CONSENT TO ACT AS A PARTICIPANT IN A RESEARCH STUDY

PROSPECTIVE INVESTIGATION OF MULTIPLE SCLEROSIS IN THE THREE RIVERS REGION | Adult

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People are different due to their distinct biology and environment. The purpose of this observational research study is to investigate the factors that influence individual differences in patients with multiple sclerosis (MS). The study will ultimately help realize precision medicine and guide personalized care for MS patients. Our research team plans to eventually enroll 5000 patients with MS and 2500 control participants. We are asking you to participate in this research study because you are ≥18 years AND either have a diagnosis of multiple sclerosis or related disorder or do not have such diagnosis (control). As MS is a chronic neurologic condition, we are asking you to participate in this study for **30 years**. Because many factors could influence the individual differences, this research study will involve the following activities, some of which are optional. You may still participate in the overall study, even if you opt out of a specific research activity.

- We will ask you to **complete questionnaires**: (1) a primary questionnaire about your basic information, medical history, environmental exposure and family history,10-15 minutes, once every three years; (2) a self-reported outcome questionnaire about how you feel, 15-20 minutes, once per year. There may be supplementary questionnaires in the future as our understanding of the disease evolves.
- We may ask you to **donate blood** upon enrollment and then at least once (but no more than four times) per year, up to 120 mL (or about eight tablespoons) per draw. We may ask for blood samples if you have a relapse.
- We may ask you to **donate stool** samples, up to four times per year. We may ask you to complete questionnaires at the time of stool donation: (1) a participant questionnaire, 10 minutes; (2) a diet questionnaire, 15-20 minutes.
- We may ask you to **donate urine** samples, up to twice per year.
- We may ask you to **donate saliva** samples, up to twice per year.
- We will request any unused cerebrospinal fluid, collected as part of your routine clinical care.
- We will ultimately study your **entire genome** (i.e., overall genetic makeup).
- We may ask you to complete a series of **standard tests that gauge your ability to think, see, move arms / hands, moves leg function and walk**, once per year, 20-30 minutes.
- We may ask you to complete a series of more detailed **tests that measure your thinking process, including concentration, attention and memory**, once per year, 10-20 minutes.
- We may ask you to participate in **biosensor testing** that measure thinking, movement / walking, balance, fatigue, and/or stress. For example, we may ask you to wear an activity watch continuously on your wrist for 14 days.
- We may ask you about your **social circle** (e.g., family, friends), one questionnaire per year, 10-20 minutes.
- We will ask you to update **your contact information** annually.
- We will ask you to provide **two contact persons** and update annually. To ensure that we do not lose contact with you throughout this long-term study, we will reach out to the designated contact persons only in case we exhaust all means of reaching you (by phone, email, or mail). When considering a potential person as the contact, please be sure that this person would agree to be the contact person and should be aware that it is OK to provide the research team with your contact information.

Medical Records. We will request your authorization or permission to review your medical records to obtain past, present, and future medical information from hospitals and other medical facilities (at UPMC or non-UPMC entities), including diagnoses, age, past medical history, imaging or laboratory tests, medical, surgical or psychiatric evaluations. This authorization is valid for the length of the study, or until you formally withdraw your authorization.

This research study involves minimal risk. Some questions in the questionnaires are personal and may make a person uncomfortable. For blood draw, people commonly feel a brief amount of pain at the needle site, which may become sore and red; a temporary, harmless “black and blue” mark may infrequently occur; rarely an infection develops, which can be treated; very rarely some people may faint. There is no risk for donating stool, urine or saliva samples. Some people may feel uncomfortable donating stool. There is no risk for completing tests that measure thinking or physical ability. There is no risk for wearing biosensors such as an activity watch. Although every reasonable effort will be taken, confidentiality (including Internet communication activities) cannot be guaranteed and it is possible that additional information beyond that collected for research purposes may be captured and used by others not associated with this study.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies and group health plans to use genetic information in making decisions regarding your eligibility or premiums. GINA also makes it illegal for employers with 15 or more employees to use your genetic information when making

decisions regarding hiring, promoting, firing, or setting the terms of employment. This federal law does not protect you against genetic discrimination by companies that sell life, disability, or long-term care insurance.

If you believe that the research activities have resulted in an injury to you, immediately contact the principal investigator who is listed on the first page of this form. Emergency medical treatment for injuries solely and directly related to your participation in this research study will be provided to you by UPMC. Your insurance provider may be billed for the costs of this emergency treatment, but none of those costs will be charged directly to you. If your research-related injury requires medical care beyond this emergency treatment, you will be responsible for the costs of this follow-up care. At this time, there is no plan for any additional financial compensation. You do not waive any legal rights by signing this form.

Study Benefits. Participation in this research study may not provide direct benefit to you. This research could potentially benefit the society and patients worldwide by helping to guide individualized care. We will describe findings from this research in general terms in newsletters. This research *might* someday lead to the development of commercial products (such as a medical test) that could be sold by a company. You will not receive payment from the sale of such product.

Return of Research Results. Because the tests from this research study are considered experimental, individual results from the study will not be returned to you and will not be placed in your medical record.

Protection of Confidentiality. The University of Pittsburgh and UPMC will take all possible measures to protect your information and follow all federal confidentiality regulations, but we cannot guarantee absolute confidentiality. The unique study code number that each participant receives following enrollment will serve to label all research data and biological samples. A master list relating the unique study number with identifiable information (e.g., name, sex, address, date of birth) will be kept in a separate secure file and accessible to approved and trained research staff. All research data are kept in firewall-protected, password-required, encrypted, institution-approved research databases that are separate from any hospital medical records or databases. All manipulations of research data and samples will be performed using this unique study number. All research team members have password-protected access to the research database.

Per University of Pittsburgh policy, all research records must be maintained for at least 7 years following final reporting or publication of a project. For projects involving children, records must be maintained for 5 years past age of majority (age 23 per PA State law) after study participation ends. Coded research data and samples may be stored for an indefinite period of time in the principal investigator's laboratory or institution-approved data warehouse and biobank.

Coded research data (including genetic data) and samples may be shared with external academic or commercial entities for research purpose. These external entities will not have access to a participant's identifiable information. Per federal regulation on sharing research findings, research data (including genetic data) may be submitted to a central repository at the National Institute of Health or other repositories. Personal information may be reviewed by regulatory officials from the University or Hospital Research Conduct and Compliance Office, local, state or federal regulatory agencies.

Protection of Privacy. All in-person research activities will be conducted in private clinic exam or office rooms.

Voluntary Participation. Participation in this research is entirely voluntary. If there are any words you do not understand, please ask us. A research team member will be available to answer your current and future questions. Whether or not you provide your consent for participation in this study will have no effect on your current or future relationship with the University of Pittsburgh. Whether or not you provide your consent for participation in this study will have no effect on your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider. Your physician may be involved as an investigator in this study. Before agreeing to participate, or at any time during study participation, you may discuss care with another doctor who is not associated with this research study. You are not under any obligation to participate in any research study offered by your physician.

Right to Withdraw. You can at any time withdraw from this research study. To formally withdraw from this research study, please provide a written and dated notice of this decision to the principal investigator below. Your decision to withdraw from this study will have no effect on your current or future relationship with the University of Pittsburgh or your current or future medical care at a UPMC hospital or affiliated health care provider or your current or future relationship with a health care insurance provider.

Costs. There will be no cost to you or your insurance company if you agree to participate in this study. However, you will be responsible for the cost of any routine clinical care, just as if you were not participating in this study.

Payment. There will be no compensation for complete or partial completion of the research activities except control participants may receive up to $25 for blood draw.

Questions. If you have questions or concerns about this research, you can call or write to us. You can call principal investigator Zongqi Xia, MD, PhD, at 412-383-5377, M-F 9am-5pm. The address is Biomedical Science Tower 3, Suite 7019, 3501 Fifth Avenue, Pittsburgh, PA 15260. You can also call the research study coordinators at 412-624-9126, M-F 9am-5pm, or email us at <msstudy2@pitt.edu>. If you want to speak with someone **not** directly involved in this research study about your rights as a research participant, your concerns about the research, and/or a complaint, please contact the Human Subject Protections Advocate of the IRB Office, University of Pittsburgh at 1-866-212-2668.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.
- This research study has been explained to me, including the potential benefits and risks.
- I have had the opportunity to ask questions. I understand that I may always ask questions, voice concerns or complaints about any aspect of the research study during the course of this study.
- I understand the information given to me.

By signing this form, I agree to participate in this research, and authorize the use and disclosure of my medical record information for the purposes described above. A copy of this consent will be provided to me.

_____ _____

Person Providing Consent (Print | Signature) Date | Time

Certification of Informed Consent

- I have explained the research to the above-named individual and have discussed the potential benefits and risks of study participation.
- I have answered all questions about this research study to the best of my ability and will always be available to address future questions, concerns, or complaints as they arise.
- I further certify that no research component of this protocol was begun until after this consent form was signed.

_____ _____

Person Obtaining Consent (Print | Signature) Date | Time