NCT02213575

UF | Institutional Review Board
UNIVERSITY of FLORIDA

INFORMED CONSENT FORM to Participate in Research, and AUTHORIZATION to Collect, Use, and Disclose Protected Health Information (PHI)

INTRODUCTION

Name of person seeking your consent:_____

Place of employment & position: _____

Please read this form which describes the study in some detail. A member of the research team will describe this study to you and answer all of your questions. Your participation is entirely voluntary. If you choose to participate you can change your mind at any time and withdraw from the study. You will not be penalized in any way or lose any benefits to which you would otherwise be entitled if you choose not to participate in this study or to withdraw. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

GENERAL INFORMATION ABOUT THIS STUDY

1. Name of Participant ("Study Subject")

_____

2. What is the Title of this research study?

Effect of Minocycline Treatment on Drug-Resistant Hypertensive Patients-Study 3

3. Who do you call if you have questions about this research study?

Principal Investigator: Dr. Carl J. Pepine (352) 273-9082 (during office hours)

Other research staff:

Dana Leach, DNP, ARNP (352) 273-8933 during office hours

Evenings, weekends, and holidays: call (352) 265-0111 and ask for the Cardiology Fellow on call.

4. Who is paying for this research study?

The sponsor of this study is the National Institutes of Health.

5. In general, what do you need to know about this Research Study?

Agreeing to become involved in any research is always voluntary. By signing this form, you are not waiving any of your legal rights. If you decide not to participate in this research, you will not be penalized in any way and you will not lose any benefits to which you are entitled. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

a.) In general, what is the purpose of the research, how long will you be involved?

The purpose of this study is to observe the effects the drug, minocycline, and how it works with the chemicals in your brain and to determine the best dose to use in future studies. Your participation will last 180 days.

b.) What is involved with your participation, and what are the procedures to be followed in the research?

This study involves specialized imaging of the brain, and you must be willing to travel to Montreal, Canada for these tests, which will be done at the Montreal Neurological Institute (McConnell Brain Imagine Centre) and the Jewish General Hospital. These images will be collected before taking study medication and will be performed again between two to six months after treatment.

c.) What are the likely risks or discomforts to you?

The study drug is a well-tolerated antibiotic but can have some side effects, which are described in full detail later in this form.

You may experience some discomfort caused by the insertion of the fine needle catheter into your veins used to inject the radioactive substance as well as to draw blood. The main risk of taking part in this study is exposure to radiation from the short-lived tracer substance injected for the PET scan.

The conditions imposed by the use of magnetic resonance imaging can cause a certain amount of discomfort due to the fact that you may have to remain completely still during the examination and the noise generated by the scanner while it is capturing images could cause you some discomfort as well, however, you will be provided with earplugs to reduce this effect.

For the Autonomic Nervous System Testing you will be positioned in a head-up tilt which may cause lightheadedness or fainting.

The risks to the ambulatory blood pressure monitoring generally relate to the annoyance of the repeated inflations and may become uncomfortable and/or could irritate the skin. Careful monitoring of the arm and removal during non-recording periods can alleviate any irritation.

The risks of drawing blood from vein and/or intravenous catheter (small plastic tubing inserted into your vein to obtain blood samples) include discomfort at the site of puncture; possible bruising and swelling around the puncture site; rarely an infection and uncommonly faintness from the procedure.

d.) What are the likely benefits to you or to others from the research?

You may or may not benefit from participating in this study. You may potentially benefit from taking minocycline and see improvement in your hypertension. Information generated from this study may help others in the future with hypertension.

e.) What are the appropriate alternative procedures or courses of treatment, if any, that might be helpful to you?

The alternative treatment would be to continue your normal clinical care as directed by your physician.

Twenty to thirty percent of patients with high blood pressure (BP) have difficulty keeping it controlled with medications. This is because their high BP is controlled by the brain and most known blood pressure medications do not cross the blood-brain barrier to affect the responsible cells in the brain. The purpose of this study is to observe the effects the drug minocycline and how it works with the chemicals in your brain and to determine the best dose to use in future studies. Minocycline is an FDA approved drug used to treat infections.

You are being asked to be in this research study because you have been diagnosed with high blood pressure that is difficult to control and you have participated in the first study for the project and it was determined that your blood pressure was responsive to minocycline.

Additional and more detailed information is provided within the remainder of this Informed Consent form, please read before deciding if you wish to participate in this study

WHAT CAN YOU EXPECT IF YOU PARTICIPATE IN THIS STUDY?

6. What will be done as part of your normal clinical care (even if you did not participate in this research study)?

Your normal clinical care will continue as previously determined by your physician. There will be no changes to your normal clinical care if you decide to participate in this study.

7. What will be done only because you are in this research study?

To participate in this study, you must meet certain qualifications, which the study staff will discuss with you. You are being asked to participate because you qualify for and have already participated in the first study of this project. If you decide to take part in this study, we will ask you to provide written informed consent. This study involves specialized imaging of the brain, and you must be willing to travel to Montreal, Canada for these tests, which will be done at the Montreal Neurological Institute (McConnell Brain Imagine Centre) and the Jewish General Hospital. These images will be collected before taking study medication and will be performed again between two to six months after treatment.

In order to participate you will have a baseline visit where a complete medical history will be taken and a brief physical examination and ambulatory monitor will be performed.

Visit 1 Baseline 1 (Screen)

- You will have a medical history taken and will be asked about the medication you are currently taking.
- You will have a physical examination: Your study doctor will listen to your heart and lungs, your vital signs (temperature, blood pressure, heart rate, and breathing rate) will also be measured. Your height and weight will be recorded.
- You will have your office blood pressure measured
- The “office” blood pressure (BP) measurement (meaning your blood pressure while at the study doctor’s office). At each visit, office BP will be recorded as an average of 3 BP readings after you have rested for 5 minutes in a quiet room.. In preparation for your office blood pressure measurements you will be asked to try to follow the below guidelines:
- Take all prescribed medications at your usual times on the day of these office BP measurements. If you have not taken your medications as usual, you will be asked to return for another office BP visit when you have taken your medications.
- At least thirty minutes before you go in for your study visit, avoid caffeine, smoking and exercising.

- During the measurements you will be asked to sit quietly in a chair with both of your feet flat on the ground for at least 5 minutes before multiple BP readings are taken.
- If you are a woman able to become pregnant, you will be asked to take a pregnancy test that must have a negative result before you can continue in this study. If sexually active, you must agree to use two appropriate contraceptive measures while taking part in this study. Medically acceptable contraceptives include: (1) surgical sterilization (such as tubal ligation or hysterectomy), 2) approved hormonal contraceptives (such as birth control pills, patches, implants or injections), (3) barrier methods (such as a condom or diaphragm) used with a spermicide, or (4) intrauterine device (IUD). If you become pregnant while taking part in this study or if you have unprotected sex, you must inform the study doctor and discontinue the use of Minocycline immediately.
- You will be instructed to begin recording your home blood pressure monitor readings if you are not currently doing so. You will need to record your blood pressure readings at least 3 times a week. These recordings will need to be brought with you to your clinic visits.
- You will be fitted with a 24 hour ambulatory blood pressure monitor (ABPM). This is described under “Visit 1
- You will be scheduled to go to Montreal for Baseline Imaging as noted below.
- You will have blood drawn (3 tablespoons)

Travel to Montreal:

Prior to starting study medication you will be asked to undergo specialized imaging of your brain using magnetic resonance imaging (MRI) and positron emission tomography (PET) scanning to determine how the brain is affected by this medication and how it impacts your blood pressure. In addition, you will also undergo Autonomic Nervous System Testing. The PET and MRI will take place at the Montreal Neurological Hospital. These will take place either over one or possibly two days, whichever is easier to schedule. Each scan takes approximately one to one and half hours. The Autonomic Nervous System Testing will take place at the Jewish General Hospital, also in Montreal and will take approximately 1 ½ to 2 hours.

During the PET scan, a blood sample will be taken from you for genetic analysis, approximately (3 tablespoons). The purpose of this genetic analysis is only to enable the investigators to properly analyze your PET images. If you agree to participate in this study, your blood sample will be sent to the McGill University and the Genome Quebec Innovation Centre for analysis. The sample will be stored here for the duration of this study, after this time the blood sample will be destroyed. Your sample will be used only for the purposes of this research project.

Positron Emission Tomography (PET):

Positron Emission Tomography or PET, is a nuclear medicine imaging technique which produces 3D images or pictures of the brain (specific to this study).

Prior to scanning, two fine needle-catheters will be inserted into the veins of your arm. One will be used to administer small amounts of a radioactive substance, the other to take four blood samples of 10 mL, equal to two teaspoons each. A portion of the blood drawn will be used to determine blood levels related to the imaging and a portion of the sample will be used to determine if a specific genetic component is present that may affect the imaging so that all patients can be categorized according to the specific genotype group that they belong to. This will allow us to properly interpret the PET-image results. The radioactive substance you will receive prior to commencing the study medication and then at the end of the study is ^{11}C-PBR28 . This substance is labelled with the short-lived radioactive atom Carbon 11 (physical half-life = 20 minutes). The dose of ^{11}C-PBR28 you will receive is 1200 MBq. You will receive this dose initially at the baseline visit and then again at the end of the study. MBq is short for megabecquerels, a unit used to measure how much radioactivity there is in a sample; the quantity you will receive is towards the low end of what is used for diagnostic clinical tests performed on a regular basis in Nuclear Medicine. The substance being injected to perform the PET study is not currently approved for general human use in Canada; however, its use for research purposes is permitted by Health Canada.

The scanning session will take approximately one and a half hour for each scan, during which time you will be asked to lie still on the mattress in the scanner. All procedures during the PET study will be carried out by a qualified nuclear medicine technician, and supervised by a qualified nuclear medicine physician.

Magnetic Resonance Imaging (MRI):

A magnetic resonance examination is a medical technique that provides high quality images of the brain. This technique uses a natural force around us; magnetism. This intense magnetic field is created by a magnet. For the MRI session, you will lie on a mattress that will slowly slide into a large cylindrical tube where pictures of your head will be taken during a period of 45 to 60 minutes. The tube is open at both ends; it has excellent air circulation, and is well lit. An intercom system will enable you to talk with the technician, if necessary. For your comfort you will be asked to wear protective earplugs, this is in order to cut out the large amount of noise made by the scanner. It is important that you remain completely still when the instrument is capturing images. To this end, a small cushion will be placed around your head to hold it still during the scan.

You will not be injected with any substances during this examination.

Autonomic Nervous System Testing:

The Autonomic Nervous System Testing will take place at the Autonomic Reflex Laboratory of the Jewish General Hospital. Prior to the test, your height and weight

will be obtained. You will then be required to lie on a special table that can be tilted to a standing position. Electrodes will be placed on your chest and abdomen to record heart function. You will wear a finger cuff that continuously measures blood pressure. A small device will be placed near your nose to record breathing. An elastic headband will be placed around your forehead to measure brain blood flow and oxygen. You will then lie quietly for 10 minutes. The tilt table will then be placed upright for 30 minutes. After the 10 minutes of standing, the tilt table will be returned to the lying position. After a few minutes of rest, you will be asked to take several slow deep breaths for about 1 minute. You will then be asked to blow into a tube on 2 separate occasions for 15 seconds each time. During these breathing tests we will continue to measure blood pressure and heart function. The tilt table test and the breathing tests are all routinely used in clinical practice to diagnose patients with low blood pressure or other autonomic nervous system disorders.

For the second part of the test, small capsules will be placed on your forearm, leg and foot. These capsules will be filled with a liquid containing a drug called acetylcholine. The capsules will be connected to a small battery and for 5 minutes you will feel a mild tingle or buzzing sensation over the area of the capsule. This test causes sweating over the area covered by the capsule. The sweating lasts about 15 minutes and we measure it for 10 minutes. The capsules are then removed. This test is called a QSART and is also routinely used to diagnose patients with autonomic nervous system disorders.

The cardiology research team will assist you in getting prepared for the trips to Montreal, Canada. More information about the costs of the travel can be found below in the “If you participate in this study, what will it cost you” section.

When you return, you will then be followed and treated as outlined in the Study 1 consent.

Between two and six months, you will be scheduled to return to Canada for repeat imaging, depending on when your blood pressure normalizes.

Tests done only for research purposes will not be evaluated or used to diagnose or treat any of your medical problems. This/these test(s) may need to be repeated if required for your medical care in the future.

When you return you will be scheduled for study visits as outlined below and restarted on the dose of minocycline that lowered your blood pressure during your previous participation. After you are considered a responder to minocycline, you will be scheduled to return to Montreal for repeat imaging.

Visit 2 (Day 0- ±3 days)

- You will be dispensed study medication (the dose of minocycline you responded to previously)

- Your home blood pressure monitor readings that you recorded will be reviewed and you will be given a new home blood pressure log.
- You will have your office blood pressure measured. This is described under "Visit 1".

Visit 3 (2 week + 7 days)

- Bring any unused study medication and bottles including empty bottles to this visit.
- You will have an updated medical history taken and will be asked about the medication you are currently taking.
- You will have a brief physical examination and vital signs. This is described under "Visit 1".
- You will have your office blood pressure measured. This is described under "Visit 1".
- Your home blood pressure monitor readings that you recorded will be reviewed and you will be given a new home blood pressure log.
- You will be re-dispensed study medication (minocycline). You will be instructed to continue to take study medication (minocycline by mouth once a day).

Visit 4 (Day 60 + 14 days)

- Bring any unused study medication and bottles including empty bottles to this visit
- You will have an updated medical history taken and will be asked about the medication you are currently taking.
- You will have a brief physical examination and vital signs. This is described under "Visit 1".
- You will have your office blood pressure measured. This is described under "Visit 1".
- Your home blood pressure monitor readings that you recorded will be reviewed and you will be given a new home blood pressure log.
- You will have blood drawn (1 tablespoon approximately) for analysis and additional biomedical tests.
- You will be re-dispensed study medication (minocycline). You will be instructed to continue to take study medication (minocycline by mouth once a day).
- You will be fitted with a 24 hour ambulatory blood pressure monitor (ABPM). This is described under "Visit 1".

Visit 5 Phone Call (within 10 days of Visit 4)

- You will be given results of your ABPM blood pressures by the study team and told if your participation in this study will end or continue on to the next visit.
- If you are told by the study staff that your participation is continuing, you will be asked to return to clinic within approximately 1 week to increase your study medication dose mouth once a day.

- If you are told by the study staff that your participation has ended, you will be asked to have your final visit scheduled to have repeat imaging in Montreal. When you return you will be asked to return to clinic within approximately 1 week for a final visit (see Visit 12 Final Visit for description).

Visit 6 (within 7 days of Visit 5)

- Bring any unused study medication and bottles including empty bottles to this visit
- You will have an updated medical history taken and will be asked about the medication you are currently taking.
- Your home blood pressure monitor readings that you recorded will be reviewed and you will be given a new home blood pressure log.
- You will have a brief physical examination and vital signs. This is described under "Visit 1".
- You will have your office blood pressure measured. This is described under "Visit 1".
- You will be dispensed study medication (minocycline). You will be instructed to continue to take study medication (minocycline by mouth once a day).

Visit 7 (Day 90 + 14 days)

- Bring any unused study medication and bottles including empty bottles to this visit
- You will have an updated medical history taken and will be asked about the medication you are currently taking.
- You will have a brief physical examination and vital signs. This is described under "Visit 1".
- You will have your office blood pressure measured. This is described under "Visit 1".
- Your home blood pressure monitor readings that you recorded will be reviewed and you will be given a new home blood pressure log.
- You will be re-dispensed study medication (minocycline). You will be instructed to continue to take study medication (minocycline by mouth once a day).

Visit 8 (Day 120 + 14 days)

- Bring any unused study medication and bottles including empty bottles to this visit
- You will have an updated medical history taken and will be asked about the medication you are currently taking.
- You will have a brief physical examination and vital signs. This is described under "Visit 1".
- You will have your office blood pressure measured. This is described under "Visit 1".
- Your home blood pressure monitor readings that you recorded will be reviewed and you will be given a new home blood pressure log.
- You will have blood drawn (1 tablespoon approximately). This is described under "Visit 4".

- You will be re-dispensed study medication (minocycline). You will be instructed to continue to take study medication (minocycline by mouth once a day).
- You will be fitted with a 24 hour ambulatory blood pressure monitor (ABPM). This is described under “Visit 1”.

Visit 9 Phone Call (within 10 days of Visit 8)

- You will be given results of your ABPM blood pressures by the study team and told if your participation in this study will end or continue on to the next visit.
- If you are told by the study staff that your participation is continuing, you will be asked to return to clinic within approximately 1 week to increase your study medication dose mouth once a day.
- If you are told by the study staff that your participation has ended, you will be asked to have your final visit scheduled to have repeat imaging in Montreal. When you return you will be asked to return to clinic within approximately 1 week for a final visit (see Visit 12 Final Visit for description).

Visit 10 (within 7 days of Visit 9)

- Bring any unused study medication and bottles including empty bottles to this visit
- You will have an updated medical history taken and will be asked about the medication you are currently taking.
- You will have your office blood pressure measured. This is described under “Visit 1”.
- You will have a brief physical examination and vital signs. This is described under “Visit 1”.
- Your home blood pressure monitor readings that you recorded will be reviewed and you will be given a new home blood pressure log.
- You will be dispensed study medication (minocycline). You will be instructed to continue to take study medication (minocycline by mouth twice a day).

Visit 11 (Day 150 +14 days)

- Bring any unused study medication and bottles including empty bottles to this visit
- You will have an updated medical history taken and will be asked about the medication you are currently taking.
- You will have a brief physical examination and vital signs. This is described under “Visit 1”.
- Your home blood pressure monitor readings that you recorded will be reviewed and you will be given a new home blood pressure log.
- Your home blood pressure monitor readings that you recorded will be reviewed
- You will be re-dispensed study medication (minocycline). You will be instructed to continue to take study medication (minocycline by mouth twice a day).

Final Visit (Day 180 +14 days or at any time your participation ends)

- Bring any unused study medication and bottles including empty bottles to this visit

- You will have an updated medical history taken and will be asked about the medication you are currently taking.
- You will have a brief physical examination and vital signs. This is described under "Visit 1".
- You will have your office blood pressure measured. This is described under "Visit 1".
- Your home blood pressure monitor readings that you recorded will be reviewed
- You will have blood drawn (4 tablespoons approximately). This is described under "Visit 1".
- You will be fitted with a 24 hour ambulatory blood pressure monitor (ABPM). This is described under "Visit 1".

Once this research study is completed, any information that could identify you might be removed from any identifiable private information or identifiable biospecimens collected and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative

If you have any questions now or at any time during the study, please contact one of the research team members listed in question 3 of this form.

8. How long will you be in this research study?

Your participation could last up to 180 days.

9. How many people are expected to take part in this research study?

Nine (9) subjects will need to complete this protocol.

WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY AND WHAT ARE YOUR OPTIONS?

10. What are the possible discomforts and risks from taking part in this research study?

Minocycline

The study medication is an FDA approved drug and is a well-tolerated antibiotic used every day to treat many different types of infections. Side effects of this drug may include abdominal cramping, diarrhea, nausea, dry mouth, headache or hypersensitivity (skin sensitivity after sun exposure, dizziness or mild skin rashes). Please inform the study doctor if you experience any of these side effects. New signs of infection e.g. fever, chills, persistent sore throat, oral thrush or new yeast infection; ringing in the ears. The drug can cause fetal harm when taken during pregnancy.

Special note to women:

Being part of this study while pregnant may expose the unborn child to significant risks, some of which may be currently unforeseeable. Therefore, pregnant women will be excluded from the study. If you are a woman able to become pregnant, a pregnancy test will be done and it must be negative before you can continue in this study. If sexually active, you must agree to use appropriate contraceptive measures while taking part in this study. Medically acceptable contraceptives include: (1) surgical sterilization (such as tubal ligation or hysterectomy), 2) approved hormonal contraceptives (such as birth control pills, patches, implants or injections), (3) barrier methods (such as a condom or diaphragm) used with a spermicide, or (4) intrauterine device (IUD). If you become pregnant while taking part in this study or if you have unprotected sex, you must inform the study doctor immediately. A pregnancy test will be repeated at the 6 month visit. Due to the possible drug interaction of minocycline with oral contraceptives, women of child bearing age who are using oral contraceptives will be required to utilize a second form of birth control while participating in this study.

Positron Emission Tomography (PET):

You may experience some discomfort caused by the insertion of the fine needle catheter into your veins used to inject the radioactive substance as well as to draw blood. Although the taking of the blood sample causes no serious problems for most people, it can cause some bleeding, bruising and/or discomfort at the site where the needle is inserted. Also, you may experience some discomfort as a result of lying on the mattress in the scanner for a long time without moving.

The main risk of taking part in this study is exposure to radiation from the short-lived tracer substance injected for the PET scan. The administered radioactive substance ^{11}C-PBR28 will expose you to a maximal dose of 4 mSv per scan, total of 8 mSv for the two scans according to our best scientific estimates. This small dose of radiation 8mSv, is above that which you are inevitably exposed to in daily life (natural radiation in the environment, cosmic rays, etc.), or to that which you might receive for medical reasons (diagnostic x-rays, radiation therapy). Nationally accepted limits on radiation doses which can be administered for research purposes have been defined (50 mSv/year), and in order to ensure that you do not go above the recommended limit you must make sure to let the investigators know about any other research protocol that you might have been part of that would have involved radiation exposure, as well as to mention the current protocol, if you do take part in it, to any investigator asking

you to take part in another protocol in the future. Most of the radioactivity you will receive will be gone from your body in a matter of hours. The risk which is alluded to when discussing risk associated with radiation exposures of the level seen in PET scanning (specifically in the current study, the radiation exposure is estimated at 8 mSv) is that of developing a cancer at some point in the future, which would not have happened if you had not received that radiation dose. Although radiation clearly increases the risk of developing cancer over certain doses, its ability to do so at the levels used in PET imaging has never been observed, is certainly at most very low and could conceivably not even exist.

The radiation exposure in this study is thought to be minor. However, the effects of radiation add up over your lifetime. Repeated exposures may increase your risk of injury or disease. When deciding to enter this study you should consider previous and future potential exposures. Examples would include x-rays taken for a broken bone or radiation therapy treatments for cancer.

The substance being injected to perform the PET study is not currently approved for general human use in Canada. However, its use for research purposes is allowed by Health Canada.

Magnetic Resonance Imaging (MRI):

The conditions imposed by the use of magnetic resonance imaging can cause a certain amount of discomfort due to the fact that you may have to remain completely still during the examination and the noise generated by the scanner while it is capturing images could cause you some discomfort as well, however, you will be provided with earplugs to reduce this effect.

Based on current knowledge, your participation in a MRI examination will not pose any medical risks to you, as long as you do not have any contraindications.

Autonomic Nervous System Testing:

Head-up tilt may cause lightheadedness or fainting. The tilt will be stopped if you feel lightheaded, or if we feel that your blood pressure has become too low or that your heart is beating too quickly. After the QSART, your skin may become slightly red around the area where the capsules had been placed, however, this will disappear after a few hours. The exercise test may cause leg discomfort, shortness of breath or lightheadedness. The exercise test will be stopped if you find it to be too tiring or if for any reason it is felt that it would be unsafe for you to continue.

Risks of twenty-four hour ambulatory blood pressure cuff

The risks to the ambulatory blood pressure monitoring generally relate to the annoyance of the repeated inflations and may become uncomfortable and/or could

irritate the skin. Careful monitoring of the arm and removal during nonrecording periods can alleviate any irritation.

Risk of Blood Collection

The risks of drawing blood from vein and/or intravenous catheter (small plastic tubing inserted into your vein to obtain blood samples) include discomfort at the site of puncture; possible bruising and swelling around the puncture site; rarely an infection and uncommonly faintness from the procedure. Blood drawn for this study will be approximately 15 tablespoons over the year of the study.

Potential Risks and the Genetic Information Non-Discrimination Act (GINA):
There is a potential risk of loss of confidentiality. Every effort will be made to protect your confidential information, but this cannot be guaranteed. The genetic information obtained as a result of your participation in this research will not be included in your medical record. Information from which you may be personally identified will be maintained in a confidential, secure location, accessible only by authorized members of the study team, and will not be disclosed to third parties except as described in this consent form, with your permission, or as may be required by law.

The Genetic Information Nondiscrimination Act (GINA) is a Federal law that will protect you in the following ways:

- Health insurance companies and group plans may not request genetic information from this research;
- Health insurance companies and group plans may not use your genetic information when making decisions regarding your eligibility or premiums;
- Employers with 15 or more employees may not use your genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination based on an already-diagnosed genetic condition or disease.

Samples collected as part of this study may be valuable for scientific, research, or teaching purposes or for the development of a new medical product. The sponsor and/or the developers will assert all rights of ownership in the samples and all rights arising from use of the samples and may profit from this. In this event, there is no plan to compensate you.

Confidentiality:

There is a potential risk of loss of confidentiality. Every effort will be made to protect your confidential information but this cannot be guaranteed. Study records that identify you will be kept confidential, as required by law.

Researchers will take appropriate steps to protect any information they collect about you. However, there is a slight risk that information about you could be revealed inappropriately or accidentally. Depending on the nature of the information, such a release could upset or embarrass you, or possibly affect your insurability or employability. Questions 17-21 in this form discuss what information about you will be collected, used, protected, and shared.

This study may include risks that are unknown at this time.

Participation in more than one research study or project may further increase the risks to you. If you are already enrolled in another research study, please inform one of the research team members listed in question 3 of this form or the person reviewing this consent with you before enrolling in this or any other research study or project.

Throughout the study, the researchers will notify you of new information that may become available and might affect your decision to remain in the study.

If you wish to discuss the information above or any discomforts you may experience, please ask questions now or call one of the research team members listed in question 3 in this form.

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. The NCT number for this study is NCT02213575.

11a. What are the potential benefits to you for taking part in this research study?

You may or may not benefit from participating in this study. You may potentially benefit from taking minocycline and see improvement in your hypertension.

11b. How could others possibly benefit from this study?

Information generated from this study may help others in the future with hypertension.

11c. How could the researchers benefit from this study?

In general, presenting research results helps the career of a scientist. Therefore, the Principal Investigator listed in question 3 of this form may benefit if the results of this study are presented at scientific meetings or in scientific journals.

12. What other choices do you have if you do not want to be in this study?

You are free not to participate in this study. The alternative to being in this study includes standard of care medical treatment for hypertension which includes blood pressure medications and lifestyle changes. If you do not want to take part in this study, tell the Principal investigator and do not sign this Informed Consent Form.

13a. Can you withdraw from this study?

You are free to withdraw your consent and to stop participating in this study at any time. If you do withdraw your consent, you will not be penalized in any way and you will not lose any benefits to which you are entitled.

If you decide to withdraw your consent to participate in this study for any reason, please contact one of the research team members listed in question 3 of this form. They will tell you how to stop your participation safely.

If you have any questions regarding your rights as a research subject, please call the Institutional Review Board (IRB) office at (352) 273-9600.

13b. If you withdraw, can information about you still be used and/or collected?

If you withdraw, the investigators will report the results of the testing that you have completed, but only as part of the overall study results. Your individual results will not be reported.

13c. Can the Principal Investigator withdraw you from this study?

You may be withdrawn from the study without your consent for the following reasons:

- If it is medically necessary;
- the sponsor stops the study;
- you become pregnant;
- if you do not follow the instructions given to you by the investigator;

WHAT ARE THE FINANCIAL ISSUES IF YOU PARTICIPATE?

14. If you choose to take part in this research study, will it cost you anything?

Study Drugs, Devices

The study drug Minocycline and an ambulatory blood pressure monitoring device will be provided at no cost to you while you are participating in this study.

Study Services

The Sponsor will pay for all medical services required as part of your participation in this study **and travel to Montreal Neurological Institute, in Montreal Canada for the specialized imaging of the brain and the autonomic nervous system testing.** There will be no cost to you. If you receive a bill related to this study, please contact Dr. Carl J. Pepine (352) 273-9082 (during office hours).

Items/Services Not Paid for by the Sponsor

All other medical services provided to you that are not directly required by this study will be billed to you or your insurance company in the usual manner.

15. Will you be paid for taking part in this study?

All costs and arrangements for travel to the Canadian study center for imaging will be provided by the study. You will receive a stipend, in the form of a pre-paid cash card, of $300.00 to compensate you for loss of wages during your time off of work and incidentals. You will receive this compensation prior to your departure to Canada on both occasions. You will also be paid $25.00 for the cost of mileage and parking expenses for all study related visits that require you to come to clinic here at UF to complete the visit. You will be paid with a pre-paid debit card at the conclusion of the visit. The total amount of money you could be paid for your participation in this study will not exceed $850.00. You will not be paid for phone call visits (Visit 5 and Visit 9).

16. What if you are injured because of the study?

If you are injured as a direct result of your participation in this study, only the professional services that you receive from any University of Florida Health Science Center healthcare provider will be provided without charge. These healthcare providers include physicians, physician assistants, nurse practitioners, dentists or psychologists. Any other expenses, including Shands hospital expenses, will be billed to you or your insurance provider.

You will be responsible for any deductible, co-insurance, or co-payments. Some insurance companies may not cover costs associated with research studies or research-related injuries. Please contact your insurance company for additional information.

The Principal Investigator will determine whether your injury is related to your participation in this study.

This study requires international travel to Montreal Canada. Medicare, Medicaid and most U.S. medical insurance plans do not pay for healthcare costs outside the United States. If you are injured and require medical care in Canada you will be responsible for these expenses.

No additional compensation is routinely offered. The Principal Investigator and others involved in this study may be University of Florida employees. As employees of the University, they are protected under state law, which limits financial recovery for negligence.

Please contact one of the research team members listed in question 3 of this form if you experience an injury or have questions about any discomforts that you experience while participating in this study.

17. How will your health information be collected, used and shared?

If you agree to participate in this study, the Principal Investigator will create, collect, and use private information about you and your health. This information is called protected health information or PHI. In order to do this, the Principal Investigator needs your authorization The following section describes what PHI will be collected, used and shared, how it will be collected, used, and shared, who will collect, use or share it, who will have access to it, how it will be secured, and what your rights are to revoke this authorization.

Your protected health information may be collected, used, and shared with others to determine if you can participate in the study, and then as part of your participation in the study. This information can be gathered from you or your past, current or future health records, from procedures such as physical examinations, x-rays, blood or urine tests or from other procedures or tests. This information will be created by receiving study treatments or participating in study procedures, or from your study visits and telephone calls. More specifically, the following information may be collected, used, and shared with others:

- Complete past medical history
- Laboratory, x-ray imaging reports and other test results
- Records about medications
- Ability or potential to conceive a child, or document pregnancy

This information will be stored in locked filing cabinets or on computer servers with secure passwords, or encrypted electronic storage devices.

Some of the information collected could be included in a "limited data set" to be used for other research purposes. If so, the limited data set will only include information that does not directly identify you. For example, the limited data set cannot include your name, address, telephone number, social security number, photographs, or other codes that link you to the information in the limited data set. If limited data sets are created and used, agreements between the parties creating and receiving the limited data set are required in order to protect your identity and confidentiality and privacy.

18. For what study-related purposes will your protected health information be collected, used, and shared with others?

Your PHI may be collected, used, and shared with others to make sure you can participate in the research, through your participation in the research, and to evaluate the results of the research study. More specifically, your PHI may be collected, used, and shared with others for the following study-related purpose(s):

- to observe the effects the drug minocycline and its interaction with the chemicals in your brain and its ability to inhibit the activation of these brain cells

Once this information is collected, it becomes part of the research record for this study.

19. Who will be allowed to collect, use, and share your protected health information?

Only certain people have the legal right to collect, use and share your research records, and they will protect the privacy and security of these records to the extent the law allows. These people include:

- the study Principal Investigator (listed in question 3 of this form) and research staff associated with this project.
- other professionals at the University of Florida or Shands Hospital that provide study-related treatment or procedures.
- the University of Florida Institutional Review Board (IRB; an IRB is a group of people who are responsible for looking after the rights and welfare of people taking part in research).
- McGill University (the IRB residing over the procedures performed at the Montreal Neurological Institute)

20. Once collected or used, who may your protected health information be shared with?

Your PHI may be shared with:

- the study sponsor (listed in Question 4 of this form).
- United States and foreign governmental agencies who are responsible for overseeing research, such as the Food and Drug Administration, the Department of Health and Human Services, and the Office of Human Research Protections .
- Government agencies who are responsible for overseeing public health concerns such as the Centers for Disease Control and federal, state and local health departments.
- Montreal Neurological Institute

Otherwise, your research records will not be released without your permission unless required by law or a court order. It is possible that once this information is shared with authorized persons, it could be shared by the persons or agencies who receive it and it would no longer be protected by the federal medical privacy law.

21. If you agree to take part in this research study, how long will your protected health information be used and shared with others?

Your PHI will be used and shared with others until the study is completed.

You are not required to sign this consent and authorization or allow researchers to collect, use and share your PHI. Your refusal to sign will not affect your treatment, payment, enrollment, or eligibility for any benefits outside this research study. However, you cannot participate in this research unless you allow the collection, use and sharing of your protected health information by signing this consent and authorization.

You have the right to review and copy your protected health information. However, we can make this available only after the study is finished.

You can revoke your authorization at any time before, during, or after your participation in this study. If you revoke it, no new information will be collected about you. However, information that was already collected may still be used and shared with others if the researchers have relied on it to complete the research. You can revoke your authorization by giving a written request with your signature on it to the Principal Investigator.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. Additional information can be obtained at: http://irb.ufl.edu/gina.html or call 1-800-669-3362. If you think this law has been violated, it will be up to you to pursue any compensation from the offending insurance company and/or employer.

SIGNATURES

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this research study; the alternative to being in the study; and how the participant's protected health information will be collected, used, and shared with others:

Signature of Person Obtaining Consent and Authorization	Date

You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your protected health information will be collected, used and shared with others. You have received a copy of this Form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask questions at any time.

You voluntarily agree to participate in this study. You hereby authorize the collection, use and sharing of your protected health information as described in sections 17-21 above. By signing this form, you are not waiving any of your legal rights.

Signature of Person Consenting and Authorizing	Date