1. Recruit individuals between the ages of 18-65 with no diagnosed disorder/disease, no family history of a genetically-linked disease/disorder, and no condition requiring hospitalization or immune suppression.

2. Obtain informed consent from qualifying individuals via a process approved by the Mount Sinai Institutional Review Board (IRB).

3. Schedule a consenting individual to undergo an examination at the Mount Sinai Clinical Research Center (CRC; established and operated through the Clinical and Translational Science Award (UL1TR000067) from the National Center for Advancing Translational Sciences (NCATS), a component of the National Institutes of Health).
   a. The examination performed by qualified CRC nurses and fellows from the Department of Medicine, Division of General Internal Medicine, includes assessment of the participant’s clinical history, vital signs and examination of the cardiovascular (including an EKG), respiratory, gastrointestinal and neurological systems. Data and results are reported in the Clinical Report Form.
   b. Blood is drawn to obtain complete blood counts, chemistries, and additional factors detailed in the Clinical Report Form.

4. Once the blood test results are available, a clinical panel consisting of the examining physicians, the head of the Mount Sinai Internal Medicine Associates outpatient clinic, and an interventional cardiologist, will determine the health status of each participant based on the physical and laboratory findings recorded in the Clinical Report Form (QA/QC). Only participants certified as healthy by the panel will be allowed to proceed with the skin biopsy (see SOP C-6.0).
Metadata

1. Consent document. Note that each participant’s completed consent document is stored in accordance with HIPAA, Mount Sinai, New York State and Federal regulations. An unsigned document is appended to this SOP.

2. Clinical Report Form. Note that each participant’s completed clinical report is stored in accordance with HIPAA, Mount Sinai, New York State and Federal regulations. A blank report form is appended to this SOP.


Quality Assurance/Control Steps (QA/QC)

**QA/QC1**: To maximize the possibility that only healthy individuals are included as cell donors, a panel of physicians must reach consensus on each participant's health status based on the extensive physical examination and laboratory findings detailed in the Clinical Report Form appended to this SOP.
TITLE OF RESEARCH STUDY:

Title: Drug Combination Signatures for Prediction and Mitigation of Toxicity

PRINCIPAL INVESTIGATOR (HEAD RESEARCHER) NAME AND CONTACT INFORMATION:

Name: Ravi Iyengar, PhD

Physical Address: Icahn Medical Institute, 12th floor, room 12-70C

Mailing Address: One Gustave L, Levy Place
Box 1215
New York, NY 10029

Phone: (212)-659-1707

WHAT IS A RESEARCH STUDY?

A research study is when scientists try to answer a question about something that we don’t know enough about. Participating may not help you or others.

People volunteer to be in a research study. The decision about whether or not to take part is totally up to you. You can also agree to take part now and later change your mind. Whatever you decide is okay. It will not affect your ability to get medical care within the Mount Sinai Health System.

Someone will explain this research study to you. Feel free to ask all the questions you want before you decide. Any new information that develops during this research study that might make you change your mind about participating will be given to you promptly.

Basic information about this study will appear on the website http://www.ClinicalTrials.gov. There are a few reasons for this: the National Institutes of Health (NIH) encourages all researchers to post their research; some medical journals only accept articles if the research was posted on the website; and, for research studies the U.S. Food and Drug Administration (FDA) calls "applicable clinical trials" 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.

PURPOSE OF THIS RESEARCH STUDY:

The purpose of this study is to understand adverse events caused by useful drugs in normal tissues of humans. For this we plan to obtain skin samples of healthy human subjects. Using this skin sample, we intend to establish fibroblast lines that will subsequently be reprogrammed to cells with the potential to give rise to any cell of the body and then differentiated to cells of the heart, liver and peripheral sensory (neurons) system for the purpose of the generation of molecular signatures for prediction and reduction of drug side effects caused by an specific drug and drug combinations.

This Consent Document is approved for use by an Institutional Review Board (IRB)

Form Approval Date: 7/9/2015
DO NOT SIGN AFTER THIS DATE » 6/30/2016
Rev. 4/1/15

IRB Form HRP-502a
Another purpose of this research project is to collect and store human samples (such as skin samples) and health information. Researchers can then use the stored materials in future studies. Through such studies, they hope to find new ways to detect, treat, and maybe even prevent or cure health problems. Some of these studies may be about how genes affect health, or how genes affect response to treatment. (Genes, which are made up of DNA, have the information needed to build and operate a human body.) Some of the studies may lead to new products, such as drugs or tests for diseases.

You may qualify to take part in this research study because your examination by the clinical research center indicates that you are a healthy person between the ages of 18-65.

Funds for conducting this research are provided by NIH.

**LENGTH OF TIME AND NUMBER OF PEOPLE EXPECTED TO PARTICIPATE**

Your participation in this research study is limited to a maximum of two visits. During the first visit to the clinical research center you will give informed consent and only then undergo a physical exam to establish your healthy status. Once your healthy status has been determined you will be contacted again to schedule an appointment during which we will obtain a skin sample. This visit will take approximately 10 to 15 minutes to complete the skin biopsy. The tissue sample will be collected during a clinic visit arranged at your convenience and will require no extra time involvement after obtaining the tissue specimen.

The number of people expected to take part in this research study at Mount Sinai is 100 individuals between 18-65 with no gender bias but about 30% ethnic minorities (African American, Asians and Hispanics) in order to obtain 40 healthy individuals from which to take a skin biopsy. The total number of people expected to take part in this research study is 100.

**DESCRIPTION OF WHAT’S INVOLVED:**

If you agree to participate in this research study, the following information describes what may be involved.

During a visit to the clinical research center you will give informed consent prior to undergoing a physical exam to establish your healthy status. The exam will involve assessment of your clinically history, taking of vital signs and major system examinations (including pulmonary, cardiovascular, GI), an electrocardiogram (ECG; describe in the next paragraph) and having blood drawn (approximately 23 mL) to test heart, liver and sensory/touch system function parameters. Your blood will also be tested for HIV. HIV is the term used for the virus that produces HIV infection and may ultimately lead to AIDS. You must be told that you are being tested for HIV and give consent. You will sign an additional consent form prior to the HIV blood test. You have a right to know the results of the test. If you test positive you will be given more tests to confirm the results of the first test. If you are HIV positive, the study doctor will also give you a list of referrals for further information and counseling. Female subjects only will have to provide a urine sample to determine their pregnancy status in order to rule out any eventual problems from the lidocaine (for local anesthesia) and the skin punch biopsy. Specifically, the physical exam will involve first checking of weight, height, waist and hip
circumference, heart rate, blood pressure, rate of breathing (breaths per minute) and peripheral oxygen saturation by pulse oximeter placed on a finger (this is a non-invasive measurement that takes only 10-20 seconds and is not painful). The doctor will then perform a complete physical examination that will include examination of the cardiovascular, respiratory, gastrointestinal and neurological systems. Particular aspects will involve listening to the heart and lungs with a stethoscope, palpation (feeling with the hands) of the abdomen, and examination of the sensori-motor system. A rectal exam will not be performed. This complete physical examination will take about 1 hour.

An ECG is the recording of the electrical activity of the heart captured over time by external electrodes attached to the skin. This involves placing 10 recording electrodes on the skin, with a gel-like substance contacting the skin (which can conduct the heart electricity). Six electrodes go across the left chest, while one electrode is attached to each limb (left and right arm and leg). For persons with a "hairy chest", shaving of some of the chest hair may be required to achieve good contact of the sensing electrodes and the skin. The entire process takes 5-10 minutes and is painless. Because an ECG is only recording the activity of the heart, there are no "electrical" or other sensations felt.

If you continue to qualify to take part in this study, you will have a skin sample taken at your convenience. If it is determined that you are not healthy and cannot continue in this study, you will be provided the results of the test by the study physician and be recommendation to see your personal physician. If you do not have a personal physician, we will refer you to the Mount Sinai Internal Medicine Associates.

After determination of your healthy status, a skin samples will be collected during a second visit arranged at your convenience. No further time involvement is required. We will obtain and save these samples and store the tissue in a bank with other samples that will be used for the research testing described as above and will be stored for a minimum of five years and for as long as deemed useful for research purposes. The skin sample will be assigned a 4-digit number (de-identification) for confidentiality during the research study.

The skin biopsy is called a punch biopsy and involves using a small 3 mm bore needle to obtain a sample of skin from either the forearm or behind the knee. The size of the sample taken will be approximately similar to the size of this typed letter “O”, approximately 3 mm in size. A numbing anesthetic will be injected locally to numb the area before the sample is obtained. The area will then be covered with a small gauze or bandage. The risks involved are listed below. The punch biopsy will be obtained by a clinician who is a member of our research team.

We may wish to do future testing of your skin samples and derivatives, including but not limited to generated induced pluripotent stem cells and differentiated target cells such as heart, liver and peripheral nerve cells, based on potential future scientific developments and discoveries.

The researchers would like to ask your permission to keep specimens (like blood, tissue, hair, or any other body matter) collected or derived from you during this study to use them in future research studies. They would also like to know your wishes about how they might use your specimens in future research studies. You should also know that it is possible that products may someday be developed with the help of your specimens, and there are no plans to share any profits from such products with you.
(1) Will you allow the researchers to store your specimens to use in future research studies?

Yes _______  No _________  If no, please stop here. If yes, please continue to the next question.

(2) The researchers can keep your specimens stored in one of two different ways: one way will store your specimens in a way that it is linked to your identity (through the use of a code that can indicate the information came from you personally) and the other way will store your specimens anonymously (no one will know who the information is from). It will not be stored both ways, so you must choose one of these two options. Please note that if you choose to have your specimens stored anonymously, you will not be able to change your mind to ask for your specimens to be destroyed at a future date.

How would you like your specimens stored? Please initial ONE choice:
I would like my specimens stored with a link to my identity______________
I would like my specimens stored anonymously _______________

(3) Do you give the researchers permission to contact you in the future to collect additional information about you, discuss how your specimens might be used, or to discuss possible participation in another research project? Please initial your choice:

Yes_________ No____________

(4) Do you give the researchers permission to keep the specimens indefinitely and use them for future studies that are directly related to the purpose of the current study? Please initial your choice:

Yes_________ No____________

(5) Do you give the researchers permission to keep the specimens indefinitely and use them for future studies that are not related to the purpose of the current study (for example, a different area of research)? Please initial your choice:

Yes_________ No____________

(a) If the future research in a different area can be done without having to know that the specimens came from you personally, that will be done.
(b) If the future research in a different area requires that it is known specifically who the specimens came from, then one of the following will be done:

(i) If you allowed the researchers to contact you in the future, they will be able to contact you to explain why your specimen is needed and what will be done with it. Your permission will be asked to use your specimens in that research project.

(ii) If you do not give permission to be contacted in the future, or if it is found that contacting you is not practical, for example, because you have moved, your specimens may still be used. Either all links to your identity will be removed from the specimens, or an Institutional Review Board will be asked for permission to use the specimens linked to your identity. The Institutional Review Board (IRB) is a committee of doctors and scientists and non-scientists and people not associated with this hospital or medical school whose job it is to protect people who participate in research. The IRB can give permission for researchers to use and share health information connected to specimens that are linked to people’s identities, but only if it determines that doing this will not be more than a minimal risk to people or their privacy.

(6) Do you give permission to have portions of the specimens given to other researchers at Mount Sinai or other institutions for use in research that is either related or not related to the purpose of this study? Please initial your choice:

Yes_________ No__________

As part of this study and do more powerful research (also in the future), it is helpful for researchers to share information they get from studying human samples. The scientific data collected in this study (but not your personal information such as name, address or social security number; see also below) will be deposited with the National Institutes of Health (an agency of the federal government) funded Data Coordination and Integration Center for the LINCS-BDK2 consortium, and possibly more scientific databases that may be maintained by Mount Sinai, by the federal government, or even by private companies, where it is stored along with information from other studies. Researchers can then study the combined information to learn even more about health and disease. A researcher who wants to study the information must adhere to rules set for by the Data Coordination and Integration Center for the LINCS-BDK2 consortium and conjunction with National Institutes of Health guidelines. Your name and other information that could directly identify you (such as address or social security number) will never be placed into a scientific database. However, because your genetic information is unique to you, there is a small chance that someone could trace it back to you. The risk of this happening is very small, but may grow in the future. Researchers will always have a duty to protect your privacy and to keep your information confidential.

In general, results from this research project will not be shared with you or put into your medical records. In some situations, the results (including genome sequencing results) might be important to your health or medical care. If this occurs, we will contact you to see if you want to learn more and if so refer you to your personal physician.

This Consent Document is approved for use by an Institutional Review Board (IRB)
Form Approval Date: 7/9/2015  DO NOT SIGN AFTER THIS DATE → 6/30/2016
Rev. 4/1/15
IRB Form HRP-502a
YOUR RESPONSIBILITIES IF YOU TAKE PART IN THIS RESEARCH:

If you decide to take part in this research study you will be responsible for the following things: undergoing a physical exam, an electrocardiogram and provide a blood sample for lab tests to establish your healthy status and only if such is confirmed to provide a skin sample, which will be obtained at a separate visit arranged at your convenience.

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

If you agree to take part in this research study, after completion of the skin punch biopsy, we will pay you $150 in cash as reimbursement for your time and effort.

Checks require some time to be prepared and will be given to you as available.

Tax law may require the Mount Sinai Finance Department to report the amount of payment you receive from Mount Sinai to the Internal Revenue Service (IRS) or other agencies, as applicable. Generally this reporting would take place if you receive payments that equal $600 or more from Mount Sinai in a calendar year. You would be responsible for the payment of any tax that may be due.

POSSIBLE BENEFITS:

You are not expected to get any benefit from taking part in this research study. Others may not benefit either. However, possible benefits to others include gaining valuable knowledge about specific drug and/or drug combinations and why they may be toxic on a molecular level to cells of the heart, liver and peripheral sensory system (neurons). Even if such knowledge is gained it will not be shared with you.

REASONABLY FORESEEABLE RISKS AND DISCOMFORTS:

The risks of a blood draw include pain, bruising, and the slight possibility of infection at the place where the needle goes in. Some people feel dizzy or may faint during or after a blood draw.

Possible risks and discomforts include those associated with obtaining the skin biopsy, which are bleeding, localized collection of blood outside the blood vessels, infection, and pain and/or physical discomfort at the time of the sampling. The sampling will be done during a routine clinic visit. Risks of the local anesthetic Lidocaine, used for skin biopsy, are pain at the site of sampling/injection. Additionally, lidocaine can pass very quickly through the placenta and reports exist of negative side effects on infants born to mothers using the anesthet. Several lidocaine studies with human case reports have showed no negative side effects, pregnancy complications or birth defects. In addition, there is minimal risk for an allergic reaction to the local anesthetic. However, allergic reactions are
immediate and since you will be watched by the study doctor during the procedure, the doctor can will watch for and treat any allergic reaction that may occur.

Group Risks

Although we will not give researchers your name, we will give them basic information such as your race, ethnic group, and sex. This information helps researchers learn whether the factors that lead to health problems are the same in different groups of people. It is possible that such findings could one day help people of the same race, ethnic group, or sex as you. However, they could also be used to support harmful stereotypes or even promote discrimination.

Privacy Risks

There always exists the potential for loss of private information; however, there are procedures in place to minimize this risk.

Your privacy is very important to us and we will use many safety measures to protect your privacy. However, in spite of all of the safety measures that we will use, we cannot guarantee that your identity will never become known. Although your genetic information is unique to you, you do share some genetic information with your children, parents, brothers, sisters, and other blood relatives. Consequently, it may be possible that genetic information from them could be used to help identify you. Similarly, it may be possible that genetic information from you could be used to help identify them.

As part of this study and do more powerful research (also in the future), it is helpful for researchers to share information they get from studying human samples. The scientific data collected in this study (but not your personal information such as name, address or social security number; see also below) will be deposited with the National Institutes of Health funded Data Coordination and Integration Center for the LINCS-BDK2 consortium, and possibly more scientific databases, where it is stored along with information from other studies. Researchers can then study the combined information to learn even more about health and disease. A researcher who wants to study the information must adhere to rules set for by the Data Coordination and Integration Center for the LINCS-BDK2 consortium and conjunction with National Institutes of Health guidelines.

Your name and other information that could directly identify you (such as address or social security number) will never be placed into a scientific database. However, because your genetic information is unique to you, there is a small chance that someone could trace it back to you. The risk of this happening is very small, but may grow in the future. Since the database includes genetic information, a break in security may also pose a potential risk to blood relatives as well as yourself. For example, it could be used to make it harder for you (or a relative) to get or keep a job or insurance. If your private information was misused it is possible you would also experience other harms, such as stress, anxiety, stigmatization, or embarrassment from revealing information about your family relationships, ethnic heritage, or health conditions.

People may develop ways in the future that would allow someone to link your genetic or medical information in our databases back to you. For example, someone could compare information in our databases with information from you (or a blood relative) in another database and be able to identify you (or your blood relative). It also is possible that there could be violations to the security of the computer systems used to store the codes linking your genetic and medical information to you.
Since some genetic variations can help to predict the future health problems of you and your relatives, this information might be of interest to health providers, life insurance companies, and others. Patterns of genetic variation also can be used by law enforcement agencies to identify a person or his/her blood relatives. Therefore, your genetic information potentially could be used in ways that could cause you or your family distress, such as by revealing that you (or a blood relative) carry a genetic disease.

There is a Federal law called the Genetic Information Nondiscrimination Act (GINA). In general, this law makes it illegal for health insurance companies, group health plans, and most large employers to discriminate against you based on your genetic information. However, it does not protect you against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

There also may be other privacy risks that we have not foreseen.

OTHER POSSIBLE OPTIONS TO CONSIDER:

You may decide not to take part in this research study without any penalty. The choice is totally up to you.

IN CASE OF INJURY DURING THIS RESEARCH STUDY:

If you believe that you have suffered an injury related to this research as a participant in this study, you should contact the Principal Investigator.

ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop taking part in this research study at any time without any penalty. This will not affect your ability to receive medical care at any of the Mount Sinai Health System hospitals or to receive any benefits to which you are otherwise entitled.

If you decide to stop being in the research study, please contact the Principal Investigator or the research staff.

You may also withdraw your permission for the use and disclosure of any of your protected information for research, but you must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use the information that was already collected if that information is necessary to complete the research study. Your health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from participating in the research study.

Withdrawal without your consent: The study doctor, the sponsor or the institution may stop your involvement in this research study at any time without your consent. This may be because the research study is being stopped, the instructions of the study team have not been followed, the investigator believes it is in your best interest, or for any other reason. If specimens or data have been stored as part of the research study, they too can be destroyed without your consent.
If you chose to end your participation in this study, all specimens, i.e. fibroblasts derived from the biopsy (skin sample) as well as the induced pluripotent stem cells generated from those fibroblasts can easily be discarded/destroyed.

CONTACT PERSON(S):

If you have any questions, concerns, or complaints at any time about this research, or you think the research has hurt you, please contact the office of the research team and/or the Principal Investigator at phone number (212)-659-1707 or Christoph Schaniel, Ph.D., at (212)-659-8276.

If you experience an emergency during your participation in this research, contact Dr. Jason Kovacic at (212)-241-7300.

This research has been reviewed and approved by an Institutional Review Board. You may reach a representative of the Program for Protection of Human Subjects at the Icahn School of Medicine at Mount Sinai at telephone number (212) 824-8200 during standard work hours for any of the reasons listed below. This office will direct your call to the right person within the Mount Sinai Health System:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You are not comfortable talking to the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

DISCLOSURE OF FINANCIAL INTERESTS:

Sometimes, physicians/researchers receive payments for consulting or similar work performed for industry. Effective September 2014 Mount Sinai reviews only payments to an individual totaling more than $5,000 a year per entity when determining potential conflicts of interest. If you have questions regarding industry relationships, we encourage you to talk your physician/researcher or visit our website at http://icahn.mssm.edu/ where Mount Sinai publicly discloses the industry relationships of our faculty.

MAINTAINING CONFIDENTIALITY – HIPAA AUTHORIZATION:

As you take part in this research project it will be necessary for the research team and others to use and share some of your private protected health information. Consistent with the federal Health Insurance Portability and Accountability Act (HIPAA), we are asking your permission to receive, use and share that information.

What protected health information is collected and used in this study, and might also be disclosed (shared) with others?
As part of this research project, the researchers will collect your name, address, telephone number, and medical record number at Mount Sinai Hospital. The researchers will also get information from your medical record at Mount Sinai Hospital.

During the study the researchers will gather information by:

- taking a medical history (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc.)
- doing a physical examination that generally also includes blood pressure reading, heart rate, breathing rate and temperature
- completing the tests, procedures, questionnaires and interviews explained in the description section of this consent.
- reviewing HIV-related information, which includes any information indicating that you have had an HIV related test, or have HIV infection, HIV related illness or AIDS, or any information which could indicate that you have been potentially exposed to HIV

Why is your protected health information being used?

Your personal contact information is important to be able to contact you during the study. Your health information and the results of any tests and procedures being collected as part of this research study will be used for the purpose of this study as explained earlier in this consent form. The results of this study could be published or presented at scientific meetings, lectures, or other events, but would not include any information that would let others know who you are, unless you give separate permission to do so.

The Principal Investigator may also use and share the results of these tests and procedures to treat you in collaboration with others in the Mount Sinai Health System.

The research team and other authorized members of The Mount Sinai Health System ("Mount Sinai") workforce may use and share your information to ensure that the research meets legal, institutional or accreditation requirements. For example, the School's Program for the Protection of Human Subjects is responsible for overseeing research on human subjects, and may need to see your information. If you receive any payments for taking part in this study, the Mount Sinai Finance Department may need your name, address, social security number, payment amount, and related information for tax reporting purposes. If the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.

Who, outside Mount Sinai, might receive your protected health information?

As part of the study, the Principal Investigator, study team and others in the Mount Sinai workforce may disclose your protected health information, including the results of the research study tests and procedures, to the following people or organizations: (It is possible that there may be changes to the list during this research study; you may request an up-to-date list at any time by contacting the Principal Investigator.)
In all disclosures outside of Mount Sinai, you will not be identified by name, social security number, address, telephone number or any other direct personal identifier unless disclosure of the direct identifier is required by law. Some records and information disclosed may be identified with a unique code number. The Principal Investigator will ensure that the key to the code will be kept in a locked file, or will be securely stored electronically. The code will not be used to link the information back to you without your permission, unless the law requires it, or rarely if the Institutional Review Board allows it after determining that there would be minimal risk to your privacy. It is possible that a sponsor or their representatives, a data coordinating office, a contract research organization, may come to inspect your records. Even if those records are identifiable when inspected, the information leaving the institution will be stripped of direct identifiers. Additionally, when applicable, the monitors, auditors, the IRB, the Office of Human Subjects Protection (OHRP) of the Department of Health and Human Services as well as the Food and Drug Administration (FDA) will be granted direct access to your medical records for verification of the research procedures and data. OHRP and FDA are authorized to remove information with identifiers if necessary to complete their task. By signing this document you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

For how long will Mount Sinai be able to use or disclose your protected health information? Your authorization for use of your protected health information for this specific study does not expire.

Will you be able to access your records?

During your participation in this study, you will not be able to access your medical records. This will be done to prevent the knowledge of study results from affecting the reliability of the study. Your information will be available should an emergency arise that would require your treating physician to know this information to best treat you. You will have access to your medical record and any study information that is part of that record when the study is over or earlier, if possible. The investigator is not required to release to you research information that is not part of your medical record.

Do you need to give us permission to obtain, use or share your health information?

NO! If you decide not to let us obtain, use or share your health information you should not sign this form, and you will not be allowed to volunteer in the research study. If you do not sign, it will not affect your treatment, payment or enrollment in any health plans or affect your eligibility for benefits.

Can you change your mind?

You may withdraw your permission for the use and disclosure of any of your protected information for research, but you must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use your protected information that was already collected if that information is necessary to complete the study. Your health information may still be used or shared after you withdraw your authorization if you should have an adverse event (a bad effect) from being in the study. If you withdraw your permission
THE MOUNT SINAI HEALTH SYSTEM
CONSENT FORM TO VOLUNTEER IN A RESEARCH STUDY
AND AUTHORIZATION FOR USE AND DISCLOSURE OF MEDICAL INFORMATION
Icahn School of Medicine at Mount Sinai,

Page 12 of 13

Study ID #: HSM14-00530 (GCO#:13-1953) Form Version Date: 6/29/2015
to use your protected health information for research that means you will also be withdrawn from the research study, but standard medical care and any other benefits to which you are entitled will not be affected. You can also tell us you want to withdraw from the research study at any time without canceling the Authorization to use your data.

If you have not already received it, you will also be given The Hospital’s Notice of Privacy Practices that contains more information about how The Hospital uses and discloses your protected health information.

It is important for you to understand that once information is disclosed to others outside Mount Sinai, the information may be re-disclosed and will no longer be covered by the federal privacy protection regulations. However, even if your information will no longer be protected by federal regulations, where possible, Mount Sinai has entered into agreements with those who will receive your information to continue to protect your confidentiality.

If as part of this research project your medical records are being reviewed, or a medical history is being taken, it is possible that HIV-related information may be revealed to the researchers. If that is the case, the following information concerns you. If this research does not involve any review of medical records or questions about your medical history or conditions, then the following section may be ignored.

________________________________________________________________________________
Notice Concerning HIV-Related Information
If you are authorizing the release of HIV-related information, you should be aware that the recipient(s) is (are) prohibited from re-disclosing any HIV-related information without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (888) 392-3644 or the New York City Commission on Human Rights at (212) 306-5070. These agencies are responsible for protecting your rights.

________________________________________________________________________________
Study ID #: HSM14-00530 (GCO#:13-1953)
Form Version Date: 6/29/2015

Signature Block for Capable Adult

Your signature below documents your permission to take part in this research and to the use and disclosure of your protected health information. A signed and dated copy will be given to you.

DO NOT SIGN THIS FORM AFTER THIS DATE  
6/30/2016

____________________
Signature of subject

____________________
Printed name of subject

____________________
Date

____________________
Time

[required if used for FDA documentation purposes]

Person Explaining Study and Obtaining Consent

____________________
Signature of person obtaining consent

____________________
Date

____________________
Printed name of person obtaining consent

____________________
Time

Witness Section: For use when a witness is required to observe the consent process, document below (for example, subject is illiterate or visually impaired, or this accompanies a short form consent):

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject, and that consent was freely given by the subject.

____________________
Signature of witness to consent process

____________________
Date

____________________
Printed name of person witnessing consent process

____________________
Time
TITLE OF RESEARCH STUDY:

Title: Drug Combination Signatures for Prediction and Mitigation of Toxicity

PRINCIPAL INVESTIGATOR (HEAD RESEARCHER) NAME AND CONTACT INFORMATION:

Name: Ravi Iyengar

Physical Address: Icahn Medical Institute, building 12-70C

Mailing Address: 1 Gustave L Levy Place, Box 1215, NY, NY 10029

Phone: 212-659-1707

INFORMATION ABOUT HIV ANTIBODY TESTING:

You have been asked to participate in a research study, for which you have signed a separate consent. As indicated on that consent, part of your participation in that study will involve undergoing an HIV antibody test. This consent is specifically for the HIV antibody test. The HIV antibody test is a blood test used to ascertain whether you have antibodies to the Human Immunodeficiency Virus (HIV), the virus which causes Acquired Immunodeficiency Syndrome (AIDS). Less than one teaspoon of blood will be drawn from a vein in your arm using a needle. This may cause some discomfort and you may develop a black and blue mark. It takes approximately one to two weeks between the time your blood is drawn and the time you are notified of the results.

Both before and after your blood is tested, you will receive counseling from trained HIV counselors involved in this research project about the implications of negative and positive results, how to prevent future transmission, and the options available to you. Your partners may be notified of the results of this test and urged to undergo testing as well. If you do not want to tell them, or you will not tell them, your doctor or local health official can inform them that a partner of theirs has been tested and what the results of the test were, but only if the doctor feels that telling them is medically appropriate. You will not incur any costs nor receive any payment for participating in this part of the study.

A positive HIV antibody test means that your body is making antibodies to HIV but it does not mean that you will necessarily develop AIDS in the future. A negative test means that you are probably not infected; however, it is possible that you may be infected but that your body has not produced antibodies to HIV. If your results are negative and you have been exposed to HIV recently, you should be retested in a few months to make sure you are not infected.

There are several possible benefits to taking the HIV antibody test. If your test results are negative, you can learn how to avoid becoming infected in the future. If your results are positive, you can learn how to avoid infecting other individuals, and if you are pregnant, or are thinking about having children, you can learn how being HIV positive will affect your decision to have children. Additionally, we can offer you enrollment in a wide variety of research projects for the treatment of AIDS or refer you to a doctor for non-experimental treatment.

This is a voluntary procedure, and all results, either positive or negative, are confidential. Under New York State law, information about your HIV antibody test can only be released to people who you designate by signing a release form, or to those people listed below:

a) You (or a person authorized by law who consented to the test for you);
b) To a health care facility (such as a hospital, blood bank, or clinical laboratory) or a health care provider (such as a physician, nurse, or mental health counselor) providing care to you or your child, and anyone working for such a facility or provider who reasonably needs the information to supervise, monitor or administer health care;

c) To a person whom your doctor believes is at significant risk for HIV infection, if you do not notify that person after being counseled to do so;

d) To a committee or organization responsible for reviewing or monitoring a health facility;

e) To a federal, state, county, or local health officer when state or federal law requires disclosure;

f) To a government agency, when the agency needs the information to supervise, monitor, or administer a health or social service;

g) To an authorized foster care or adoption agency;

h) To insurance companies and other third party payers such as Medicaid necessary for the payment of services to you;

i) To any person whom a court orders disclosure under limited circumstances set forth by law. Except in an emergency situation, advance notice and an opportunity to oppose the release of such information would be given to you;

j) To the Division of Parole, the Division of Probation, the Commission of Correction, or a medical director of a local correctional facility, as permitted by HIV confidentiality regulations of such organization.

k) By a physician to someone who may consent to health care for you if you have been counseled and won't inform such person and disclosure is medically necessary to provide timely care and treatment. Disclosure must not be against your best interest.

If you do not want anybody to know your tests results or that you have been tested, you can go to an anonymous test site. This is a place where you can have your blood tested and receive counseling without having to tell anybody your name or address. You can find the nearest anonymous test site by calling the AIDS Hotline at 1-(800)-541-2437.

If your results are positive, you should be very careful who you disclose this information to. Some HIV positive people have been discriminated against by landlords, employers, and the like. If you believe you have been discriminated against, you should call the New York State Division of Human Rights at (888) 392-3644 or the New York City Commission on Human Rights at (212) 306-5070. If you have any further questions regarding AIDS or HIV antibody testing, you can contact the New York State Department of Health AIDS Hotline at 1-(800) -TALK-HIV / 1-(800)-825-5448.
Study ID #: HSM14-00530 (GCO#:13-1953)  Form Version Date: 6/4/15

Signature Block for Capable Adult

Your signature below documents your permission for HIV Antibody Testing, pre-test counseling, post-test counseling and for a blood draw of less than one teaspoon of blood, one time from me. A signed and dated copy will be given to you.

DO NOT SIGN THIS FORM AFTER THIS DATE  →  06/30/2016

Signature of subject  Date and Time

Printed name of subject

Person Explaining Study and Obtaining Consent

Signature of person obtaining consent  Date and Time

Printed name of person obtaining consent

If the individual cannot read, a witness is required to observe the consent process and document below:

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject, and that consent was freely given by the subject.

Signature of witness to consent process  Date and Time

Printed name of person witnessing consent process

This Section For IRB Official Use Only

This Consent Document is approved for use by Mount Sinai’s Institutional Review Board (IRB)

Form Approval Date:  07/01/2015  DO NOT SIGN AFTER THIS DATE  →  06/30/2016

Rev. 4/15/14  IRB Form HRP-507a
# Drug Combination Signatures for Prediction and Mitigation of Toxicity

## ENROLLMENT FORM

<table>
<thead>
<tr>
<th>Pt. Initials</th>
<th>Pt. ID Number</th>
<th>Date: / / (mm/dd/yyyy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[98x754]</td>
<td>[58x691]</td>
<td>[58x651]</td>
</tr>
</tbody>
</table>

### INCLUSION CRITERIA

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient ≥18 and ≤65 years of age and freely willing to participate</td>
<td></td>
</tr>
<tr>
<td>Signed written Informed Consent</td>
<td></td>
</tr>
</tbody>
</table>

### EXCLUSION CRITERIA

<table>
<thead>
<tr>
<th>Abnormal EKG</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Any family history of any cardiovascular disorder, excluding hypertension, in any first or second degree relative(s), at age &lt; 50. This includes stroke, myocardial infarction, angina, peripheral vascular disease, aortic dissection, aortic aneurysm, vasculitis, vasculopathy</td>
<td></td>
</tr>
<tr>
<td>Any family history of non-ischemic cardiomyopathy in any first or second degree relative(s), at any age</td>
<td></td>
</tr>
<tr>
<td>More than 2 pack-year of lifetime smoking</td>
<td></td>
</tr>
<tr>
<td>Positive for: HIV, Hepatitis B, Hepatitis C</td>
<td></td>
</tr>
<tr>
<td>Pts. who are currently participating in another investigational drug/device study</td>
<td></td>
</tr>
<tr>
<td>Patients with liver disease</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
</tr>
<tr>
<td>Pregnant women and/or nursing mothers</td>
<td></td>
</tr>
<tr>
<td>Patients having undergone heart transplantation or any other organ transplantation.</td>
<td></td>
</tr>
<tr>
<td>Personal or family history of neuropathy, at any age in a first or second degree relative, with the exception of diabetic neuropathy in another family member over the age of 60 at first diagnosis</td>
<td></td>
</tr>
<tr>
<td>Personal or family history of myopathy, at any age in a first or second degree relative</td>
<td></td>
</tr>
<tr>
<td>Body Mass Index ≥ 30 kg/m²</td>
<td></td>
</tr>
<tr>
<td>Creatinine ≥ 1.3 mg/dL or known renal disease</td>
<td></td>
</tr>
<tr>
<td>Abnormal Chem14 panel, renal function or liver function studies</td>
<td></td>
</tr>
<tr>
<td>Abnormal BNP (Brain natriuretic peptide)</td>
<td></td>
</tr>
<tr>
<td>Abnormal hemoglobin, platelet count or white cell count</td>
<td></td>
</tr>
<tr>
<td>Other disorders, clinically manifest or detected by screening labs, that are associated with cardiovascular disease, including but not limited to hemochromatosis, hyperthyroidism or hypothyroidism.</td>
<td></td>
</tr>
<tr>
<td>Active autoimmune disease</td>
<td></td>
</tr>
<tr>
<td>Taking any medications other than occasional aspirin, occasional NSAIDS, occasional acetaminophen or the oral contraceptive pill.</td>
<td></td>
</tr>
<tr>
<td>Asthma requiring any regularly inhaled therapy</td>
<td></td>
</tr>
<tr>
<td>Epilepsy requiring any form of ongoing therapy (medication or other)</td>
<td></td>
</tr>
</tbody>
</table>
Drug Combination Signatures for Prediction and Mitigation of Toxicity

**DEMOGRAPHICS**

Date of Birth: _____/____/________ (mm/dd/yyyy)  
Gender: □ Male  □ Female

Race: □ Caucasian  □ Hispanic  □ Asian  □ Other (specify) ___________
□ African-American

**Social History:**

Tobacco Use:
□ Never
□ Quit; total duration _______________
□ Current; total duration _______________

**Other Clinical History:**
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________

**EXAMINATION:**

Weight: ________ kg/lbs ; Height: ________cm/inches; Waist: ________cm/inches; Hip: ________ cm/inches
Heart Rate: _______ /min  
Blood Pressure: _____/____ mm of Hg
Respiratory Rate: _______/min
Oxygen saturation (on room air): _______%
Cardiovascular Exam:
JVP:
Carotid bruits:
Apex beat:
Auscultatory findings:
Palpable AAA:
Pedal pulses:
Pedal edema:

Respiratory Exam:
Clubbing:
Upper airway:
Trachea midline:
Chest expansion:
Auscultation:

GI/Abdominal Exam:
Sclerae (jaundice):
Spider naevi:
Abdominal distension:
General palpation:
Liver:
Spleen:
Auscultation:

Neurological Exam:
Sit to stand without using upper limbs:
Screening cranial nerve exam:
Screening upper limb (light touch, tone, strength flexion and extension):
Screening lower limb (light touch, tone, strength flexion and extension):
Neurofilament (great toe):

LABORATORY RESULTS:

<table>
<thead>
<tr>
<th>Date of collection: <em><strong>/</strong></em>/______ (mm/dd/yyyy)</th>
<th>Time: <strong><strong>:</strong></strong> (24-hr clock)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>65-139 mg/dL</td>
</tr>
<tr>
<td>Sodium</td>
<td>135-145 MEQ/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.5 – 5.0 MEQ/L</td>
</tr>
<tr>
<td>Chloride</td>
<td>96-108 MEQ/L</td>
</tr>
<tr>
<td>CO2 total</td>
<td>22 – 32 MEQ/L</td>
</tr>
<tr>
<td>Urea Nitrogen</td>
<td>10 – 30 mg/dL</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.6 – 1.4 mg/dL</td>
</tr>
<tr>
<td>eGFR African Am</td>
<td>&gt;60 ml/min/1.73m²</td>
</tr>
<tr>
<td>eGFR non African Am</td>
<td>&gt;60 ml/min/1.73m²</td>
</tr>
<tr>
<td>Calcium</td>
<td>8.5 – 10.5 mg/dL</td>
</tr>
<tr>
<td>ALT</td>
<td>1 – 53 U/L</td>
</tr>
<tr>
<td>AST</td>
<td>1 – 50 U/L</td>
</tr>
<tr>
<td>Bilirubin total</td>
<td>0.1 – 1.2 mg/dL</td>
</tr>
<tr>
<td>Alk Phos</td>
<td>30 – 110 U/L</td>
</tr>
</tbody>
</table>
**Drug Combination Signatures for Prediction and Mitigation of Toxicity**

<table>
<thead>
<tr>
<th>Albumin</th>
<th>3.5 – 4.9 g/dL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein total</td>
<td>6.0 – 8.3 g/dL</td>
</tr>
</tbody>
</table>

**CBC & Platelets Differential:**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHITE BLOOD CELL</td>
<td>4.5-11.0 / x10 3/uL</td>
</tr>
<tr>
<td>RED BLOOD CELL</td>
<td>4.50-6.00 / x10 6/uL</td>
</tr>
<tr>
<td>HEMOGLOBIN</td>
<td>13.9-16.3 / G/DL</td>
</tr>
<tr>
<td>HEMATOCRIT</td>
<td>42.0-52.0 / %</td>
</tr>
<tr>
<td>MEAN CORP. VOLUME</td>
<td>80.0-98.0 / FL</td>
</tr>
<tr>
<td>MEAN CORP. HGB</td>
<td>27.0-32.0 / PG</td>
</tr>
<tr>
<td>MEAN CORP. HGB CONC.</td>
<td>32.0-35.0 / G/DL</td>
</tr>
<tr>
<td>RED DISTRIBUT. WIDTH</td>
<td>11.5-15.0 / %</td>
</tr>
<tr>
<td>PLATELET</td>
<td>150-450 / x10 3/uL</td>
</tr>
<tr>
<td>MEAN PLT VOLUME</td>
<td>7.4-12.0 / FL</td>
</tr>
<tr>
<td>NEUTROPHIL %</td>
<td>40.0-78.0 / %</td>
</tr>
<tr>
<td>LYMPHOCYTE %</td>
<td>15.0-50.0 / %</td>
</tr>
<tr>
<td>MONOCYTE %</td>
<td>2.0-11.0 / %</td>
</tr>
<tr>
<td>EOSINOPHIL %</td>
<td>0.0-5.0 / %</td>
</tr>
<tr>
<td>BASOPHIL %</td>
<td>0.0-1.0 / %</td>
</tr>
<tr>
<td>NEUTROPHIL #</td>
<td>1.9-8.0 / x10 3/uL</td>
</tr>
<tr>
<td>LYMPHOCYTE #</td>
<td>1.0-4.5 / x10 3/uL</td>
</tr>
<tr>
<td>MONOCYTE #</td>
<td>0.2-1.0 / x10 3/uL</td>
</tr>
<tr>
<td>EOSINOPHIL #</td>
<td>0.0-0.6 / x10 3/uL</td>
</tr>
<tr>
<td>BASOPHIL #</td>
<td>0.0-0.2 / x10 3/uL</td>
</tr>
<tr>
<td>NUCLEATE RBC%</td>
<td>0.0-0.0 / %</td>
</tr>
<tr>
<td>NRBC#</td>
<td>0.0-0.0 / x10 3/uL</td>
</tr>
</tbody>
</table>

**Heart Failure, endocrine and other:**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BNP</td>
<td>0 – 100 pg/ml</td>
</tr>
<tr>
<td>Ferritin</td>
<td>30 – 400 ng/ml</td>
</tr>
<tr>
<td>Transferrin Sat</td>
<td>15 – 50%</td>
</tr>
<tr>
<td>HBA1C</td>
<td>4.0 – 6.0%</td>
</tr>
<tr>
<td>TSH</td>
<td>0.34 – 5.6 uIU/MI</td>
</tr>
</tbody>
</table>

**Infectious:**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV</td>
<td></td>
</tr>
<tr>
<td>HepC</td>
<td></td>
</tr>
<tr>
<td>HebB sAG</td>
<td></td>
</tr>
</tbody>
</table>
**Drug Combination Signatures for Prediction and Mitigation of Toxicity**

<table>
<thead>
<tr>
<th>HepB sAB</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>HepB cAB</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Other Labs:**

**Date of collection:** __/__/____ _ (mm/dd/yyyy)  **Time:** _______________(24-hr clock)

**Pregnancy Test:**
- [ ] Positive
- [ ] Negative
- [ ] Not Applicable [If male/Post menopausal/sterile female]

**ECG Date:** __/__/____ _ (mm/dd/yyyy)  **Time:** __ : ___ (24-hr clock)

**ECG comments:**

________________________________________________________

________________________________________________________

Clinician Name: _______________________________

Clinician Signature: ___________________________ **Date:** ___ / _____ / ______ (mm/dd/yyyy)

Investigator’s Signature: ______________________________ **Date:** ___ / _____ / ______ (mm/dd/yyyy)