Clinical Pharmacology and Target Validation of A Bioactive Dietary Polyphenol Preparation (BDPP) For Stress-Related Disorders

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STUDY INFORMATION:

Study Title: Clinical Pharmacology and Target Validation of BDPP for Stress-Related Disorders

Study site(s): Icahn School of Medicine at Mount Sinai, Mount Sinai Hospital

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SUMMARY OF THIS RESEARCH STUDY:

In medicine, there are many unanswered questions. A research study is when scientists try to answer a question about something that we don't know enough about. Participation in a research study may or may not directly help you or others. Participation is entirely voluntary. It is completely up to you whether or not you take part. You can also change your mind at any time and it will not affect your ability to get medical care within the Mount Sinai Health System.

Psychological stress is experienced widely throughout society and is associated with increased risk for the development of psychiatric disorders, in particular stress-related disorders such as major depressive disorder. As the majority of individuals who experience psychological stress do not develop these disorders, identifying mechanisms that promote resilience is of importance. Resilience means 'bouncing back' from a difficult experience. Current evidence suggests that our body's inflammatory response to stress may play a role in this resilience.

Polyphenols are a category of compounds typically found in plants that are thought to have anti-inflammatory effects. The purpose of this research study is to investigate how the body takes in and breaks down a polyphenol rich preparation called Bioactive Dietary Polyphenol Preparation (BDPP) as well is its effects on inflammation within the body compared to a placebo, an identical pill with no active substance.

This polyphenol rich preparation (BDPP) is made up of multiple ingredients including commercially available Concord grape juice (CGJ), a select grape seed polyphenol extract (GSPE) and trans-resveratrol (RSV).

If you choose to participate, you will be asked to complete 7 in-person visits, lasting between 1 and 6 hours, over the course of roughly 10 weeks. During the appointments, you will complete interviews,

clinical self-report scales, blood draws and urine collections. One of the visits will also include a stress task in which you will be interviewed by a panel.

You will be randomly (by chance, like the flip of a coin) assigned to a low, medium or high dose of BDPP or to a placebo which you will be asked to take daily over the course of 5 weeks. The BDPP supplement consists of taking 2 pills and an 8 oz drink once, twice, or three times a day depending on your dosage. The placebo also consists of two pills and a juice taken once, twice, or three times a day that do not contain BDPP and have no effect on the body. Neither you nor the study team will know if you have been assigned to the BDPP or placebo groups.

There are no costs associated with participation. You will be compensated for each study visit you complete.

The main risks to you if you choose to participate are discomfort associated with having blood draw and with questionnaires or interviews. The dietary supplement (BDPP) has not been associated with any side effects in previous studies but there may be unforeseen effects.

If you participate in this study, you are not expected to receive any direct benefit.

If you are interested in learning more about this study, please continue to read below.

STUDY PARTICIPATION:

This research study will be fully explained to you by a member of the study team. Feel free to ask all the questions you want before you make a decision about whether or not to participate. Any new information that develops during this research study that might make you change your mind about participating will be given to you promptly.

You may qualify to take part in this research study because you are a healthy volunteer, do not have a present or past diagnosis of a psychiatric disorder, and are willing and able to participate in this study.

Funds for conducting this research are provided by the National Center for Complementary and Integrative Health (NCCIH).

Some biological samples collected as part of this study (i.e. blood and urine) will be analyzed at Rutgers University and Metware, Inc. All identifiable information, including your name, date of birth, or contact information, will be removed from these samples.

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.

DESCRIPTION OF WHAT IS INVOLVED:

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

After receiving complete disclosure about the research and being given the opportunity to fully review the consent form, you will also be given the opportunity to ask questions. If you choose to take part in the study, you will be asked to sign this written consent form.

These visits can take place either at the Clinical Research Unit (CRU) located in 1468 Madison Ave, the Infusion suite located in the 5th floor of 1425 Madison Ave, or the DAC offices at 1399 Park Ave. Portions of the study visits can occur at home, as noted in the description below. The research staff will ensure the size are properly notified of the location before a study visit.

- ***Screening (1-3 visits; 3-5 hours):***

  A study team member will ask questions about your health and complete tests to see if you are eligible for this study. This is called the “screening visit” and the following examinations will be completed during this visit, with the expectation of this taking about 3 to 5 hours:

  o Rating scales: Research personnel will conduct assessments to determine the presence of any current or past psychiatric symptoms.

  o Medical, Psychiatric, and Personal History: Research personnel will ask you questions about your medical and psychiatric history, medications you have taken, and your family psychiatric history. You will also be asked if you have any planned surgeries or other medical procedures.

  o Physical examination: A study doctor will check you for general signs of disease.

  o Vital signs: Your heart rate, blood pressure, respiratory rate, height, and weight will be recorded.

  o Blood draw: A blood sample (14ml, approximately 3 teaspoons) will be drawn from a vein in your arm. This blood sample will be used for routine laboratory test (blood count, electrolytes, thyroid function, liver function, etc.). The study team will also compete a finger stick test of your blood sugar levels.

- Urine sample: You will be asked to pee into a cup. This urine sample will be used for determining how your body is breaking down and taking in polyphenol from your current diet, routine analysis, testing if you are pregnant, to test for illegal drugs. If you test positive for pregnancy or illegal drugs, you may be unable to participate in the study.

- Questionnaires: The research staff will ask that you complete self-report questionnaires to evaluate any symptoms of depression, anxiety, and stress. A questionnaire will also be given to evaluate your average diet.

- Diet: Study participants will be asked to limit their consumption of foods high in polyphenols throughout the course of the study. Foods known to be high in polyphenols include tea, red wine, fruit juice, coffee, whole grains, and fruit.

- Salivary sample: You will be provided with 4 cotton-based standardized sampling tubes and a standardized instruction sheet for salivary collection to measure salivary cortisol, a stress related hormone.

- 24-hour urine collection: If you are deemed eligible, the study team will ask you to complete a 24-hour urine collection which will be brought to your visit 1 appointment. You will be provided with instructions on how to complete this collection.

If you are already participating in and/or have already completed screening assessments under the screening protocol “A Screening Protocol for Adult Patients with Mood and Anxiety Disorders, Chronic Medical Conditions, and Healthy Volunteers” (GCO: 06-0945; PI Dr. Murrough), and these assessments have been completed within 6 months of signing the consent for this protocol, you do not need to repeat these assessments.

The screening period may last from 1 day up to 4 weeks. If you meet all eligibility criteria you can go on to the next phase.

- **Visit 1 (Week 0; 6-7 hours):**

At this visit you will be randomized to the study treatment. The study treatment you get will be chosen by chance, like pulling names out of a hat. You will have a one in four chance of being given each experimental treatment (low, intermediate or high dose of BDPP or placebo). Neither you nor the study doctor will know which experimental study treatment you are getting; however, this information could be obtained in an emergency.

Roughly 48 hours ahead of this visit, the study team will email you a link to a survey. With this survey, you will catalogue your diet over the course of one day.

You will be asked to fast ahead of this visit. This fast will begin at midnight the night before this appointment and will continue until the 2-hour mark of the blood collection described below.

At this visit, you will complete self-report questionnaires which will measure any symptoms of depression, anxiety, or stress. Your vital signs (i.e. heart rate, blood pressure, height, weight) will be recorded, a urine sample will be collected, and you will meet with a study physician to review any changes in your health that may have occurred since the previous visit. The study team will also compete a finger stick test of your blood sugar levels.

Ahead of the first administration of study dietary supplement/placebo, a study nurse will place an IV in a vein in your arm, which will be used to draw blood over the course of six hours. An initial blood draw (40 ml, approximately 3 tablespoons) will occur before the first study medication dosage for routine laboratory testing and to test the effect of the bioactive polyphenol supplement on inflammation and various immune cells. This blood draw will also be used to explore your RNA (how your body is expressing your genetics), to broadly characterize your metabolism (i.e. how your body breaks down foods), and to examine how your genetic expression might impact how your body breaks down food.

Subsequent blood draws (6 ml, approximately 1 teaspoon each) will occur 0.5, 1, 2, 3, 4, and 6 hours after administration of study dietary supplement/placebo, to test for the levels of the study supplement within your blood. An additional 6ml blood draw will be performed 4 hours following the supplement/placebo administration to test the level of blood inflammatory hormones. The total amount of blood draw at this visit will be roughly 82 ml or 6 tablespoons.

You will also be provided with a urine collection vessel and given instructions for a 24 hours urine collection to measure how your body breaks down the dietary supplementation.

You will be provided with 2 weeks of study dietary supplementation or placebo, which you will asked to take daily.

You will be provided a survey link that can be used to record your consumption of the study dietary supplement/placebo. A study team member may call you one week following this visit to review your study compliance and any concerns you have.

Visit 1a (24hrs follow-up; 30-60min):

This visit will take place the day following Visit 1 to complete a blood draw (12 ml, approximately 1 tablespoon) 24 hours following your first administration of study dietary supplement/placebo and prior to the morning dose of the study dietary supplementation or placebo to test for the levels of the study medication within your blood and to test the level of blood inflammatory hormones. At this visit, you will also drop-off the 24 hour urine collection.

Visit 2 (Week 2; 30 – 60 min):

At this visit, you will complete self-report questionnaires to measure any symptoms of depression, anxiety, or stress, and you will meet with a study physician to review any changes in your health that may have occurred since the previous visit.

You will be provided with 2 weeks of study dietary supplementation or placebo, which you will asked to take daily.

If necessary, this visit may be completed remotely via a HIPAA compliant video platform with all surveys sent via an email link.

You will also be provided a survey link that can be used to record your consumption of the study dietary supplement/placebo. A study team member may call you one week following this visit to review your study compliance and any concerns you have.

Visit 3 (Week 4; 6-7 hours):

At this visit, you will complete self-report questionnaires to measure any symptoms of depression, anxiety, or stress. Your vital signs (i.e. heart rate, blood pressure, height, weight) will be recorded, a urine sample will be collected, and you will meet with a study physician to review any adverse events that may have occurred since the previous visit. The study team will also compete a finger stick test of your blood sugar levels.

Roughly 48 hours ahead of this visit, the study team will email you a link to a survey. With this survey, you will catalogue your diet over the course of one day.

You will be asked to fast ahead of this visit. This fast will begin at midnight the night before this appointment and will continue until the 2-hour mark of the blood collection described below.

Ahead of the daily administration of study dietary supplement/placebo, a study nurse will place an IV in a vein in your arm, which will be used to draw blood over the course of six hours. An initial blood draw (40 ml, approximately 3 tablespoons) will occur before the study medication dosage for routine laboratory testing in order to test the level of inflammatory markers, and examine the effects of polyphenol intake on your immune cells, and characterize your metabolism (i.e. how your body breaks down foods). This blood draw will also be used to explore your RNA (how your body is expressing your genetics) and to examine how your genetic expression might impact how your body breaks down food.

Subsequent blood draws (6 ml, approximately 1 teaspoon each) will occur 0.5, 1, 2, 3, 4, and 6 hours after administration to test for the levels of the study medication within your blood. An additional 6ml blood draw will be performed 4 hours following the supplement/placebo administration to test the level of blood inflammatory hormones. The total amount of blood draw at this visit will be roughly 82 ml or 6 tablespoons.

You will also be provided with a urine collection vessel and given instructions for a 24 hours urine collection to measure how your body breaks down the dietary supplementation.

You will be provided with 1 weeks of study dietary supplementation or placebo, which you will asked to take daily.

Visit 3a (24hrs follow-up; 30-60min):

This visit will take place the day following Visit 3 to complete a blood draw (12 ml, approximately 1 tablespoon) 24 hours following your first administration of study dietary supplement/placebo and prior to the morning dose of the study dietary supplementation or placebo to test for the levels of the study medication within your blood and to test the level of blood inflammatory hormones. At this visit you will also drop-off the 24hrs urine collection.

Visit 4 (Week 5; 4 hours):

At this visit, you will complete self-report questionnaires to assess any symptoms of depression, anxiety, or stress. Your vital signs (i.e. heart rate, blood pressure, height, weight) will be recorded, a urine sample will be collected, and you will meet with a study physician to review any side effects that may have occurred since the previous visit. The study team will also compete a finger stick test of your blood sugar levels.

Roughly 48 hours ahead of this visit, the study team will email you a link to a survey. With this survey, you will catalogue your diet over the course of one day.

Ahead of the daily administration of study dietary supplement/placebo, a study nurse will place an IV in a vein in your arm, which will be used to draw blood over the course of 2 hours.

A blood draw (12 ml, approximately 1 tablespoon) will be performed prior to the morning dose of dietary supplementation or placebo for routine laboratory testing, to assess inflammation markers, and to test for the levels of the study medication within your blood.

Also, at this visit, you will undergo a stress task which involves an interview in front of a panel lasting about 10 minutes. At the end of the visit, a study team member will debrief you and you will be able to ask questions. However, if you feel too uncomfortable or distressed at any point during this visit, the study procedures will be stopped, and you will be exited from the study.

Following the stress test, you will be asked to complete a series of surveys at various time points (0, 15, 30, 45, and 60 minutes). Levels of inflammatory markers will also be assessed at various time points through saliva and blood collection (0, 15, 30, 45, 60, 90, and 120 minutes) (approximately 6 ml or 1 teaspoon of blood to be collected at each time point).

The total amount of blood draw at this visit will be roughly 54 ml or 4 tablespoons.

You will be instructed by the study team to stop taking the BDPP supplement/placebo following this visit.

Exit Visit (Week 6; 1 -2 hours):
At this final visit, you will complete self-report questionnaires to measure any symptoms of depression, anxiety, or stress and will be asked questions about your mental and physical health. Your general health we be assessed by a physical exam, and vital signs. Blood will also be drawn at this visit (25 ml or approximately 2 tablespoons) for routine laboratory tests, to determine levels of inflammatory markers within your blood, and to determine the levels of study supplement within your blood. A urine sample will be used for routine analysis, to test if you are pregnant, and to test for illegal drugs. If you test positive for pregnancy or illegal drugs, a note will be made in your research record.

Once this visit is over, your participation in the study will be complete and you will be considered exited from the study.

Electronic Medical Record

Because this project involves the use of an oral dietary supplement, it is necessary that we make a note of your participation in the electronic medical record. That way anyone treating you will be aware of your participation and may be able to avoid any unfortunate outcomes that could arise if your research participation were unknown.

Optional*:* Would you like to receive text reminders to take your medication once, twice, or three times daily based on your treatment assignment (to be delivered at approximately 9am, 1pm, and 5pm)? Please initial below with your choice.

_____**Yes,** I would like to receive text messages three times per day as a reminder.

_____ **No,** I would not like to receive text messages three times per day as a reminder.

Randomization

No one, not you, or anyone from your medical team or from the research team will be able to choose what group you are assigned to or what study supplement or placebo you get. It will be by chance, like pulling names out of a hat. *You will have a one in four chance of being given each experimental treatment (low, intermediate or high dose of BDPP or placebo). Neither you nor the study doctor will know which experimental study treatment you are getting; however, this information could be obtained in an emergency.*

Pregnancy

If you can possibly get pregnant, a urine drug test for pregnancy will be done before you begin the study and the pregnancy test will be repeated at the exit visit.

You cannot be included in the study if you are or become pregnant, as the study supplement could harm your fetus. You also should not be in the study if you are producing milk to feed a child as the study supplement could harm your baby.

Unless you are at least one year past menopause or have had a successful operation to make pregnancy impossible, you should use effective birth control. Unless you are sexually abstinent (not having genital sex) the recommended methods of birth control are:

- The consistent use of approved hormonal birth control (pill, patches, or rings),
- An intrauterine device (IUD),
- Contraceptive injection (Depo-Provera),
- Double barrier methods (Diaphragm with spermicidal gel or condoms with contraceptive foam),
- Sexual abstinence (no sexual activity),
- Sterilization (a vasectomy, getting tubes tied, or a hysterectomy).

Hormonal birth control, implants, and injections are only considered effective if used properly and started at least one month before you begin the study, continuing throughout the study and for one month after the end of the study. You should ask your study doctor if you should continue birth control for longer than 30 days after the end of the study. If you are unsure whether the method of birth control you use is acceptable to use while participating in this study, you should ask your study doctor before you begin the study. If you are less than one year post-menopausal, there is the potential that you could become pregnant.

If you or your partner becomes pregnant, or may be pregnant, at any time during the trial, it is important that you tell your study doctor immediately. The trial drug may be stopped, and a referral may be made to an obstetrician/gynecologist for follow-up. If you plan to become pregnant in the year following a clinical trial, speak with your study doctor.

Should you/your partner become pregnant, whether or not you/your partner have the baby, the people funding and overseeing the research may ask for information on the pregnancy, even if you are no longer part of the study. You/your partner will be asked for additional written consent to share this information if that happens.

Semen/Sperm:

Drugs can be found in semen and alter sperm. Since you are taking part in a study using experimental drugs or treatments, it is recommended that 1) you use a condom, 2) you do not get a partner pregnant or expose them to semen, and 3) you do not donate semen. These recommendations apply both while

you are taking the study drug, and for 3 months after you stop taking the study drug . This is because levels of the study drug may be present in the sperm and/or semen even after you stop taking the study drug. You are encouraged to tell your female partner(s) and/or their doctor(s) that you are participating in this clinical trial.

USE OF YOUR DATA AND/OR SAMPLES:

Some biological samples collected as part of this study (i.e. blood and urine) will be analyzed at Rutgers University and Metware, Inc. All identifiable information, including your name, date of birth, or contact information, will be removed from these samples.

In the future, your identifiable information may be removed from the private information and/or samples that are collected as part of this research. After this removal, the information and/or samples could be used for future research studies or shared with other research teams for future research studies. You will not be informed of the details of specific research that is done with your medical information and biospecimens. That means that a research project might be done that you would not consent to if provided with the details of that research project. Future research may or may not be related to this project, your specimens remain linked to your identifiable information by a code. These data/specimens may also be shared with commercial entities or deposited into a large public repository.

To do more powerful research, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or 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. If you agree to take part in this study, some of your genetic and health information might be placed into one or more scientific databases. There are many different kinds of scientific databases; some are maintained by Icahn School of Medicine at Mount Sinai or another institution, some are maintained by the federal government, and some are maintained by private companies. For example, the National Institutes of Health (an agency of the federal government) maintains a database called “dbGaP.” A researcher who wants to study the information must apply for permission to use the database. Different databases may have different ways of reviewing such requests. Researchers with an approved study may be able to see and use your information, along with that from many other people. Researchers will always have a duty to protect your privacy and to keep your information confidential, but there are risks associated with data collection and sharing. They are described in more detail in the risks section.

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:

- Come to all study visit appointments and be available for any telephone appointments
- Complete questionnaires yourself and participate in interviews several times
- Do not participate in other medical research studies
- Take the study supplement at the prescribed dose and time.
- Tell the study doctor about any health problems you have during the study
- Tell the study doctor about any new medicine you take during the study Do not take any other drugs or remedies unless the study doctor has approved them beforehand. This includes prescription drugs and over the counter medicine (including vitamins and herbal remedies) that you buy without a prescription.
- Use effective birth control; examples of effective birth control include barrier contraception (for example condoms), oral contraceptive pills or intrauterine devices.
- Do not get pregnant or cause your partner to become pregnant
- Do not take illegal drugs; examples of illegal drugs include marijuana, cocaine, heroin or other narcotic substances

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

If you agree to take part in this research study, we will pay you $700 for your time and effort. Please, refer to the table below:

Study Visits	***Payments***
V0 (Screening)	*$90*
V1 + V1a	*$190*
V2	*$60*
V3 + V3a	*$190*
V4	*$100*
V5	*$70*
Total	***$700***

We will also provide up to $200 in transportation reimbursement throughout the course of the study. In order to be reimbursed for travel, a receipt must be provided to the study team. If you are unable to complete the entire study, you will be paid for the part/visits you have completed.

Your visits and study-related medical tests will not cost you any money.

It can take up to 6 weeks to prepare and give you a check for study participation. If you do not get a check by then, you can first contact the research team. If further assistance is needed, please contact Mount Sinai's Program for the Protection of Human Subjects at (212) 824-8200.

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

happens 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.

It is possible that products may someday be developed with the help of your data and/or samples, and there are no plans to share any profits from such products with you.

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 a new strategy to prevent the development of stress- related disorders (like Major Depressive Disorder or Posttraumatic Stress Disorder) in at-risk populations that experience many stressors.

POSSIBLE RISKS AND DISCOMFORTS:

- Consumption of BDPP has not been associated with serious adverse effects. Our preclinical studies have demonstrated safety features of dietary BDPP; however, there may be unknown side effects.
- Participants may experience slight gastrointestinal distress, like nausea and/or vomiting, increased urgency to move bowels, loose stool, and/or heartburn associated with the BDPP supplement or study procedures, like fasting or IV placement.
- Participants may experience headaches associated with study procedures, like fasting.
- During the clinical interviews and questionnaires, you may become tired or upset about the questions. If this happens, you should tell the interviewer/study personnel and he/she will stop the examination. Depending upon how you feel, you may then 1) take a rest period and resume later, 2) reschedule for a later appointment or 3) decide not to finish the exam.
- 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.
- If you are pregnant or become pregnant, this research may hurt your baby or your pregnancy in ways that are unknown. The unknown risks could be minor or major (death) for the pregnancy. You should not become pregnant or get someone pregnant while you take part in this study. Please read the acceptable methods of birth control found under the Description of What Is Involved section of this document.
- Psychological risks - during the psychiatric interviews, participants will possibly be exposed to the discomfort of being asked personal questions they may find distressing. You may choose to not answer any questions that make you uncomfortable. The risks and discomforts associated with answering questionnaires are minimal.
- Group Risks - Although your name will not be given to researchers, basic information such as your race, ethnic group, and sex may be shared. 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 discrimination.

- Privacy Risks - Risk of loss of private information; this risk always exists, but there are procedures in place to minimize the risk. Your name and other information that could directly identify you (such as contact information or date of birth) is stored in a secure validated database in which only study team members have access to. It will never be placed into a scientific database outside of our research center. 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 contains 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 experience other harms, such as stress, anxiety, stigmatization, or embarrassment from revealing information about your family relationships, ethnic heritage, or health conditions.
- Insurance Risks - There is a Federal law called the Genetic Information Nondiscrimination Act (GINA). This law makes it illegal for health insurance companies, group health plans, and most employers of over 15 people 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.

OTHER OPTIONS TO CONSIDER:

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

This study is not a substitute for comprehensive medical or psychiatric treatment. If you are seeking treatment for a medical or a psychiatric condition, you may consider treatments that have been shown to be effective for your condition instead of participating in this study. These alternatives are available to you at Mount Sinai and elsewhere and will be described to you fully prior to agreeing to participation in this study.

IN CASE OF INJURY DURING THIS RESEARCH STUDY

If you are injured or made sick from taking part in this research study, you will get medical care. Generally, it will be billed to you or your insurance. You will be responsible for all treatment costs not covered by your insurance, including deductibles, copayments, and coinsurance. This does not prevent

you from seeking payment for injury related to malpractice or negligence. You can contact the Lead Researcher for more information.

ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop taking part in this study at any time. No matter what you choose, your care and benefits through Mount Sinai will not be negatively impacted.

If you decide to stop being in the study, please contact the Lead Researcher or the research staff. At that point, if you choose to stop participating in the study before you have completed it, you may be asked to return to the study doctor to have final safety tests done. If you stop being in the research study, already collected information may not be removed from the research study database and will continue to be used to complete the research analysis. You may be asked whether the study doctor can collect information from your routine medical care. If you agree, this data will be handled the same as research data.

You may also withdraw your permission for the researchers to use and share any of your protected information for research, but you must do so in writing to the Lead Researcher at the address on the first page. Even if you withdraw your permission, the Lead Researcher 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 taking part in the research study.

If you decide you don't want your data and/or samples to be used for research anymore, you can contact the researcher and ask to have your data and/or samples withdrawn or labeled so that they will not to be used in additional projects or shared. If your data and/or samples have already been shared with researchers, those researchers will be asked to stop using them. However, if any data and/or samples have already been shared without your identity or a linking code, it won't be possible to retrieve them. Data and/or samples that have already been used will not be affected by your decision. If your data and/or samples have already been deposited in an external repository, the study team will request that your data and/or samples be removed.

Withdrawal without your consent: The Lead Researcher, the funder or Mount Sinai 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 research team have not been followed, the Lead Researcher believes it is in your best interest, or for any other reason. If data and/or samples have been stored as part of the research study, they too can be destroyed without your consent.

CONTACT INFORMATION:

If you have any questions, concerns or complaints at any time about this research, or you think the research has harmed you, please contact the office of the research team and/or the Lead Researcher at phone number 212-585-4640.

If there is an emergency, please call 911 or go to the emergency room. Let the emergency room staff know you are in a research study so they can contact the Lead Researcher if needed.

DISCLOSURE OF FINANCIAL INTERESTS:

Researchers sometimes get paid for consulting or doing work for companies that produce drugs, biologics or medical devices. If you have questions regarding industry relationships, you are encouraged to talk to the Lead 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 part of this study, some of your private and/or protected health information will be obtained, used, and shared with your permission. There is a Federal Health Insurance Portability and Accountability Act (HIPAA) that makes sure this is done correctly and safely.

What is protected health information (PHI)?
PHI is the combination of two things:

1. PHI contains information that identifies you. It will be used to contact you and link you to your health information, like name, date of birth, medical record number, and address.
2. PHI also contains health information, including information about your mental and physical health from your visits to doctors or hospitals, or from study visits.

Every time you visit a hospital or your doctor, PHI is created and recorded in your medical record by your healthcare providers. In the same way, the PHI created as part of this study will be linked to who you are and your medical information.

What PHI is collected and used in this research study, and might also be shared with others?

As part of this research project, the research team at the hospital(s) involved in the research will collect your name, address, dates directly related to you (birth, admission, discharge, etc.), e-mail addresses, social security number, medical records number.

The researchers will also get information from your medical record. 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 mental health records

Why is your PHI being used?
Researchers need the information that identifies you so they can contact you during the study. They need your health information and the results of any tests and procedures being collected as part of this study to answer the questions posed in the study. The purpose of the study is discussed earlier in this consent form. Before researchers analyze the data, they remove any information that would let others know who you are or that you took part in the study. If researchers publish or present study results at scientific meetings, lectures, or other events, their presentations would not include any information that would let others know who you are, unless you give separate permission to do so.

The Lead Researcher may also use and share the results of these tests and procedures with other healthcare providers at Mount Sinai who are involved in your care or treatment. 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 Mount Sinai Program for the Protection of Human Subjects is responsible for overseeing research on human participants 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.
- I*f the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.*

Who, outside Mount Sinai, might receive your PHI?
As part of the study, the Lead Researcher, research team and others in the Mount Sinai workforce may disclose your PHI, 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 Lead Researcher.)

- The United States Department of Health and Human Services (DHHS) and the Office of Human Research Protection (OHRP) (the government organization that is responsible for protecting human research participants).
- The sponsoring government agency and/or their representative who need to confirm the accuracy of the results submitted to the government or the use of government funds: National Institute of Mental Health (NIMH)
- A Data Safety Monitoring Board or other committee that will monitor the study on an ongoing basis for safety.
- The United States Food and Drug Administration

- The United States Department of Health and Human Services and the Office of Human Research Protection.

In almost 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. Some records and information disclosed may be identified with a unique code number. The Lead Researcher 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 Institutional Review Board (IRB) allows it after determining that there would be minimal risk to your privacy. The Certificate of Confidentiality obtained from the Department of Health and Human Services will not be used to prevent disclosure to local authorities of child abuse and neglect, or harm to self or others. 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, *OHRP, 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.* The results of this research may be published. However, your name and other identifying information will be kept confidential.

For how long will Mount Sinai be able to use or disclose your PHI? Your authorization for use of your PHI 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 is 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 research team is not required to release research information to you that is not part of your medical record.

Do you need to give the researchers permission to obtain, use or share your PHI?
NO! If you decide not to let the research team obtain, use or share your PHI, 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?
If you decide to stop being in the study, please contact the Lead Researcher or the research staff.
The research team may ask you whether they can continue to collect information from your medical record. You will also have to decide if you wish to limit the continued use of the information collected during the study. Under US privacy laws you may also withdraw your permission for the researchers to

use and share any of your protected information for research, but you must do so in writing to the Lead Researcher at the address on the first page.

Even if you withdraw your permission, the Lead Researcher may still use the information that was already collected, but only to complete this 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 taking part in the research study.

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 PHI.

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, where possible, Mount Sinai has entered into agreements with those who will receive your information to continue to protect your confidentiality.

If researchers are reviewing your medical records or asking questions about your medical history or conditions, it is possible that they may learn information related to your HIV status. If that is the case, the following information concerns you. If researchers are not reviewing your medical records or asking questions about your medical history or conditions, then you may ignore the following section.

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.

Certificate of Confidentiality: To further protect your privacy, the researchers have obtained a Certificate of Confidentiality from the Department of Health and Human Services. This is intended to ensure that your identity as a participant in this research study will not have to be disclosed as a result from a subpoena, for the purpose of identifying you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings other than to the FDA or OHRP as identified above.

The research staff will not share any of your personal information, study data and/or samples with anyone who is not a member of the research team, including any family members or friends, other than those identified above. However, you should know that if it is learned that you or someone else is threatened with serious harm, such as a child or an elderly person being abused, the research team may notify the appropriate authorities if necessary to protect you or others. A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information

about yourself or your involvement in this research. This means that you and your family must also actively protect your own privacy. If an insurer or employer learns about your research participation, and you agree that they can have your research information, then the researchers may not use the Certificate of Confidentiality to keep this information from them.

How the Institutional Review Board (IRB) can help you:

This research has been reviewed and approved by an Institutional Review Board (IRB). You may reach a representative of the Mount Sinai Program for Protection of Human Subjects at telephone number (212) 824-8200 during regular work hours (Monday-Friday, 9am-5pm, excluding holidays) 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 participant.
- You want to get information or provide input about this research.

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

_____	_____	_____	_____
Signature of Participant	Printed Name of Participant	Date	Time

PERSON EXPLAINING STUDY AND OBTAINING CONSENT:

_____	_____	_____	_____
Signature of Consent Delegate	Printed Name of Consent Delegate	Date	Time

WITNESS SECTION:

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 participant, and that consent was freely given by the participant.

_____	_____	_____	_____
Signature of Witness	Printed Name of Witness	Date	Time