MEDICAL SCIENCES CAMPUS
UNIVERSITY OF PUERTO RICO

INFORMED CONSENT DOCUMENT

TITLE: Adopting a Precision Medicine Paradigm in Puerto Rico: leveraging ancestral diversity to identify predictors of clopidogrel response in Caribbean Hispanics.

PROTOCOL NO.: A4070417

SPONSOR: School of Pharmacy, University of Puerto Rico Medical Sciences Campus (UPR-MSC); UPR MSC RCMI Program; National Institute on Minority Health and Health Disparities (NIMHD)

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Dr. Dagmar Hernández: +1 (585) 351-8736 (Cell Phone)

I-INTRODUCTION

This consent form may contain words that you do not understand. Please ask the study investigator or the study staff to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

You have been invited to participate in a research study. However, before you agree to take part in this study, please read this consent form carefully and ask as many questions as you need in order to be sure you understand the study procedures, including risks and benefits.

II- PURPOSE OF THE STUDY

You are invited to participate in this study because you are taking or will soon start receiving a drug named clopidogrel, a.k.a. Plavix (trade name), as part of your dual antiplatelet therapy (DAPT) that also includes aspirin. This DAPT is often prescribed to patients that have had a heart attack, catheterizations or stroke since it contains medications proven to help blood platelets from sticking together. Clopidogrel actually causes your blood to become "less sticky". It is a "blood thinner" medicine commonly taken by patients like you in order to prevent platelet aggregation that gives rise to clots formation. Blood clot formation can be extremely dangerous for many reasons. A clot in your blood vessel can cause a blockage and cutting off blood supply to an organ, leading to serious health problems or even death. For someone that has already had a heart attack or stroke, there is the risk of it happening again. Clopidogrel is used in situations where future risk of these occurrences may be present. It is designed to minimize the process of blood clot formation by inhibiting the elements that cause them in the first place, and thus decreasing the likelihood of future occurrence. It has been found that some patients receiving clopidogrel do not respond to this drug as expected (i.e., they are resistant to this drug) or might have some severe cardiovascular complications upon treatment.

Resistance to clopidogrel may run in your family. In order to determine if a medical condition runs in a family, scientists study a person's "genes". You inherit your genes from your parents and these genes play a role in deciding many traits, such as how tall you are and the color of your eyes. Genes are found in the cells that make up your body; in the "DNA" (deoxyribonucleic acid) portion of your cells. Scientists can use your DNA to identify inherited traits related to heart conditions, coagulation disorders, bleedings and sensitivity or resistance to drugs. New methods allow us to study the genes in your DNA. Genes may also help explain who will be more sensitive or respondent to clopidogrel therapy, and which treatment will work the best in each individual. Using genetic and other health-related data, we can predict the optimal DAPT therapy in patients like you (i.e.,

whether you are a patient who can respond well to clopidogrel or need an alternative drug such as ticagrelor or prasugrel, instead).

In this study, we want first to determine what genes are associated with the clopidogrel response in Caribbean Hispanic patients and how the variability of these genes alter the effectiveness of the clopidogrel treatment. The second part of this study is aimed at testing a method to guide your DAPT therapy using your clinical data, genetic test results and the results of a test to measure your platelet activity (PRU, using the VerifyNow equipment). VerifyNow is a lab machine that allows us to measure *ex-vivo* the patient's residual platelet activity through a simple, fast blood test.

You may also be invited to participate as a volunteer for this study and serve as a control for certain analyses of plasma protein levels, in comparison to other participants, either because you are a cardiovascular patient who is currently not being treated with clopidogrel or a healthy subject without a cardiovascular condition. The analysis of your proteins in plasma will allow us to know if there are variations in their abundance as a result of alterations in genes related to clopidogrel. The control subjects will not participate in the second phase of this study.

Moreover, this protocol can lead to additional studies in order to apply new methods for improving the way we currently treat patients like you and determine their ideal DAPT therapy as well as for many other medical conditions in Caribbean Hispanics. Accordingly, there is an expectation that your biological specimens can be stored in a repository or bio-bank and/or your data from this study can be shared with other investigators and become available for future use in other research projects (i.e., broad research purposes), if you consent to this/these purpose(s). At the end of this informed consent document, you will find special sections for this purpose, where you can either consent to or reject such a request for future research use and broad sharing of specimens, genetic and clinical data generated from this study through controlled-access. If you agree, your totally de-identified specimens and data will be anonymously shared. However, there is always a minimal risk that your personal information can be compromised in this process, though precautions will be taken to minimize the risks.

III- STUDY PARTICIPANTS

Taking part in this study is completely voluntary. You do not have to participate if you do not want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not loose any benefits to which you are otherwise entitled.

~~The initial contact with you by the study investigators will last less than 45 minutes.~~

when the informed consent process will be completed and a blood sample for genetic and platelet function (VerifyNow) testing will be taken. This blood sample will be withdrawn by qualified personnel in the hospital at the same time of your other routine tests ordered by your doctor, including your lab tests that also require blood samples. The first part of this study will only consist of the initial contact and your authorization to perform the required genetic and platelet function tests. The volunteers who will serve as controls will only participate in the first part of the study. Upon consenting to participate in the second part of the study, which proposes to test a new method to guide your DAPT therapy based on results from your genetic testing, platelet function and clinical data, you authorize us to conduct a follow up on your therapy over a period of up to six (6) months (with checkpoints at month one and six). This means we can review your medical record and contact you, mainly on phone or during your follow-up visits, for a short follow-up interview (about 30 minutes) about your health condition and the results of your DAPT therapy.

To conduct this follow-up, you will be assigned to one of four different groups, based on the results of your genetic and platelet function tests: that is, Group 1 is for participants with high residual on-treatment platelet activity and the presence of risk genes; Group 2 for those who have a high residual function of their platelets but do not have the risk genes; Group 3 for those who have low residual platelet function but have the risk genes and Group 4 for those who have a low residual platelet function and do not have the risk genes. Depending on which group you are assigned to, a recommendation will be made to your doctor regarding your DAPT therapy (i.e., on whether you should receive clopidogrel or an alternative drug such as prasugrel or ticagrelor). However, your doctor may either accept or reject this recommendation according to his/her clinical judgment. One of the study investigators will tell you if your participation in the second part of the study is required at the time we seek for your authorization of this informed consent process. Your consent to participate in any of the study parts does not imply an obligation to participate in the other part, whatever your choice will be.

This study is intended for Caribbean Hispanic patients who have been or will be receiving clopidogrel:
(A) for at least five days with a 75 mg dose of clopidogrel or;
(B) received an initial dose of 300-600 mg in the hospital and then 75 mg daily at home.

We expect approximately 1,000 cardiac patients with an indication for clopidogrel as prescribed by a duly certified physician (i.e., DAPT with clopidogrel and aspirin). Additionally, 20 control volunteers will also be invited to participate (10 subjects who do not have cardiovascular conditions and 10 cardiovascular patients not

treated with clopidogrel). These controls will be used to compare the results of future studies. All participants will be Caribbean Hispanics residing in Puerto Rico, both genders and older than 21 years of age. Enrollment is scheduled for the period spanning from October 2017 to June 2021. In order to participate, you must be able to understand and complete the informed consent process and follow the indications of the study investigators. Adherence to treatment with clopidogrel (taking the medication as directed by your doctor) or the alternative in your DAPT is mandatory. Any factor that limits adherence to treatment, or contraindications to taking clopidogrel, excludes you from participating in the study.

Patients who have previously taken or are taking another oral antiplatelet agent (e.g., Ticagrelor, Prasugrel, Ticlopidine) or have received Abciximab or Eptifibatide (other medicines commonly used in patients with heart diseases) cannot be enrolled.

Likewise, patients diagnosed with anemia, low platelets count, renal or hepatic disease, acute illness (sepsis, infections), sickle cell anemia, HIV/AIDS, hepatitis B, cancer, alcoholism or user of illicit drugs, receiving nutrition through nasogastric tubes, suffering from mental health conditions, and patients participating in another clinical study that prohibits their enrollment in this study, are also excluded from this protocol. Pregnant women or childbearing women not using medically approved method of birth control (e.g., contraceptives pills) will be excluded. If you become pregnant during this study there may be other risks to you and your unborn child that are not known. If you are female, and able to become pregnant, must use two (2) contraceptive methods, one should be an acceptable barrier method (diaphragm with spermicidal jelly, condoms, etc.) through the study period (i.e., up to 6 months). No sexual intercourse is an acceptable method of birth control if you become pregnant during the course of the study, you must withdraw from the study, and contact your doctor.

IV-PROCEDURES

If you accept to voluntarily participate in this study, you will be asked to do the following:

- Donate two (2) small tubes of blood (approximately 15 ml, which is about one tablespoon). Blood withdrawal will be performed by qualified and trained personnel. The study investigators will label the bag with your samples using a unique study code number in order to protect your personal information. No names or any other identifiable information will be used. Only two blood tubes will be collected from the controls in the study. No further participation in the study will be required for control subjects.

- Allow access to your medical record or chart by the study investigators. The following information might be collected from your medical record by the investigators of this study: age, gender, weight, and ethnicity, the current list of medications you are taking, health conditions, and clopidogrel treatment history including any reports of adverse events. In case the information is lacking in your medical record, we might ask you to provide the information.
- Accept two short follow-up interviews (30 min. each) to be conducted by the study investigators, one at the first month and the other within 6 months of signing this consent. These follow-up interviews are only if you are invited and consent to participate in the second part of the study. The interview can be in person or by phone.
  As part of these interviews, the study investigators may ask you to complete a fact sheet, which already contains data about you and your participation in the study, in order to document any relevant event that occurred over the follow-up period (e.g., gum bleeding; blood in urine; dark stools; bruises on the arms, legs or trunk; nose bleedings; vomited blood or coffee ground-like material; chest pain; slurring of speech, arm or one-sided facial weaknesses; need hospitalization or emergency room visit, etc.) They will also ask you questions about how you feel and whether or not you have been taking your medications as directed.

  If you were invited to participate in the second part of this study, please indicate your willingness to participate by making your choice below.
  Yes, I accept___
  I do not accept___

  Initials_____ Date_____

- You may be invited to donate your samples and/or data from this study for future studies.
- You might be asked to bring the pill bottle to your scheduled appointments during the study period and count how many pills left. You will be asked if you missed any dose or took any extra dose over the span. You will be educated regarding importance of adherence to therapy and medical instructions for clopidogrel use, as well as on how to use drug calendars, pill box or other methods to aid compliance.

The blood samples donate by you will be coded (i.e., identified by a unique 7-digit code that does not include your name or personal information). The coded samples will be sent to Dr. Duconge's laboratory for DNA analysis and for performing the VerifyNow test (Pharmacogenomics lab, B-214, 2nd floor, main

bldg., MSC). The researchers at the laboratory will not have access to any information that might identify you. A change in your DAPT treatment might be recommended based on the results of this DNA analysis and the VerifyNow test, depending on what group you were assigned to. However, your doctor (cardiologist) will make the final decision on this recommended change. Your doctor may choose to cancel your participation in this study if, in his/her judgment, it is of no benefit to you. If this is the case, you will continue receiving the best available treatment for your condition.

This study is experimental; therefore, the tests and data collection will be used for investigational purposes only. The study will last about 5 years. The participation of each patient, including you, will last about 45 minutes (first part) or up to six months (24 weeks of follow up) if you also participate in the second part of the study. The investigators of this study will have no plan to inform you of any result from your tests, though you have the right to request this information if you will. We will not re-contact you in the future based on the information obtained from this study. Please, tell us if you want to be re-contacted after finishing this study or if you wish to receive information about the result of your tests (including the DNA test). If you decide not to take action this time it will not prevent you to change your mind in the future.

The PI of the study (Dr. Duconge) will keep secured any information that might reveal your identity. This information will be kept in a password-protected separate file from the study data and will reside in the PC of the PI (Dr. Duconge, 2nd floor, main bldg., MSC). The original records will be destroyed as soon as the investigators collect all the data from the study, the analyses can be performed, and the IRB permits this action. Once this is done, there will be no manner to track your test sample.

However, if you provide authorization for future use of your data in other research projects (i.e., broad research purposes), we could deposit your totally de-identified individual genetic and clinical data (i.e., genotypes and phenotypes) on a database repository (i.e., dbGaP) with controlled-access. Likewise, if you provide authorization, we can also store your blood-derived biological specimens (such as a portion of your DNA) in a repository or bio-bank of the UPR MSC for future studies. At the end of this informed consent document, you will find special sections for these purposes, where you can either consent to or reject such requests for future research use and broad sharing of specimens, genetic and clinical data generated from this study through controlled-access.

V- RISKS AND DISCOMFORTS

You may experience the following mild physical discomforts or risks as a result of participating in this research study:

- Blood sample collections might cause bruises, slight stress, anxiety and discomfort. To minimize discomfort, qualified and well-trained personnel will perform this procedure.
- The idea of testing can cause pre- and post-test anxiety.
- The risks of sharing your DNA test results with your employer and/or any insurance company representative, like your health insurance company, are minimal since this personal information is confidential and therefore protected by the PI of the study and will not be shared with other persons outside the study. It is possible that an authorized member of the study site and/or a member of the committee that protect your human rights in this study (IRB) can also request access to your information derived from the study, but only for overseeing ethic and scientific conduction of this research study.
- The disclosure of genetic information might negatively affect a person's insurance coverage, employment, or social-economic standing. The risk of such a disclosure is low in this study because the samples disclosed to the clinical laboratory will be coded (de-identified) and safeguards are in place to keep the information secure and prevent any privacy violations. Once all data is collected for the study, the master list linking you to your sample will be destroyed.

VI- BENEFITS

The purpose of the study is to determine the association between genetic variants and clopidogrel response in Caribbean Hispanic patients from Puerto Rico like you. If we can be able to demonstrate any association between gene variations and the effect of clopidogrel in patients like you, it could be possible in the future to modify the treatment and reduce the risks of adverse effects after DAPT therapy (e.g., serious bleeding, strokes, etc.).

However, there may be no direct benefit to you from participating in this study. Yet, it is possible that the information learned during this study will help us understand better how to modify the clopidogrel therapy, justify a change to an alternative drug and reduce the burden of adverse events. This will ultimately help future patients that need clopidogrel therapy to optimize their therapies and achieve proper and sooner control and clinical outcomes.

VII- COSTS

There are no charges for your participation in this study.

VIII- COMPENSATION FOR PARTICIPATION

You will be paid $25 for each completed study visit (second part of the study) to cover the transportation and meals expenses. If you do not complete the study, you will be paid for the visits you have completed.

IX-ALTERNATIVE TO PARTICIPATE

If you decide not to enter this study, you will still be provided all the medical care and benefits for which you are otherwise eligible. The doctor will discuss the other alternatives of therapy with you. You do not have to be in this study to be treated with clopidogrel for your medical condition.

X- PRIVACY AND CONFIDENTIALITY

If you choose to be in this study, the investigators will get personal information about you. This may include information that might identify you. You will give blood samples for DNA analysis and the VerifyNow test. The investigators will code your samples with a unique study number in order to protect your identity. Once the study is completed, your de-identified DNA specimens and blood samples will be properly destroyed and disposed as per current policy at UPR-MSC for safety disposal of biohazard materials. This is the plan unless you give your consent to the storage of these specimens in the UPR MSC repository/ bio-bank for future studies, as part of the authorization in appendix A2 at the end of this document.

Your health information, as described in this document, will be used for the purposes of this research study only. During this study your personal information, including genetic and health information, will be collected by the study investigators. The information that will be collected also includes your name, telephone, address and social security number, which may be used to contact you during the follow up period and to obtain information about your health condition from medical records at the participating medical facilities. These HIPAA identifiers will also be necessary in case we need to re-contact you for future studies (only if you authorize this action by giving your consent to share your data/store your specimens, as part of the special sections at the end of this document, in Appendices A1 and/or A2). Date of birth will be used to confirm you are eligible for this study as only individuals older than 21 years can be enrolled.

Individual names, telephones, social security numbers and any other personal identifiers are irrelevant for the purposes of the data analyses and, accordingly, will be kept safely by the PI of the study in encrypted and separated files apart from the study database and codes. No one, except the PI (Dr. Duconge), will have access to these records at any time. Accordingly, there will be a code that identifies you as a participant of this study, which will not present any information that is

related to your personal identifiers. Any study investigator other than the PI will only see this code and, therefore, cannot identify whom this code belongs to.

Apart from the genetic information derived from the analysis of your DNA sample, the health-related information that will be collected includes your past and present medical history, diagnosis, medications use, clopidogrel dose and regimen, information obtaining during this research about your laboratory tests results (VerifyNow), compliance and reports of adverse events (questionnaire form).

We will protect all the information about you and your part in this study, just as is done for all patients at the participating medical facilities. Your records will be maintained safeguarded as stated by HIPAA regulations and in accordance with applicable state and federal laws. Besides, your personal information concerning the results of the analysis of your DNA sample are protected by provisions of Title II of GINA (Genetic Information Non-discrimination Act). This new federal law will generally protect you in the following ways:

• Health insurance companies and group health plans may not request your genetic information obtained from this research.

• Health insurance companies and group health plans may not use your genetic information obtained from this research when making decisions regarding your eligibility or premiums.

• Employers with 15 or more employees may not use your genetic information obtained 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.

The master files with your health information and related study records will be maintained (either electronically as encrypted files in the password-protected PC of the PI or physically in a locked cabinet at the PI's office) for a minimum of five years following the end of the study as required by law. The PI's PC is protected from outside access by a two-tiered firewall system. Your signature on this Consent form authorizes us to use your health information.

Private identifiable information about you may be used or disclosed for purposes of this research project as described in the study's authorization form. The information may also be used to meet the reporting requirements of NIH. The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed. During the research study, you will not have access to the research data that is collected about you.

Alexander-Cuprill DI, et al. BMJ Open 2020;10:e038936. doi: 10.1136/bmjopen-2020-038936

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From 06/29/2020 To 06/29/2021

This information will be made available to you (if you so request) after completion of the study when the results have been determined and/or published. However, the majority of the health information collected about you during this study is already included in your regular patient medical record so that it is available to you, your doctor and others providing you care.

This study involves multiple recruiting and performance sites (i.e., the University Hospital at Carolina and UDH at Centro Medico, the Cardiovascular Center of Puerto Rico and the Caribbean and School of Medicine, medical offices of Drs. Eileen Ramirez, Marta Diaz-Nater, Steven Rivas, Raul Garcia-Rinaldi and Hilton Franqui-Rivera and Dr. Duconge's lab of pharmacogenomics, B-214, 2nd floor, main bldg., UPR-MSC) and other collaborating sites (i.e., the Genetics and Genomics department, Icahn School of Medicine at Mount Sinai, New York, NY; CLIA-certified Genomas Inc. Lab, Hartford, CT; PROMICs lab of the UPR Comprehensive Cancer Center; nursing services at the *Puerto Rico Clinical and Translational Research Consortium* (PRCTRC), and the RCMI Molecular Genetics lab, A-639, 6th floor, main bldg., UPR-MSC). The data shared with these sites will be coded so that investigators therein cannot identify you.

The study data may be reviewed by the ethics committee overseeing the research. Your identity will not be disclosed to the public domain. However, your medical records and study information may need to be reviewed by the members of the UPR Medical Sciences Campus Institutional Review Board (UPR MSC IRB) and other federal or local Regulating Agencies. The UPR MSC IRB is a group of people who perform independent review of research as required by regulations. By signing this form, you authorize such inspection. In addition, the research files identifying you and the consent form you sign may be inspected by a representative of the sponsor (i.e., the University of Puerto Rico School of Pharmacy).

You have the right to revoke (or take back) your permission for use of your personal health information for research purposes. However, if your information has already been combined with other patient's information in the study, such as when numbers are averaged, they will continue to use the information on file but no new information about you will be forwarded.

If you have any questions concerning your right to revoke or take back your permission, you may contact

Dr. Jorge Duconge at 787-758-2525 ext. 5312, and 5410 (Work) or at 787-449-3692 (Cell Phone), principal investigator.
Dr. Kyle Melin al 787-758-2525 ext. 3711 (trabajo) y 787-662-4925 (celular),
Dr. Dagmar F Hernández Suárez 585-351-8736 (celular).

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The request to revoke your permission should be submitted in writing at the following address:

Dr. Jorge Duconge
Department of Pharmaceutical Sciences, R-325-14
Pharmacy Bldg, 3rd Floor
School of Pharmacy,Medical Sciences Campus
University of Puerto Rico, PO Box 365067
San Juan, PR 00936-5067

If you cancel this authorization, the PI will no longer use or disclose your personal health information under the authorization for this study, unless he needs to use or disclose some of your personal health information to preserve the scientific integrity of the study. Information submitted before you cancel this authorization can still be used by the associates.

The Authorization for Use and Disclosure of Protected Health Information for research purposes is completely voluntary. However, if you do not sign this document you will not be able to participate in this study. If in the future you cancel this authorization, you will not be able to continue participating in this study.

Who Will Have Access to your Study Data?
Since all NIH-funded clinical trials like this one are expected to register and submit results information to Clinicaltrials.gov official website, as per the new "*NIH Policy on Dissemination of NIH-Funded Clinical Trial Information*", we will be posting this study at Clinicaltrials.gov in order to be in full compliance with the new requirements.

ClinicalTrials.gov is an official website that provides information about clinical trials. A description of this clinical trial will be available on http://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.

XI- COMPENSATION FOR INJURY
In the event of physical and/or mental injury resulting from this research study, you will receive medical treatment free of change at the University Hospital or any other hospital designated by the Chancellor or the Medical Sciences Campus of the University of Puerto Rico. The University of Puerto Rico has no plans to provide any form of compensation directly to you for any injury or lost wages. However, by signing this consent form you do not give up any legal rights. You will not be required to pay for treatment received as part of your participation in this study.

XII- VOLUNTARY PARTICIPATION AND WITHDRAWAL

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From 06/29/2020 TO 06/29/2021

Your participation in this research is voluntary. You may refuse to participate, or withdraw your consent and discontinue participation in the research at any time. You may do so without penalty, or loss of benefits to which you are otherwise entitled. Your decision whether to participate will not affect your future medical care at the participating medical institutions.

XIII- SOURCE OF FUNDING FOR THE STUDY

This study is funded with the RCMI U54 grant from the National Institute on Minority Health and Health Disparities (NIMHD) of the NIH.

XIV- QUESTIONS

Should any problem or question arise before or during the study with regards to this research, or with regards to any research related injury, you understand that you should contact

Dr. Jorge Duconge at 787-758-2525 ext. 5312, 5410 (work) or 787-449-3692 (cell phone).
Dr. Kyle Melin at 787-758-2525 ext. 3711 (work) or 787-662-4925 (cell phone),
Dr. Dagmar F. Hernández Suárez at 585-351-8736 (cell phone).

If you have questions about your rights as a research subject, you may contact:

Human Research Subjects Protection Office (OPPHI/ IRB)
University of Puerto Rico Medical Sciences Campus
EPS Bldg, 2nd floor, R-210
Telephone: 787-758-2525 ext. 2510 to 2515.
E-mail: opphi.rcm@ upr.edu

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions. If you agree to be in this study, you will receive a signed and dated copy of this consent form with the stamp of IRB approval for your records.

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From 06/29/2020 To 06/29/2021

XV- CONSENT

I have read the information in this consent form (or it has been read to me). All my questions about the study and my participation in it have been answered. I freely consent to be in this research study.

I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above (except for the special section).

By signing this consent form, I have not given up any of my legal rights.

_____
Subject Name

_____ _____
Signature of Subject Date

_____
Name of the Person Conducting Informed Consent Discussion

_____ _____
Signature of Person Conducting Informed Consent Discussion Date

---------- Use the following only if applicable ----------

If this consent form (addendum) is read to the subject because the subject (or legally authorized representative) is unable to read the form, an impartial witness not affiliated with the research or investigator must be present for the consent and sign the following statement:

I confirm that the information in the consent form (addendum) and any other written information was accurately explained to, and apparently understood by, the subject (or the subject's legally authorized representative). The subject (or the subject's legally authorized representative) freely consented to be in the research study.

_____ _____

IRB APPROVED (MSC/UPR)
From 06/29/2020 To 06/29/2021

Signature of Impartial Witness Date

Note: This signature block cannot be used for translations into another language. A translated consent form is necessary for enrolling subjects who do not speak English.

Appendix A1:

Consent to Use Data for Future Studies and Broad Sharing:

There is an expectation that your individual data (i.e., totally de-identified genotypes, clinical or phenotypic data as well as any other data relevant for the study such as disease status) can be available for future use in other research projects. Accordingly, you are herein asked to give authorization for future research use and broad sharing of your own genetic and clinical data generated from this study.

Prior to submitting the data to the NIH-designated data repository (dbGaP), data will be stripped of identifiers such as names, phone numbers, SS numbers and others by standard procedures consistent with the Common Rule. Safeguards to protect the data according to federal standards for information protection will be implemented. Access to your totally de-identified, anonymous data will be controlled at any time.

Your personal health information will be kept as confidential as possible under the law. However, your personal health information may no longer be protected by the privacy rule once it is shared with others. Because it may still be possible to re-identify anonymous genetic data, even if access to data is controlled and data security standards are met, confidentiality cannot be 100% guaranteed, and re-identified data could potentially be used to discriminate against or stigmatize you, a member of your family or ethnic group. In addition, there may be other unknown risks. You may want to discuss this special authorization with your family before making a decision.

Once your consent is given for this special authorization, your data may be used for future research on any topic and shared broadly in a manner consistent with this informed consent and all applicable federal and state laws and regulations. No direct benefits to you are expected from any secondary study that may be conducted in the future under this special authorization. Nonetheless, it is possible that the information learned during such future studies will ultimately help scientists understand the patient's susceptibility to diseases or who are at higher risk for adverse events or not response, and thus be able to use these data to improve medical outcomes.

You may withdraw consent for any future research use of your individual genetic or phenotypic data at any time without penalty or loss of benefits to which you are otherwise entitled. In this event, be advised that your individual data will be withdrawn from the NIH-designated data repository (dbGaP), if possible, but data already distributed for research use will not be retrieved.

As a result of using your data in the NIH repository for future investigations, new relevant information about your health may emerge (for example, a predisposition to develop certain disease or a high risk to response adversely to a particular drug, etc.), as well as on your ancestry (that is, if you are likely a descendant of Europeans, Africans or Amerindians, and to what extent, according to the information obtained from your genes and the use of certain algorithms to analyze that information). If you wish to be re-contacted in the future to be totally or partially informed about the results of these studies, especially if there is a relevant finding that merits a disclosure according to the opinion of the investigators, let us know by selecting the option of your preference below this paragraph. If you change your mind in the future about this decision you can notify us and we will make the arrangements to satisfy your choice.

___ Yes, I want to be re-contacted in the future to be notified about findings with the analysis of my data.
___No, I do not want to be re-contacted in the future to be notified about findings with the analysis of my data.

If you decline to consent to future research use and broad sharing of your data, you will not be excluded from the current study protocol on that basis. Therefore, you can still give your informed consent to participate in the present study and/or store your biological specimens in a bio-bank at the UPR MSC (appendix A2) for future studies and, at the same time, reject an authorization to share your data broadly for any future use in research projects.

Should any question arise with regards to this special authorization, you should contact
Dr. Jorge Duconge, principal investigator, at 787-758-2525 ext. 5312, 5410 (work) or 787-449-3692 (cell phone).
Dr. Kyle Melin at 787-758-2525 ext. 3711 (work) y 787-662-4925 (cell phone),
Dr. Dagmar F. Hernández Suárez at 585-351-8736 (cell phone).

By writing my initials below, I freely consent to future research use and broad sharing of my data.

_____
Subject Name

_____ _____
Signature of Subject Date

Appendix A2:

IRB APPROVED (MSC/UPR)
From 06/29/2020 TO 06/29/2021

Consent to Store Biological Specimens for Future Studies and Broad Sharing:

The investigators of this study are interested in creating a sample repository named "UPR MSC CV Genotypes and Phenotypes Database and Biobank", which would serve as a valuable resource for future research. This is expected to help addressing a current problem in genomic research, which is the lack of relevant information about Caribbean Hispanic patients with cardiovascular disease like you. For this reason, it is possible that the blood samples you will provide for this study and the biological specimens derived from these samples (i.e., DNA, plasma and the blood cells called PBMC) can be useful for future studies, including those that would be carried out by other investigators. We ask you to authorize the use of your specimens to be stored in our UPR repository (bio-bank) as well as for future studies.

Your samples and biological specimens will be stored safely in our UPR repository with controlled acess, and they can be shared anonymously for future studies following a request process that also need authorization by the study PI.
Prior to submitting your samples and/or biological specimens to be stored at the UPR repository (bio-bank), they will be stripped of identifiers by folowing standard procedures consistent with the Common Rule. Safeguards to protect the speciemns according to federal standards for sample protection will be implemented. Access to your totally de-identified, anonymous specimens will be controlled at any time.

Privacy of your samples and biological specimens will be garanteed under the law. Your personal health information will be kept as confidential as possible under the law. However, your personal health information derived from the use of your anonymous samples may no longer be protected by the privacy rule once it is shared with others. Because it may still be possible to re-identify anonymous genetic data, even if access to data is controlled and data security standards are met, privacy of your specimens and confidentiality of derived data cannot be 100% guaranteed, and re-identified data could potentially be used to discriminate against or stigmatize you, a member of your family or ethnic group. In addition, there may be other unknown risks. You may want to discuss this special authorization with your family before making a decision.

Once your consent is given for this special authorization, your samples may be used for future research on any topic and shared broadly in a manner consistent with this informed consent and all applicable federal and state laws and regulations. No direct benefits to you are expected from any secondary study that may be conducted in the future under this special authorization. Nonetheless, it is

possible that the information learned during such future studies will ultimately help scientists understand the patient's susceptibility to diseases or who are at higher risk for adverse events or not response, and thus be able to use these data to improve medical outcomes.

You may withdraw consent for any future research use of your specimens at any time without penalty or loss of benefits to which you are otherwise entitled. In this event, be advised that your individual specimens will be withdrawn from the UPR repository, if possible, but data already distributed for research use will not be retrieved.

As a result of using your biological specimens in the UPR repository for future investigations, new relevant information about your health may emerge (for example, a predisposition to develop certain disease or a high risk to response adversely to a particular drug, etc.), as well as on your ancestry (that is, if you are likely a descendant of Europeans, Africans or Amerindians, and to what extent, according to the information obtained from your genes and the use of certain algorithms to analyze that information). If you wish to be re-contacted in the future to be totally or partially informed about the results of these studies, especially if there is a relevant finding that merits a disclosure according to the opinion of the investigators, let us know by selecting the option of your preference below this paragraph. If you change your mind in the future about this decision you can notify us and we will make the arrangements to satisfy your choice.

___ Yes, I want to be re-contacted in the future to be notified about findings with the analysis of my specimens.
___No, I do not want to be re-contacted in the future to be notified about findings with the analysis of my specimens.

If you decline to consent to future research using and broad sharing of your specimens, you will not be excluded from the current study protocol on that basis. Therefore, you can still give your informed consent to participate in the present study and/or share your data in the NIH repository (appendix A1) for future studies and, at the same time, reject an authorization to store your specimens and share them for any future use in research projects.

Should any question arise with regards to this special authorization, you should contact

Dr. Jorge Duconge, principal investigator, at 787-758-2525 ext. 5312, 5410 (work) or 787-449-3692 (cell phone).

Dr. Kyle Melin at 787-758-2525 ext. 3711 (work) y 787-662-4925 (cell phone),
Dr. Dagmar F. Hernández Suárez at 585-351-8736 (cell phone).

By writing my initials below I freely consent to future research use and broad sharing of my data.

Supplemental material

BMJ Open

Subject Name

Signature of Subject

Date