### Project Title

Contagious Phenotypes of Acute Respiratory Infection: Identification, Characterization, and Biomarkers {Characterizing And Tracking College Health (CATCH)-- the Virus Study}

### Purpose of the Study

This research is being conducted by Donald Milton, MD, DrPH and a team of researchers at the University of Maryland with funding from the U.S. Defense Advanced Research Projects Agency. We are inviting you to participate in this part of the research project because you are a college student living in certain residence halls or enrolled in a particular Living Learning Community and you have either recently developed symptoms of an Acute Respiratory Infection (ARI) or have developed an ARI while being followed as a close contact. The purpose of this research project is to identify biomarkers (measurable substances within a person) that can indicate which individuals, when exposed to viruses and bacteria that cause Acute Respiratory Infections (ARI), are likely to become contagious and spread the ARI to others, and to improve our understanding of how ARI are transmitted so that we may better prepare to mitigate or prevent epidemics and pandemics of influenza and other ARIs.

### Procedures

**IN-DEPTH CASE ASSESSMENT**

If you have cold or flu symptoms and were selected for additional testing or you have a positive virus test through contact testing in our laboratory, are at least 18 years old, and you agree to participate in this part of the study, we invite you to come to our case evaluation lab in the School of Public Health (Room 0117) for up to two visits and to complete an online survey once or twice.

If you are being enrolled because you developed an ARI while being followed as a contact, we will measure and record your oral temperature using a standard thermometer, and we will ask you to complete a set of standard respiratory infection symptom questions and a brief questionnaire, which contains questions about health care visits for evaluation of your symptoms, recent use of cold and flu medications, and use of the phone app.

No matter how you got to enroll in this part of the study, unless you answered the baseline questionnaire today, we will you about recent exposures, stress, sleep, exercise, smoking, and alcohol intake. We will also ask about your class attendance and time spent in various campus locations over the past 24 hours, and will ask you to characterize your contact with up to 4 close contacts during that time period who are in the
group we wish to study. We will provide you with contact recruitment flyers that you can give your contacts to encourage them to enroll in the study, if you would like to do that.

In addition, if you haven’t already done so, we will ask you to download and use a cell phone app (separate consent required) that tracks your location and the amount of time that 2 or more users spend together. This app will help to assess and measure the exposure between you and your contacts.

We will then collect samples from you, including a swab of your cell phone to look for infectious agents. A professional study staff member (physician, nurse, professional medical technician or highly trained graduate student) or an undergraduate research assistant under physician supervision will collect 2 nasal swabs by using a sterile soft-tipped stick (similar to a large Q-tip) to swab the nostrils, just inside the opening of your nose. We will collect 2 throat swabs by using a tongue depressor and swabbing the back of your throat. One set of nose and throat swabs will be combined and tested for a wide variety of respiratory infectious agents within 24 hours to confirm that you have an infection. The other set will be saved for a later more detailed analysis of the infectious agents, microbiome (the microbes that typically live at the entrances to your respiratory tract), and biomarkers of infection, susceptibility, and contagiousness. We will then ask you to sit in a booth with clean, filtered air and breathe into a large funnel or cone, which is part of an apparatus that collects particles in your exhaled breath, coughs, and sneezes. You will sit in the booth for 30 minutes, and during this time you will be asked periodically to talk or recite the alphabet (three times). We will also count the number of times you cough and sneeze while providing the exhaled breath sample, either by direct observation or by asking you to wear a microphone so that we can count your coughs and sneezes later. We estimate the entire visit (including answering questions, swabbing your phone, nose, and throat, and sitting in the booth) will take 45-60 minutes. If the breath collector is not available, you will have a shorter visit but receive the same compensation.

At the end of your in-depth case visit we may ask you to temporarily attach a portable CO2 monitor to your backpack and carry it with you wherever you go for the next week to help us measure and understand your environmental exposures. If you want to stop carrying the monitor before a week is over, you can return it early; we will retain the data collected unless you specifically request it to be deleted. In the event that you think you have lost the monitor, please notify us; you will not be charged, but can earn compensation if the monitor turns up and you
On the day after your visit we will ask you to complete a short questionnaire (which can be done as an online survey from a smartphone or computer) updating your symptoms, medication use, class attendance and location data, and close contacts over the past 24 hours. If any new contacts are identified that are not enrolled in the study AND your contacts are eligible, we may ask you to give your contacts a recruitment flyer. We estimate the questionnaire or survey will take about 5-10 minutes.

**IF** we confirm that you are infected with one of several respiratory infectious agents we are studying (e.g. influenza virus) by analysis of the swabs we collect from you, we will also ask you to return to our lab in SPH for a short case follow-up visit approximately 1 week after your in-depth case visit. At this follow-up visit, you will be asked to complete a questionnaire to update your symptoms, related medications, healthcare visits, and course of illness. Your oral temperature will be measured and recorded, and you will be instructed and assisted by trained study personnel to obtain a self-collected nasal swab from each nostril: you will be guided to carefully insert a small, soft, sterile swab that is made specifically for this procedure into your nostril until the stopper along the swab shaft is just outside the opening of the nose, and to rotate the swab several times to collect a sample from inside your nostril. You will then be asked to place the swab into a collection tube, and to repeat the process for the other nostril. We estimate this follow-up visit will take about 10-15 minutes.

**IF** we do not detect one of the specific respiratory infectious agents we are targeting in the swabs collected at your in-depth visit, we will cancel your 1-week follow-up visit and will instead ask you to complete the same questionnaire as an on-line survey to update your symptoms, medications, healthcare visits, and course of illness.

**PLEASE NOTE:** Your test results may be reported anonymously on our study website to update a summary of the numbers and types of infections detected in the study group. Many of the infectious agents we are testing for do not typically require treatment with prescription medication. We will notify you if you have an infection that should be treated and refer you to a healthcare provider. Otherwise, if you are curious to know what kind of virus we found in your swabs, you are free to call us and talk with one of the senior clinical research staff. If we do not confirm the presence of one of the targeted respiratory pathogens in the swabs we collect at your first visit, you will not be eligible to
complete the follow-up visit or receive compensation for recruiting your contacts.

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| Your participation in this portion of the study will take time away from other activities or time you may have spent resting and recuperating from your illness; we will try to keep each visit as short as possible and minimize wait times through efficient scheduling of appointments. You may not feel well while participating in this part of the study due to symptoms of your illness, but participation should not exacerbate your symptoms any more than a visit to a health care provider. You may feel some embarrassment when providing information about your recent illness, medical history, and habits, but this will be minimized by collecting the information in a private setting on a computer or tablet and should be no greater than experienced during a doctor visit. There is a small risk to your privacy and confidentiality, as we will be collecting a variety of personal information from you; we will do our best to keep your personal information confidential and limit access to only essential study personnel. All data will be transmitted between the tablet or computer used to enter the data and the server via encrypted connections and the server will be housed in a secure data.

You may experience some mild pressure or discomfort, a tickling or gagging sensation, or occasional eye watering or sneezing when the nose and throat swabs are collected. In rare instances, swabbing inside the nose may cause very minor bleeding. There is no known risk from breathing warm, humidified HEPA (High Efficiency Particulate Arresting -- removes ≥99.94% of particles in the air) filtered air, but you may feel uncomfortable sitting in the booth with your face at the entrance to the large funnel used to collect your exhaled breath, particularly if you suffer from claustrophobia. You may wear headphones and listen to your own entertainment during the session. If you are selected and agree to carry a portable CO₂ monitor, this will add a small amount of extra weight (approximately 10 ounces) and may be slightly inconvenient, but poses no other risk.

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| There is a potential benefit to you that through your participation in this part of the study, we may be able to identify the respiratory pathogen responsible for your symptoms or illness. Although most of the pathogens that cause ARI do not require specific treatment (such as the viruses that cause common colds) and it would of no benefit to know which one you have, you may benefit from early detection of certain infections such as influenza or strep throat, as this may give you the chance to seek early medical treatment from a healthcare provider, if...
appropriate.

We hope that, in the future, other people might benefit from this study through improved understanding of how acute respiratory infections spread and identification of biomarkers that can predict contagiousness, in order to limit the spread of respiratory infections like influenza.

**Confidentiality**

Potential loss of confidentiality will be minimized by storing all data in an encrypted database maintained on a secure server housed in a high security data center. Only essential study personnel will have access to this data. Access to data elements will also be controlled so that only staff with an operational need for particular information will have access to sensitive information (for example social security numbers), and undergraduate research assistants will only have access to the clinical research database while working in the clinic under senior staff supervision.

If you are eligible, we will seek to enroll your closest contacts and follow them to see if they develop an acute respiratory infection, and it may become obvious to those contacts that you are the case who referred them to the study, even if you do not tell them yourself (for example by giving them a recruiting flyer). We will not voluntarily disclose who you are, but may not be able to prevent disclosure. If one of your contacts develops an infection, we will not tell them what you have or tell you what they have. There are many viruses circulating at the same time and you may have different things. However, if you ask, we will tell you what we found in your own swab. It is up to you whether you want to share that information. Unless disclosure is required by law that requires reporting certain illnesses to the State of Maryland as described below, we will not disclose personally identifiable information about who was infected with what to anyone outside of the research team.

If you decide to participate in the study, you will be assigned a subject ID number which will be used to access your records in the database. All biologic samples will be labeled with a unique sample ID that can only be linked to your subject ID number by Dr. Milton and his designated research staff.

Collaborators within and outside the University of Maryland may conduct analyses on samples or data for research purposes, but all such samples or data will always be de-identified. If we write a report or article about this research project or post information on the study website, your identity will be protected to the maximum extent possible. Your information may be shared with representatives of the University of Maryland, College Park or governmental authorities if you or
someone else is in danger or if we are required to do so by law.

The Code of Maryland Regulations (COMAR) 10.06.01.03 C, requires reporting to the Maryland Department of Health and Mental Hygiene of certain illness including personally identifiable information in the event of “any grouping or clustering of patients having similar disease, symptoms, or syndromes that may indicate the presence of a disease outbreak,” that poses a danger to public health. It also requires reporting of cases of Measles, Mumps, Pertussis and Legionellosis, which will be tested for in samples that we collect. Measles is a highly contagious virus that causes respiratory infection and rash, and Mumps is a somewhat less contagious viral illness that typically causes swollen tender salivary glands. Pertussis, also known as whooping cough, is a highly contagious bacterial respiratory infection, and Legionellosis is a bacterial infection that can cause pneumonia or flu-like illness. Measles, Mumps, and Pertussis can all be prevented through proper vaccination.

Any unanticipated problems involving risks to participants or others such as unexpected or serious adverse events, non-compliance, audits, and investigation reports will be promptly reported to the University of Maryland Institutional Review Board, as well as both the U.S. Department of the Navy and Space and Naval Warfare Systems Center Pacific Human Research Protection Programs.

| Medical Treatment | The University of Maryland does not provide any medical, hospitalization or other insurance for participants in this research study, nor will the University of Maryland provide any medical treatment or compensation for any injury sustained as a result of participation in this research study, except as required by law. |
| Compensation | IN-DEPTH CASE ASSESSMENT |
| | You have the potential to earn up to $90, IF you are eligible for and complete both visits and a follow-up questionnaire/survey on time (see details below): |
| | ● You will receive up to $60 for completing the in-depth case visit (this includes a $10 bonus for being on-time to your appointment). |
| | ● You will receive $10 if you complete the follow-up online survey within 24-36 hours of your in-depth case visit. |
| | ● You will receive $20 (includes a $10 on-time bonus) for completing the 1 week follow-up visit within 6-8 days of your in- |
depth case visit, IF eligible because your swabs are positive for a targeted infection. Otherwise, you will receive $10 if you complete the 1 week follow-up online survey within 24 hours of it being sent to you.

ADDITIONAL COMPENSATION

You may also qualify for additional compensation (see details below):

- IF your swabs are positive for one of the targeted pathogens and you are in the core group we are studying, you have the potential to earn an additional $40 if close contacts you name become enrolled in the study within 2 days of your initial case visit. (For each of the first four of your named contacts that become enrolled within 2 days, you will be compensated $10.)

- IF you are selected and agree to carry a portable CO2 monitor, you will receive an additional $10 when you return the monitor in person.

Knowing you will earn more than $100 as a research participant in this study, you must provide your name, address, and SSN to receive compensation. If you decline to provide this information you can still participate in the study, but you will not be able to receive compensation.

You will be responsible for any taxes assessed on the compensation you receive during this study.

You may choose to receive compensation payments via one of two payment vehicles: a) the Terrapin Express account linked to your University identification number (UID), which allows purchase at over 50 locations on campus and for which the Bursar’s Office will mail a check to your permanent address on cancellation of the account or b) a University issued debit card onto which funds will be electronically transferred. We will not make any cash payments other than by electronic means.

Right to Withdraw and Questions

Your participation in this research is completely voluntary. You may choose not to take part at all. If you decide to participate in this research, you may stop participating at any time. If you decide not to participate in this study or if you stop participating at any time, you will not be penalized or lose any benefits to which you otherwise qualify. Your academic standing as a student or employability at UMD will not
be affected by your participation or non-participation in this study.

Special notice for research assistants: If you are a student working on the study and are earning course credit for your work, your grade will not be affected by your decision to participate (or not participate) in this portion of the study.

If you decide to stop taking part in the study, if you have questions, concerns, or complaints, or if you need to report an injury related to the research, please contact the investigator:

Dr. Donald Milton
Room 2234V
SPH Building 255
University of Maryland
College Park, MD 20742
Telephone: 301-4405-0389
Email: dmilton@umd.edu

If you have questions about your rights as a research participant or wish to report a research-related injury, please contact:

University of Maryland College Park
Institutional Review Board Office
1204 Marie Mount Hall
College Park, Maryland, 20742
E-mail: irb@umd.edu
Telephone: 301-405-0678

This research has been reviewed according to the University of Maryland, College Park IRB procedures for research involving human subjects.

Your signature indicates that you are at least 18 years of age; you have read this consent form or have had it read to you; your questions have been answered to your satisfaction and you voluntarily agree to participate in this research study. You will be sent a copy of this signed consent form via email, which you may print.

If you agree to participate, please type your name and sign below.

NAME OF PARTICIPANT
[Please Print]

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