Aqueous Humor Dynamic Components That Determine Intraocular Pressure Variance

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The Ohio State University Combined Consent to Participate in Research and HIPAA Research Authorization

Study Title: Aqueous Humor Dynamic Components that Determine Intraocular Pressure Variance

Principal Investigator: Sayoko Moroi, MD, PhD

Sponsor: National Institutes of Health (NIH)

- **This is a consent form for research participation.** It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.
- **Your participation is voluntary.** You may refuse to participate in this study. If you decide to take part in the study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your usual benefits. Your decision will not affect your future relationship with The Ohio State University, The University of Nebraska, or Mayo Clinic. If you are a student or employee at one of these institutions, your decision will not affect your grades or employment status.
- **You may or may not benefit as a result of participating in this study.** Also, as explained below, your participation may result in unintended or harmful effects for you that may be minor or may be serious depending on the nature of the research.
- **You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate.** If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.

Key Information About This Study
The following is a short summary to help you decide whether or not to be a part of this study. More detailed information is listed later in this form.

The purpose of this research project is to identify reasons for variations in eye pressure response to glaucoma drugs between individuals. Depending on if you are currently being treated for your high eye pressures, the length of time you will be in the study will vary, between 9 and 14 weeks.

By participating in this study, you will have a course of procedures to make sure you are a good fit for the study, including a pregnancy test, vision tests, optic nerve exam, eye

pressure tests, review of your medical history, and measuring your vital signs. In later visits, you will continue to have eye pressures measurements, vision tests, and your health status reviewed. You will also take home a device that you will use to measure your eye pressures at home. You will also be asked to put drops provided by the research study in your eyes at certain times and also asked to washout, or stop your current medications for a certain period of time, so the medication can leave your body. Some of the study activities may be done in only one of your eyes, based on the health of your eyes. You will also be asked to provide a blood sample or spit specimen which will be analyzed for genetic traits related to glaucoma drug response and eye pressure changes. Data collected in this study may be entered into your medical record where authorized employees may see the information.

The known or expected risks are similar to those associated with your normal clinical care. There is a risk of loss of privacy and confidentiality while participating in this study. We put in place extra measures to protect your privacy and to minimize this risk. During the eye pressure measurements, there is the rare risk of a corneal scratch. The eye drop medications used during this study may cause eye irritation, including eye redness, eye burning or stinging, and blurry vision. All of these effects are short lived (less than 24 hours) and you will be appropriately monitored. More serious but rare side-effects include shortness of breath, changes in heart rate and blood pressure, and nausea. At the doses used in this study, these more serious side-effects are not expected. If applicable, there are risks associated with the washout period when you stop glaucoma medications, like a rise in eye pressure. You will be monitored very closely and a plan is in place to lower elevated eye pressure during the washout period if this becomes necessary. Participation in the study has the potential to benefit you by informing you of your eye pressure response and eye pressure changes during and outside of standard office hours, and both with and without different glaucoma medications.

1. Why is this study being done?

Glaucoma is a major cause of blindness caused by permanent damage to the optic nerve. However, blindness can be prevented by effectively treating and lowering eye pressure. The purpose of this research project is to identify reasons for the variations in eye pressure response to glaucoma drugs between individuals.

2. How many people will take part in this study?

This study will enroll approximately 200 participants across 3 study sites. Approximately 66 participants will be enrolled at each site.

3. What will happen if I take part in this study?

By participating in this study, you will have the following study procedures over a series of 6 visits:

Consent/authorization/personal questions: If you agree to participate in this study, you will be asked to sign this informed consent form and provide identifying information about yourself, such as your name, date of birth, gender and race. (Screening)

Health and medication questions: You will be asked to answer questions about your health, medical and family history, demographics, eye history and medications. At every visit, you will be asked about how you have been feeling. (All visits)

Pregnancy testing: If you are a woman who could become pregnant, you will have a urine test to check for pregnancy. The results of the pregnancy test must be negative in order for you to continue in the study. (Screening)

Vital signs: Your blood pressure, height, and weight will be measured. (Screening)

Assessment of adverse events: You will be asked about your current state of health and any health changes since your last study visit. (All visits)

Vision: You will be asked to read letters on an eye chart to determine how clearly you see. (All visits)

Biomicroscopy (eye examination): This test will look at your eyelids, front of your eye, and through your lens using a light and a microscope. (Screening)

Optic Disc Examination: This test will be used to look at the optic nerve at the back of your eyes. (Screening)

Gonioscopy: This test will look at the inside front portion of your eyes using drops to numb your eyes and a special mirrored lens. (Screening unless already obtained within a year)

Corneal thickness assessment (Pachymetry): This test will measure the thickness of your corneas (the clear front part of your eyes) using drops to numb your eyes. (Screening, Visits 3, 4 and 6)

Pupil Dilation for Fundus Examination: After placing eye drops on your eyes to make your pupils (the black part of your eyes) large or dilation, the study doctor can examine the inside of your eyes. Since dilation of your pupils may affect your vision and cause sensitivity to light, you should plan in advance for driving or other activities that require your normal vision. (Screening)

Optos Retinal Examination: If you do not wish to have your pupils dilated, the inside of your eyes can be examined using a special camera. (Screening)

Eye Pressure measurements (Tonometry): the pressure of your eyes will be measured with the following devices:

- **Reichert Ocular Response Analyzer (ORA)** measures the pressure in your eye using a light air-puff directed at the front of the eye. ORA also analyzes the function and motion of the clear front part of your eye. (Screening, Visits 3, 4, and 6)
- **Goldmann and Model-30** measure the pressure in your eye by touching your eye. Before measurements are taken, you will receive a numbing drop in each eye to minimize any possible discomfort when the instrument touches your eye. There may be a mild stinging sensation when the numbing drops are applied. (Goldmann at screening unless already obtained within a year, Model-30 during all visits) The change of the eye pressure (Pneumatonography) will be measured by placing a 10 gram weight to the probe of the Mode-30 device and your eye pressure changes will be measured for 2 minutes. (Visits 3, 4 and 6)
- **Icare® HOME** is a device designed to be used outside of the clinic setting to measure eye pressures. No numbing drops are needed for you to take these measurements. You will be trained and certified to use the device by a study team member at the screening visit and assigned a device to take home with you for the duration of the study. We will ask you to bring in the device to each study visit so the data can be downloaded by the study team and you can be informed of your eye pressures. The device will also be used to measure your eye pressure while in the office during Visit 3. Your study coordinator will instruct you about which days you should use this device at home, and whether to use it with both or only one of your eyes.
- **Falck Medical FMAT1** (May not be used at your study site) This instrument uses a clear, disposable prism to measure your eye pressure, as well as your change in eye pressure (tonography). Your eyes will be given numbing drops to minimize any possible discomfort. You may feel a mild stinging sensation when the drops are put in. The prism of the FMAT1 will be brought into contact with the center of your eye for a brief period to take the measurement.

Ultrasound Biomicroscopy Uses a probe to capture image data inside your eye. The probe will touch your eye. The technician will use an anesthetic and lubricant gel to minimize any possible discomfort. The images captured will be of the ciliary body, and ciliary muscles, in one of your eyes.**Washout period:** If you are currently prescribed glaucoma medication(s), the study team will tell you when to stop your current medications. This is called a “washout” (time for the medicines to leave your body). This time will allow your eye pressure to return to an unmedicated level.

The washout period may be between 4 to 42 days depending on the medications(s) you are currently using. You will be followed closely by your study doctor during this time. You will be asked by the study doctor to return to the site for safety checks during this time. (Visit 2) If your glaucoma or eye pressure gets worse during washout, you will receive appropriate rescue medications and will be asked to return to the clinic for another check of your eye pressures. (Visit 2.1). You will be asked to record what time you take the rescue medication each day.

Based the health of your eyes, you may be asked to do this washout from only 1 of your eyes.

ANTERION Imaging: One or both of your eyes will be imaged using the Heidelberg ANTERION Anterior Segment OCT before and after your first pneumatonography measurement on Visit 3 (baseline). This is done to see how long it takes for the front part of your eye to return back to normal after pneumatonography.

Eye measurements (Biometry): Eye measurements or biometry will be taken in both of your eyes using standard imaging equipment. (Visits 3, 4, and 6)

Eye Fluid Production (Fluorophotometry): After you place a temporary orange dye (fluorescein) using eye drops on the surface of your eyes, this dye will absorb into your eye and allow us to determine the rate at which your eye fluid circulates. You will be asked to record what time you take the fluorescein medication each day. The dye content in the front portion of the eye will be measured by shining a blue light into your eye for approximately 30 seconds. We calculate the fluid movement by measuring the change in the dye content in the front of your eye over the course of the day. This imaging, called fluorophotometry, will be measured during Visits 3, 4, and 6 and you will be asked to put the fluorescein in your eyes the night before Visits 3, 4, and 6.

Eye vein pressure (Episcleral venomanometry): Eye pressure is determined in part by the pressure in the eye. After placing a numbing drop on your eye, a study team member will look for an appropriate vein on the white portion of your eye. We estimate the vein pressure the pressure needed to change the shape of the vein. (Visits 3, 4, and 6)

Treatment with Timolol and Latanoprost: This study will examine how your eye pressures respond to two commonly used glaucoma drugs: timolol and latanoprost. We will provide you with these medications during Visits 3 and 4. The order that you receive them is randomized, like the flip of a coin. If you have a known sensitivity or serious concern to either timolol or latanoprost, you may still participate in the study with one of the treatments. You will be asked to put the drops in your eyes for 7 days prior to Visits 4 and 6. Specifically, you will use latanoprost for 7 days in the evening before the study visit, and you will use timolol for 7 days in the morning and evening before the study visit. Depending on the health of your eyes, we may ask you to use these medications in only one of your eyes. You will be asked to record what time you take the medications

each day.

Blood/Saliva sample: You will be asked to provide a one-time blood sample equal to approximately 3 tablespoons for genetic testing. Trained study personnel will draw a sample of your blood. If you are unable or unwilling to donate blood, we can collect a sample of your saliva. Your blood/saliva sample will be assigned a code number. Researchers will test the blood/saliva sample to look for genes related to glaucoma and response to glaucoma medications. The genetic (DNA or RNA) or protein analyses will be done in the laboratory of one of the investigators listed at the top of this form and/or in the laboratory of a collaborator and/or at a commercial lab. Your name or any other identifiers will not be given. The results of this test will not impact the clinical care of your condition; therefore, you will not be informed of any results related to the genetic testing portion of the study. Your DNA will be removed or "extracted" from your blood or saliva samples. The DNA will be studied or better known as "sequenced" by either single nucleotide polymorphisms methods for genome-wide association studies, whole genome sequencing, exome sequencing, or other similar techniques. Depending upon the genome sequencing method that is used, there is the possibility that mutations in genes causing other conditions could be discovered unrelated to the scope of the study. These findings will not be shared with you or anyone else. Given the findings may not be understood for some time, you will not be informed of new developments related to the genetic testing portion of the study.

_____ I choose to OPT-IN to the blood/saliva sample portion of this study
initials

_____ I choose to OPT-OUT to the blood/saliva sample portion of this study
initials

4. How long will I be in the study?

The total duration of the study will vary for each participant. For those participants enrolled who are currently taking glaucoma medications, the study involves up to 8 study visits over the course of 14 weeks. For those participants not currently on treatment, the study involves up to 8 visits over the course of 9 weeks. The estimated total study time commitment will be approximately 30-50 hours depending on the group you are in and how many visits are required. This includes both the time spent at home obtaining eye pressure measurements and the in-person clinic visits. If requested, the study coordinator will be able to provide a more precise estimate of the total time commitment based on the group to which you are assigned.

5. Can I stop being in the study?

You may leave the study at any time. If you decide to stop participating in the study,

there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship with The Ohio State University, The University of Nebraska, Mayo Clinic or your regular eye care provider.

6. What risks, side effects or discomforts can I expect from being in the study?

The known or expected risks are similar to those associated with your normal clinical care. All study procedures are standard clinical procedures and established research procedures.

The following are possible physical risks:

During the eye pressure measurements and ultrasound biomicroscopy, there is the rare risk of a corneal scratch. This discomfort will be managed by the study doctor and typically heals with a couple of days.

For ultrasound biomicroscopy, there is the rare risk of physical injury or illness from the low-power sound waves. This risk from this is extremely unlikely.

You will be asked to put fluorescein 2% dye in your eye(s) at home prior to research visits with fluorophotometry scans. This will be done using eye drops containing the dye. Depending on site availability, the fluorescein 2% drops you receive may vary between two forms: in the form of an FDA approved fluorescein injectable product that is used off-label by being compounded by a pharmacy into eye drops, OR a Fluorescein product approved in Canada, but under investigational use only status in the USA. Our study sources these forms of fluorescein as they have a known concentration of dye with minimal to no additives. Your study coordinator will inform you in advance of the fluorescein source.

Both forms of fluorescein drops may possibly cause your eye to become red, irritated, and swollen if you are allergic to fluorescein. If you are very allergic you may experience difficulty in breathing and an itchy rash on your skin. These side-effects are rare. More commonly, you may experience some minor temporary stinging or irritation, yellowish mucus and tears, or mild nausea after the drop goes into your eye. These side-effects are temporary and will resolve on their own. There are no other known risks associated with the use of either form of fluorescein 2%.

All other drugs are approved by the U.S. Department of Health and Human Services, Food and Drug Administration (FDA). There may be some mild eye irritation from the eye drops, which is typically minor and goes away on its own. If you are known to be allergic to any of the drops used in this study, you will not receive those specific drops.

You will be asked to return to the study team all empty, used, and unused drugs provided in the study.

A topical numbing drop (also known as an anesthetic drop) with or without fluorescein dye (applied as a drop or using a small paper strip) will be used for tests that require contact with the surface of your eye to help make you more comfortable and prevent a corneal scratch from occurring. These types of drops may cause temporary eye redness, temporary dry eye, and/or brief stinging/burning sensations in your eye. More serious side-effects are rare, but include possible allergic reactions that may damage the surface of the eye or cause eye inflammation. As such, patients with a known hypersensitivity to any of these components will not receive these drops. If fluorescein dye is used with the numbing drop, the same risks listed in the previous paragraph apply.

If you have not had a recent clinical dilated eye exam, a dilated eye exam will be performed as part of this study. Side-effects associated with the drops used to dilate your eyes are typically mild and include eye pain and stinging, temporary blurred vision and sensitivity to light, and eye redness and dryness. The eye pain and stinging will resolve within a few minutes and the blurred vision, sensitivity to light, redness, and dryness will resolve within a few hours. More serious side-effects are rare and typically associated with higher doses than the doses used in this study. These more serious side-effects include changes in heart rate, changes in blood pressure, fainting, heart attack, irregular heartbeat, dry mouth, headache, nausea, vomiting, and muscle pain.

The possible risks associated with the glaucoma eye drop timolol include shortness of breath and decreased pulse/heart rate. Blood pressure and heart rate will be monitored. Individuals with severe asthma or heart failure will not be allowed to participate in our study using beta-adrenergic antagonists, such as timolol. Any side effects will be short lived (typically less than two weeks). It is not known whether timolol ophthalmic drop is harmful to an unborn baby, but this is typically the glaucoma medication used for people who have juvenile glaucoma and are pregnant.

Timolol may also cause some stinging or irritation of the eye. Such side effects are temporary and will resolve on their own.

For latanoprost, the possible risks include irritation of the eye, which you may experience as a red eye or blurring of vision. These side effects reverse after stopping latanoprost. Animal studies have revealed evidence of embryo toxicity at high doses. There are no controlled studies in human pregnancy, so latanoprost is not typically given to pregnant people.

For ANTERION imaging, there is a risk of fatigue associated with fixation on a bright light. The timeframe of measurements will be acquired appropriately to limit the risk of fatigue.

Before participating in this study, please tell your doctor if you are pregnant or plan to become pregnant. To prevent any risks to a fetus or your nursing child, we will not allow

pregnant people or those who are breastfeeding to participate in this study. People of childbearing potential will only be allowed to participate after a negative pregnancy test and after agreement to use contraceptive measurements to prevent pregnancy during the course of the study. The pregnancy test will be given as part of your initial screening tests.

It is unlikely, but there is a possible risk of breach of confidentiality. The databases developed for this project will not contain information that is traditionally used to identify you, such as your name, address, telephone number, or social security number. It also is possible that there could be violations to the security of the computer systems used to store the codes linking your genetic and medical information to you. These codes will be maintained only at The Ohio State University.

Your personal health information (e.g., name, date of birth, and address) will need to be provided to an outside pharmacy to allow tracking of supplied study medication to you as a safety precaution (i.e., to ensure the study medication being supplied is provided only for you). If your personal health information is shared with an outside pharmacy, this information will not be linked to any other study data.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

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

All health insurance companies and group health plans must follow this federal law. This law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Under Ohio law, health insurance companies cannot ask about the results of a genetic test or use any information obtained from genetic testing to make decisions about providing coverage or benefits for health care services. Research using your specimens may include mapping your DNA (whole genome sequencing). This information could identify you. Ask the study team if you have questions.

If located in a state other than Ohio, please consult with someone in your respective state if you have questions regarding state laws associated with genetic testing and your individual protections.

7. What benefits can I expect from being in the study?

Participation in the study has the potential to benefit you by informing you of your eye pressure response and eye pressure changes during and outside of standard office hours, and both with and without different glaucoma medications.

8. What other choices do I have if I do not take part in the study?

You may choose not to participate without penalty or loss of benefits to which you are otherwise entitled.

9. What are the costs of taking part in this study?

There are no costs for taking part of this study However, there may be a parking cost associated with participation at certain sites. Your study coordinator will discuss the possibility of parking costs and the availability of study provided parking vouchers.

10. Will I be paid for taking part in this study?

For those who complete the screening visit (visit 1), you will be paid $70. For Visits 3, 4, and 6, you will be paid $175. If you need to come in for pressure checks (Visits 2, 2.1, 5, and 5.1) you will be paid $20 for each visit. The total maximum payment for study visits is up to $675. You will be compensated after visit 1, after visit 4, and after visit 6 using a re-loadable debit card known as a “ClinCard”, check, or cash depending on the site where you are participating.

For participating in the Icare® HOME measurements, you will be compensated $50 for each time period you use the device between visits, for a total of up to $200. You will be compensated up to $100 after visit 4 and up to $100 after visit 6 for Icare® HOME measurements using the same re-loaded debit card, check, or cash depending on the site where you are participating.

For participating in the Ultrasound Biomicroscopy, you will receive 25$ for the test at screening. You will receive an additional $25 for the test again at either Visit 4 or Visit 6. You will be compensated using the same re-loaded debit card, check, or cash depending on the site where you are participating.

You will not be reimbursed for travel or mileage.

By law, payments to participants are considered taxable income.

11. What happens if I am injured because I took part in this study?

For Ohio State Wexner Medical Center Participants:

If you suffer an injury from participating in this study, you should notify the researcher or study doctor immediately, who will determine if you should obtain medical treatment at The Ohio State University Wexner Medical Center.

The cost for this treatment will be billed to you or your medical or hospital insurance. The Ohio State University has no funds set aside for the payment of health care expenses for this study.

For University of Nebraska Medical Center Participants:

Your welfare is the main concern of every member of the research team. If you are injured or have a medical problem as a direct result of being in this study, you should immediately contact one of the people listed at the end of this consent form. Emergency medical treatment for this injury or problem will be available at The Nebraska Medical Center. If there is not sufficient time, you should seek care from a local health care provider.

UNMC and the Nebraska Medicine has no plans to pay for any required treatment or provide other compensation. If you have insurance, the insurance company may or may not pay the costs of medical treatment. If you do not have insurance, or if the insurance company refuses to pay, you will be expected to pay for the medical treatment.

Agreeing to this does not mean you have given up any of your legal rights.

For Mayo Clinic Participants:

Where to get help:
If you think you have suffered a research-related injury, you should promptly notify the Principal Investigator listed in the Contact Information at the beginning of this form. Mayo Clinic will offer care for research-related injuries, including first aid, emergency treatment and follow-up care as needed.

Who will pay for the treatment of research related injuries:

Care for such research-related injuries will be billed in the ordinary manner, to you or your insurance. You will be responsible for all treatment costs not covered by your insurance, including deductibles, co-payments and coinsurance.

12. What are my rights if I take part in this study?

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study.

You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subjects research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of research participants.

13. Will my de-identified information be used or shared for future research?

Yes, your de-identified information may be used or shared with other researchers without your additional informed consent.

14. Will my study-related information be kept confidential?

The NIH has issued a Certificate of Confidentiality for this study. This Certificate provides extra protection for you and your study information, documents, or samples (blood, tissue, etc.). The Certificates are issued so that we cannot be required to disclose any identifiable, sensitive information collected about you as a part of this study in a lawsuit or legal proceeding. We are also prevented from releasing your study information without your consent. This is a layer of protection over and above the already existing protections in place for you and your information, documents, or samples.

However, these protections do not apply in some situations. For example, we may have to release your information if a law requires us to do so, the Agency that is funding this study requests the information, or if the FDA tells us to release this information. We may also use your information to conduct other scientific research as allowed by federal regulations.

Study information that has health implications may be placed in your medical record where authorized employees may see the information. Further, authorized requests for your records (medical record release for continuity of care) may result in research-related information being released.

Please talk to your study team, or contact the Office of Responsible Research Practices at 614-688-8641, if you have questions. You may also visit the NIH website at https://humansubjects.nih.gov/coc/faqs to learn more.

Efforts will be made to keep your study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

Also, your records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies;
- U.S. Food and Drug Administration;
- The Ohio State University Institutional Review Board or Office of Responsible Research Practices;
- The sponsor supporting the study, their agents or study monitors; and
- Your insurance company (if charges are billed to insurance).

If we find information that significantly impacts your health, we will share it with you. Specifically, the pressure readings from the Icare® HOME device will be downloaded at each study visit. The eye pressure measurements will be given to you by the study ophthalmologist or research team member to inform you of how your eye(s) pressure may change while outside of the clinic setting.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search the website at any time.

15. HIPAA AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

Please use institution specific information underlined below:

HIPAA Authorization for Ohio State Wexner Medical Center and University of Nebraska Participants:

I. What information may be used and given to others?

- Past and present medical records;
- Research records;
- Records about phone calls made as part of this research;
- Records about your study visits;
- Information that includes personal identifiers, such as your name, or a number associated with you as an individual;
- Information gathered for this research about:
  Physical exams
  Laboratory, x-ray, and other test results
  Diaries and questionnaires
- Records about any study drug you received;

II. Who may use and give out information about you?

Researchers and study staff.

III. Who might get this information?

- The sponsor of this research. "Sponsor" means any persons or companies that are:
  - working for or with the sponsor; or
  - owned by the sponsor.
- Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information;
- If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic, or physician's office record;
- Others: Our collaborators at The University of Nebraska Medical Center and The Mayo Clinic. Authorized University of Nebraska Medical Center may be aware that you are participating in a research study and have access to your information subject to their local research and clinical medical record policies

IV. Your information <u>may</u> be given to:

- The U.S. Food and Drug Administration (FDA), Department of Health and Human Services (DHHS) agencies, and other federal and state entities;
- Governmental agencies in other countries;
- Governmental agencies to whom certain diseases (reportable diseases) must be reported; and
- The Ohio State University units involved in managing and approving the research study including the Office of Research and the Office of Responsible Research Practices.

V. Why will this information be used and/or given to others?

- To do the research;
- To study the results; and
- To make sure that the research was done right.

VI. When will my permission end?

There is no date at which your permission ends. Your information will be used indefinitely. This is because the information used and created during the study may be analyzed for many years, and it is not possible to know when this will be complete.

VII. May I withdraw or revoke (cancel) my permission?

Yes. Your authorization will be good for the time period indicated above unless you change your mind and revoke it in writing. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the researchers. If you withdraw your permission, you will not be able to stay in this study. When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others. Data collected and entered into your medical record during the course of the study may remain in your medical record.

VIII. What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study and receive research-related treatment. However, if you are being treated as a patient here, you will still be able to receive care.

IX. Is my health information protected after it has been given to others?

There is a risk that your information will be given to others without your permission. Any information that is shared may no longer be protected by federal privacy rules.

X. May I review or copy my information?

Signing this authorization also means that you may not be able to see or copy your study-related information until the study is completed.

Additional HIPAA Authorization Information for University of Nebraska Participants:

We may share information about you with other groups:

- The UNMC Institutional Review Board (IRB)
- Institutional officials designated by the UNMC IRB

HIPAA Authorization for Mayo Clinic Participants:

How will your privacy and the confidentiality of your records be protected?

Mayo Clinic is committed to protecting the confidentiality of information obtained about you in connection with this research study.

All paper records will be kept in a locked file cabinet in a locked room. Research documents will only refer to participants with a coded subject ID number. The code to the subject ID numbers will be kept on a secure and encrypted shared electronic folder that is only accessible to those on the research team involved with the study. Electronic records will be uploaded to a study specific electronic data capture (REDcap) for secure online storage and transfer of data. Additionally, data collected in this study may be entered into your secure medical record where authorized employees may see the information. During this research, information about your health will be collected. Under Federal law called the Privacy Rule, health information is private. However, there are exceptions to this rule, and you should know who may be able to see, use and share your health information for research and why they may need to do so. Information about you and your health cannot be used in this research study without your written permission. If you sign this form, it will provide that permission (or "authorization") to Mayo Clinic.

Your health information may be collected from:

- Past, present and future medical records.
- Research procedures, including research office visits, tests, interviews and questionnaires.

Your health information will be used and/or given to others to:

- Do the research.
- Report the results.
- See if the research was conducted following the approved study plan, and applicable rules and regulations.

Your health information may be used and shared with:

- Mayo Clinic research staff involved in this study.

- Other Mayo Clinic staff involved in your clinical care.
- Researchers involved in this study at other institutions.
- The sponsor(s) of this study and the people or groups hired by the sponsor(s) to help perform this research.
- The Mayo Clinic Institutional Review Board that oversees the research.
- Federal and State agencies (such as the Food and Drug Administration, the Department of Health and Human Services, the National Institutes of Health and other United States agencies) or government agencies in other countries that oversee or review research.
- A group that oversees the data (study information) and safety of this research.

How your information may be shared with others:

While taking part in this study, you will be assigned a code that is unique to you, but does not include information that directly identifies you. This code will be used if your study information is sent outside of Mayo Clinic. The groups or individuals who receive your coded information will use it only for the purposes described in this consent form.

If the results of this study are made public (for example, through scientific meetings, reports or media), information that identifies you will not be used.

In addition, individuals involved in study oversight and not employed by Mayo Clinic may be allowed to review your health information included in past, present, and future medical and/or research records. This review may be done on-site at Mayo Clinic or remotely (from an off-site location). These records contain information that directly identifies you. However, the individuals will not be allowed to record, print, copy (using paper, digital, photographic or other methods), or remove your identifying information from Mayo Clinic.

Is your health information protected after it has been shared with others?

Mayo Clinic asks anyone who receives your health information from us to protect your privacy; however, once your information is shared outside Mayo Clinic, we cannot promise that it will remain private and it may no longer be protected by the Privacy Rule.

Your Rights and Permissions

Participation in this study is completely voluntary. You have the right not to participate at all. Even if you decide to be part of the study now, you may change your mind and stop at any time. You do not have to sign this form, but if you do not, you cannot take part in this research study.

Deciding not to participate or choosing to leave the study will not result in any penalty. Saying ‘no’ will not harm your relationship with your own doctors or with Mayo Clinic.

If you cancel your permission for Mayo Clinic to use or share your health information, your participation in this study will end and no more information about you will be collected; however, information already collected about you in the study may continue to be used.

You can cancel your permission for Mayo Clinic to use or share your health information at any time by sending a letter to the address below:

Mayo Clinic
Office for Human Research Protection
ATTN: Notice of Revocation of Authorization
201 Building 4-60
200 1st Street SW
Rochester, MN 55905

Alternatively, you may cancel your permission by emailing the Mayo Clinic Research Subject Advocate at: researchsubjectadvocate@mayo.edu.

Please be sure to include in your letter or email:

- The name of the Principal Investigator,
- The study IRB number and /or study name, and
- Your contact information.

Your permission for Mayo Clinic to use and share your health information lasts until the end of this study, unless you cancel it. The study does not end until all data has been collected, checked (or audited), analyzed, and reported. Because research is an ongoing process, we cannot give you an exact date when the study will end. Sometimes this can be years after your study visits and/or activities have ended.

The Sponsor (The Ohio State Wexner Medical Center) will store your coded samples for a maximum of 10 years.

There is no expiration or end date related to the Sponsor's use of your health information received from Mayo Clinic as part of this study.

16. Who can answer my questions about the study?

For Ohio State Wexner Medical Center Participants:

For questions, concerns, or complaints about the study, or if you feel you have been harmed as a result of study participation, you may contact

Dr. Sayoko Moroi, MD, PhD (Study-Principal Investigator)
915 Olentangy River Rd.
Columbus, Ohio 43212
(614)-293-5287

For questions related to your privacy rights under HIPAA or related to this research authorization, please contact

HIPAA Privacy Officer
650 Ackerman Road,
Columbus, OH 43202
(614) 293-4477

For University of Nebraska Medical Center Participants:

You have rights as a research subject. These rights have been explained in this consent form and in " The Rights of Research Subjects" and " What Do I Need to Know" handout that you have been given. If you have any questions concerning your rights or want to discuss problems, concerns, obtain information or offer input, or make a complaint about the research, you can contact any of the following:

Dr. Vikas Gulati, MD (Site-Principal Investigator)
3902 Leavenworth Street
Omaha, Nebraska 68105
(402)-559-2020

UNMC Institutional Review Board
IRBORA@unmc.edu
987830 Nebraska Medical Center
Omaha, Nebraska 68198-7830
(402)-559-6463

UNMC Research Subject Advocate
unmcrsa@unmc.edu
(402)-559-6941

For Mayo Clinic Participants:

For questions, concerns, or complaints about the study, or if you feel you have been harmed as a result of study participation, you may contact

Dr. Arthur Sit, MD (Site-Principal Investigator)
200 1st Street SW
Rochester, Minnesota 55905
(507)-284-2511

For questions related to your privacy rights under HIPAA or related to this research authorization, please contact

Research Subject Advocate (RSA)

(507)-266-9372
researchsubjectadvocate@mayo.edu

For All Participants:

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team at Ohio State University, you may contact the Office of Responsible Research Practices at Ohio State University at 1-800-678-6251.

If you are injured as a result of participating in this study or for questions about a study-related injury, you may contact

Dr. Sayoko Moroi, MD, PhD
915 Olentangy River Rd.
Columbus, Ohio 43212
(614)-293-5287

Signing the consent form

I have read (or someone has read to me) this form and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this combined consent and HIPAA research authorization form**.**

Printed name of participant	**Signature of participant** **AM/PM** **Date and time**
Printed name of person authorized to consent for participant (when applicable)	**Signature of person authorized to consent for participant (when applicable)** **AM/PM**
Relationship to the participant	**Date and time**

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent	**Signature of person obtaining consent** **AM/PM** **Date and time**

Witness(es) - *May be left blank if not required by the IRB*

Printed name of witness	**Signature of witness** **AM/PM** **Date and time**
Printed name of witness	**Signature of witness** **AM/PM** **Date and time**