or information we have learned from other scientists doing similar research in other places.

Return of research results

SARS-CoV-2 antibody test results and the COVID-19 infection test results will be made available to you. You will be able to login to a secure website to view your test results. These tests are the same as those that your doctor may order. These tests we are using in this study are experimental use tests (investigational tests) and have not been approved by the FDA. The FDA has allowed these tests to be used under its Emergency Use Authorization. We will provide an information sheet about these tests so you can better interpret the test results, and better understand the tests' Emergency Use Authorization status.

If the COVID-19 infection test results are positive for an infection, a member of the study staff will directly contact you, so you can contact your local medical provider. The study staff is also required to report your name to the North Carolina Department of Health and Human Services.

EARLY WITHDRAWAL FROM THE STUDY

Taking part in this study is completely voluntary. If you choose to take part, you have the right to stop at any time, for any reason, with no consequence to you. You will not lose any benefits or medical care to which you are entitled. To withdraw, you should contact the study staff at the NIEHS CRU at 919-541-9899. If you discontinue participation, your study paperwork will be confidentially archived in a password-protected database and a locked, dedicated study cabinet accessible only by authorized study staff. If you are enrolled in the study but decide to not participate further, samples collected from you may still be used in future experiments.

Unless you tell the study doctor or research staff that you do not wish to be contacted again, you may possibly be contacted in the future by the study staff and asked if you wish to take part in another study.

The study doctor may decide to stop your participation without your approval if the study doctor thinks that being in the study may cause you harm or for not completing your study visits or study assessments.

STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

Will your specimens or data be saved for use in other research studies?

As part of this study, we are obtaining specimens and data from you. We will remove all the identifiers, such as your name, date of birth, address, or medical record number and label your specimens and data with a code so that you cannot easily be identified. However, the code will be linked through a key to information that can identify you. We plan to store and use these specimens and data for studies other than the ones described in this consent form that are going on right now, as well as studies that may be conducted in the future. These studies may provide additional information that will be helpful in understanding C*OVID-19*, or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to the development of a commercial product by the NIH and/or its research or commercial partners. There are no plans to provide financial compensation to you if this happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you.

I give permission for my coded specimens and data to be stored and used for future research as described above.

_____ Yes _____ No

Initials Initials

Will your specimens or data be shared for use in other research studies?

We may share your coded specimens and data with other researchers. If we do, while we will maintain the code key, we will not share it, so the other researchers will not be able to identify you. They may be doing research in areas that are similar to this study or in other unrelated areas. These researchers may be at NIH, other research centers and institutions, or commercial entities.

I give permission for my coded specimens and data to be shared with other researchers and used by these researchers for future research as described above.

_____ Yes _____ No

Initials Initials

If you change your mind and do not want us to store and use your specimens and data for future research, you should contact the research team member identified at the top of this document. We will do our best to comply with your request but cannot guarantee that we will always be able to destroy your specimens and data. For example, if some research with your specimens and data has already been completed, the information from that research may still be used. Also, for example, if the specimens and data have been shared already with other researchers, it might not be possible to withdraw them.

In addition to the planned use and sharing described above, we might remove all identifiers and codes from your specimens and data and use or share them with other researchers for future research at the NIH or other places. When we or the other researchers access your anonymized data, there will be no way to link the specimens or data back to you. We will not contact you to ask your permission or otherwise inform you before we do this. We might do this even if you answered "no" to the above questions. If we do this, we would not be able to remove your specimens or data to prevent their use in future research studies, even if you asked, because we will not be able to tell which are your specimens or data.

NIH policies require that your clinical and other study data be placed in an internal NIH database that is accessible to other NIH researchers for future research. Usually, these researchers will not have access to any of your identifiers, such as your name, date of birth, address, or medical record number; and your data will be labeled with only a code. We cannot offer you a choice of whether your data to be placed in this database or not. If you do not wish to have your data placed in this database, you should not enroll in this study.

How long will your specimens and data be stored by the NIH?

Your specimens and data may be stored by the NIH indefinitely.

Risks of storage and sharing of specimens and data

When we store your specimens and data, we take precautions to protect your information from others that should not have access to it. When we share your specimens and data, we will do everything we can to protect your identity, for example, when appropriate, we remove information that can identify you. Even with the safeguards we put in place, we cannot guarantee that your identity will never become known or someone may gain unauthorized access to your information. New methods may be created in the future that could make it possible to re-identify your specimens and data.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will be compensated for your time and effort. Compensation will be based on the number of completed visits and provided samples.

- For the Screening Pre COVID-19 Visit and Final Visit, you will be compensated $35 for blood collection, $40 for nasal swab collection, $10 for cheek swab collection and $15 for saliva collection procedures.
- For the COVID-19 Antibody Screening Visits (up to 4 visits), you will be compensated $35 for blood collection procedure, $40 for nasal swab collection, $10 for cheek swab collection and $15 for saliva collection procedures.
- You may be invited to repeat the final visit if you completed the study before you received the COVID-19 vaccination. The compensation will be the same as listed for the final visit and based on the procedures you complete for a total up to $100.

If you are eligible to complete all study visits and procedures, you will receive a total of up to $800, including an additional $100 completion bonus.

VISITS	PROCEDURES	COMPENSATION
Screening Pre COVID-19 Visit	Blood	$35
	Saliva	$15
	Nasal swab	$40
	Cheek swab	$10
	Total	$100
COVID-19 Antibody Screening Visit (Repeatable **up to 4 times** until results are positive)	Blood	$35
	Saliva	$15
	Nasal swab	$40
	Cheek swab	$10
	Total	$100

Final Visit (this visit may be repeated for participants that complete the study before they received the COVID-19 vaccination)	Blood	$35
	Saliva	$15
	Nasal Swab	$40
	Cheek Swab	$10
	Total	$100
Bonus at conclusion of study after completion of Final Visit		$100
Total study compensation		Up to $800

Participants who are unable to complete reimbursable procedures at any visit will be compensated $25 for their time and effort. Payments will be made after each visit at which reimbursable procedures are completed.

If you are unable to finish the study, you will receive compensation as listed in the table above for the parts you completed.

With few exceptions, study compensation is considered taxable income that is reportable to the Internal Revenue Service (IRS). A "Form 1099-Other Income" will be sent to you if your total payments for research participation are $600 or more in a calendar year. If you have unpaid debt to the federal government, please be aware that some or all of your compensation may be automatically reduced to repay that debt on your behalf.

Will you receive reimbursement or direct payment by NIH as part of your participation?

Some NIH studies offer reimbursement or payment for travel, lodging or meals while participating in the research. The amount, if any, is guided by NIH policies and guidelines.

This study generally does not offer reimbursement for, or payment of, travel, lodging or meals. However, if you have traveled to the CRU from your home over 50 miles, one way, you will receive compensation at the government rate for your trip. Parking is provided free of charge.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIEHS Clinical Research Unit.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

A description of this clinical trial 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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

NIH and NIEHS are committed to protecting the confidentiality of study participants. Research records are maintained at the NIH Clinical Center and the NIEHS Clinical Research Unit stored in computer systems and on NIH and NIEHS servers, which are secured with dual authentication access measures, limiting access overall, and other IT security and privacy protections as additional security and privacy precautions. The information is used for research by NIH scientists, some of whom may have no personal contact with you. Much of the information will eventually be used in publications, but your identity will not be revealed.

When NIH and NIEHS studies offer compensation for participation in research, the participant's social security number (SSN) is usually collected for the purpose of providing compensation and may be used for research authentication. Should you choose not to provide your SSN, you may be able to participate in the study, but you would not receive any eligible compensation. Please note that when sharing your SSN, you should not provide your SSN via unsecure methods (regular, unencrypted, email is an unsecure method) – it is best to provide your SSN in person or to a known person via telephone.

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance that, despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.

In most cases, the NIH will not release any identifiable information collected about you without your written permission. However, your information may be shared as described in the section of this document on sharing of specimens and data, and as further outlined in the following sections.

Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.

NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.

The Certificate does not protect your information when it:

1. is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
2. is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
3. is for other research;
4. is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.

The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.

Privacy Act

The Federal Privacy Act generally protects the confidentiality of your NIH medical information that we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

POLICY REGARDING RESEARCH-RELATED INJURIES

The NIEHS will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIEHS, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

A Declaration under the Public Readiness and Emergency Preparedness (PREP) Act was issued by the Secretary of the United States Department of Health and Human Services on March 10, 2020. This Declaration limits the legal rights of a subject participating in clinical studies utilizing COVID-19 countermeasures. Because this study is covered by the PREP Act Declaration, covered persons, such as the manufacturers, study sponsor, researchers, healthcare providers and others have liability immunity (that is, they cannot be sued by you or your family under the laws of the United States).

If you believe that you may have been harmed as a result of this research study, certain claims for serious injury or death caused by the countermeasure may be eligible for compensation through the Countermeasures Injury Compensation Program. This is a program set up by the United States Government.

Information about this program can be found at https://www.hrsa.gov/cicp/about/index.html or by calling 1-855-266-2427.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Stavros Garantziotis, MD, garantziotis@niehs.nih.gov, 984-287-4412. You may also call the NIEHS Office of Human Research Compliance at 919-541-4265 or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness to the oral short-form consent process only:

Witness:

Signature of Witness*	Print Name of Witness	Date

***NIH ADMINISTRATIVE SECTION TO BE COMPLETED REGARDING THE USE OF AN INTERPRETER:**

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent and served as a witness. The investigator obtaining consent may not also serve as the witness.

____ An interpreter, or other individual, who speaks English and the participant's preferred language facilitated the administration of informed consent but did not serve as a witness. The name or ID code of the person providing interpretive support is: _____.