RESEARCH SUBJECT CONSENT FORM

TITLE: A Prospective, Non-Randomized, Multi–Center Observational Study to Establish a Physical Baseline Profile for Individual Study Subjects Using Various Modalities and Identify Deviations via Longitudinal Monitoring that May Develop Over Time and May be Relevant to Human Health and Longevity

PROTOCOL NO.: PLI001
WCG IRB Protocol #20224339

SPONSOR: PUER Research, LLC

INVESTIGATOR: Name
Address
City, State Zip
Country

STUDY-RELATED PHONE NUMBER(S): Phone Number
Phone Number (24 hours)
[24 hour number is required]

Taking part in this research is voluntary. You may decide not to participate, or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are otherwise entitled.

If you have any questions, concerns, or complaints or think this research has hurt you, talk to the research team at the phone number(s) listed in this document.

RESEARCH CONSENT SUMMARY

You are being asked for your consent to take part in a research study. This document provides a concise summary of this research. It describes the key information that we believe most people need to decide whether to take part in this research. Later sections of this document will provide all relevant details.

What should I know about this research?

- Someone will explain this research to you.
- Taking part in this research is voluntary. Whether you take part is up to you.
- If you don't take part, it won't be held against you.
- You can take part now and later drop out, and it won't be held against you

- If you don't understand, ask questions.
- Ask all the questions you want before you decide.

How long will I be in this research?
We expect that your taking part in this research will last approximately 36 months.

Why is this research being done?
The purpose of this research is to collect individual biological data, including genetic data, over a span of time to find out if a detailed evaluation of simple lab measurements, non-invasive over-the-skin-imaging and functional assessments like breathing, brain and heart measurements etc. will identify biological deviations that are different from the average population. Lab measurements will include genomics (your genetic data), levels of your circulating molecules (proteins, small molecules, amino acids, etc.) from your blood, and other biological samples, like urine, stool and saliva. If successful, this study will help establish individual monitoring over time as a method to make healthy living better.

What happens to me if I agree to take part in this research?
If you decide to take part in this research study, the general procedures include an initial assessment performed by a trained Research Associate, sample collection of blood, urine, stool and saliva, non-invasive over-the-skin-imaging, such as magnetic resonance imaging (MRI) or computerized tomography (CT) scans, and functional assessments, such as breathing, brain and heart monitoring, and eye examination. Their use in this study is experimental.

Could being in this research hurt me?
The most likely risks or discomforts that you may expect from taking part in this research include those associated with giving blood samples (vein puncture) such as pain, bruising, bleeding at the puncture site, fainting and/or inflammation of the vein. The non-invasive imaging performed as part of this research is non-radiation-based and radiation-based imaging that may include contrast agents (injected into the blood vessels to enhance imaging). These contrast agents have a very low risk of allergic reaction. Due to risks to a fetus associated with the radiation exposure, you may not take part in this study if you are pregnant at enrollment or any visit. Positive findings on these tests may cause anxiety or impact you if you decide to do further testing.

Will being in this research benefit me?
You may personally not benefit from participating in this research study. Potential benefit to you from taking part in this research may include the identification of variation and changes from your baseline profile that may be worthy of further evaluation and testing by your primary care physician. Your individual research study results may be discussed with you in detail and if you wish, may be shared with your healthcare provider.

Possible benefits to others include identifying methods of medical monitoring over time that may lead to better detection of biological deviations from the average population.

What other choices do I have besides taking part in this research?

The alternative to participating in this research study is to not participate at all.

What else should I know about this research?

Other information that may be important for you to consider so you can decide whether to take part in this research is that this study involves the collection of protected health information (data) and samples, which may be used for future research. Your name and other personal identifiers will be removed from these data and samples. Your information will be protected from disclosure to others to the extent required by law.

DETAILED RESEARCH CONSENT

You are being invited to take part in a research study. A person who takes part in a research study is called a research subject, or research participant.

What should I know about this research?

- Someone will explain this research to you.
- This form sums up that explanation.
- Taking part in this research is voluntary. Whether you take part is up to you.
- You can choose not to take part. There will be no penalty or loss of benefits to which you are otherwise entitled.
- You can agree to take part and later change your mind. There will be no penalty or loss of benefits to which you are otherwise entitled.
- If you don't understand, ask questions.
- Ask all the questions you want before you decide.
- There will be no cost to you to participate.

Why is this research being done?

The purpose of this research is to collect individual or each person's biological data over a span of time to find out if a detailed evaluation of genomics – your genetic data analyzed by collecting your blood sample, other lab measurements like levels of your circulating molecules (proteins, small molecules, amino acids, etc.) from your blood, and other biological samples like urine, stool and saliva, non-invasive, over-the-skin-imaging and functional assessments like breathing, brain and heart measurements etc., can identify if some of your individual results are different from those of the average population. This research study may help to find out if, and how, these measurements may predict biological changes over time.

Up to 10,000 subjects will take part in this research study over time.

How long will I be in this research?

We expect that your taking part in this research will last up to 36 months.

What happens to me if I agree to take part in this research?

If you decide to take part in this research study, you will have up to six (6) visits over 36 months for detailed evaluation. You will be required to participate in all study visits, provide the required blood, urine, stool and saliva samples and have non-invasive, over the skin medical imaging performed when specified in the study procedure. The study procedure schedule is available on Page 6 of this document. To complete all procedures of the study, you will be asked to come for up to six (6) visits over 36 months, including this first one. At each visit, you will undergo the following procedures:

- Initial assessment – A trained Research Associate will perform a physical evaluation and exam.
- Lab measurements – Biochemical and molecular testing ('Omics' assessment) via collection of blood, urine, stool and saliva.
    - Biochemical tests consist of a diverse spectrum of laboratory analyses of metabolites, enzyme activities, and functional assays to understand how individual results may compare to the average population
    - Molecular testing is a laboratory method that uses a sample of tissue, blood, or other body fluid to check for certain genes, proteins, or other molecules to measure different aspects of biological processes. This is also called biomarker testing, or "molecular profiling". The 'Omics' assessment via molecular testing could include Whole genome sequencing involving your genetic material DNA, whole genome DNA methylation analysis, whole transcriptome sequencing from circulating mononuclear cells (entire complement of your transcripts when your genetic material DNA is converted to RNA, that carries the message of how to build proteins within your cells), proteomics profiling (protein profile), metabolomics profiling (metabolite profile) and other conventional biomarker analysis.
- Non-invasive imaging – The need for the following will be determined by the investigator on the basis of initial assessment and biochemical and molecular testing above:
    - MRI – to include brain, head, neck and spine (may include contrast)
    - CT – to include head, chest, abdomen and pelvis (may include contrast)
    - Ultrasound – to include reproductive organs and bladder
    - X-ray – to include arms and legs

- Functional Assessments (need will be determined by the initial assessment, described above)
    - VO2-max functional testing (maximum oxygen consumption)
    - Non-invasive endothelial function testing
    - Electroencephalogram (EEG)
    - Electromyography (EMG)
    - Ophthalmologic examination for vision preservation and other pathology
    - Optional: sleep study
- Wearables and Quantified Self Assessments (need determined by the initial assessment, described above)
    - Ambulatory ECG monitoring (Apple Watch, ePatch or similar)
    - Continuous glucose monitoring
    - Oura ring (may obviate the need for formal sleep study) or similar product(s) measuring heart rate (HR), heart rate variation (HRV), sleep duration, sleep stage.

The research will include whole genome sequencing (determining the order of DNA building blocks (nucleotides) in your genetic code) only at visit 1. Samples for all other omics assessment will be conducted at all visits.

Study Procedure Schedule:

Procedure	**Visit #1 Baseline Visit**	**Visit #2 6-Month Visit ± 1 month**	**Visit #3 12-Month Visit ± 1 month**	**Visit #4 18-Month Visit ± 1 month**	**Visit #5 24-Month Visit ± 1 month**	**Visit #6 36-Month Visit ± 1 month**
Medical history and physical exam	X	X	X	X	X	X
Biochemical/Molecular Testing (omics assessment) (Blood draw)	X	X	X	X	X	X
Pregnancy testing[1]	X	X	X	X	X	X
Whole genome sequencing (Blood draw)	X					
Non-Invasive Imaging (MRI, CT and/or X-ray)	X	X	X	X	X	X

Functional Assessments (as needed)		X	X	X	X	X
Wearables and Quantified Self Assessments (as needed)		X	X	X	X	X

1. If you are able to get pregnant.

The research will be conducted at up to 20 study sites in the United States. Each study visit will be 3-6 hours on the day of visit where multiple procedures will be conducted per the study procedures schedule. A total of 6 visits will be conducted during the duration of enrollment (36 months) for a participant during the study.

- Blood will be drawn at each of the six (6) visits. Up to 155 mL or 10.5 tablespoons of blood will be drawn at each visit.
- 10 mL of urine will be collected at each of the six (6) visits.
- If you are able to get pregnant, additional pregnancy testing prior to imaging studies will be done at each visit.
- 2 mL of saliva will be collected at each of the six (6) visits.
- Single stool sample will be collected at each of the six (6) visits.
  You will be informed of any relevant research results.

What are my responsibilities if I take part in this research?

- If you take part in this research, you will be responsible to: Participate in up to six (6) study visits and complete all procedures of the study.
- Discuss any new medications or new medical issues with the Investigator during the initial assessment portion of each of the six (6) study visits.
- Advise the study doctor if you are pregnant or planning to become pregnant. Due to the risk of radiation exposure to your fetus, you may not participate in the study if you are pregnant at any visit.

Could being in this research hurt me?

The most likely risks or discomforts that you may expect from taking part in this research include side effects associated with vein puncture or blood draw. It may be necessary to try more than once to draw blood. A new needle will be used for each blood draw. You might feel pain or be lightheaded from this. You may have the following where the needle sticks you when blood is drawn: pain, bruising, bleeding at the puncture site, fainting and/or inflammation of the vein (rarely).

You will also undergo MRI. MRI is a non-radiation-based imaging method. Contrast agents may be administered in connection with the MRI examination. Contrast agents have been associated with potential risks. Allergic-like reactions are uncommon and vary in frequency from 0.004% to

0.7%. Severe life-threatening reactions are exceedingly rare (0.001% to 0.01%). Some contrast agents have also been associated with nephrogenic systemic fibrosis (NSF) in patients with compromised renal function.

You will also undergo CT. CT is a imaging method that includes exposure to ionizing radiation with or without contrast agents. The contrast is either given orally, rectally or intravenously. This contrast material can rarely cause medical problems or allergic reactions. Most of these reactions are mild and result in a rash or itchiness. In rare instances, an allergic reaction can be serious, even life-threatening.

During an abdominal ultrasound exam, a trained technician will glide a small device over your abdomen to take pictures of the tissue under your skin. There are no known side effects from taking part in an abdominal ultrasound exam. Ultrasound tests do not involve radiation and they do not penetrate the skin.

You will also undergo x-ray imaging. X-ray is an imaging method that includes exposure to a low amount of electromagnetic radiation to take pictures of structures in your body, such as bones.

There is a small risk that some of the tests you will undergo in this study will produce in a false positive result. This could result in your undergoing additional testing that would otherwise be unnecessary.

You may also learn that you have or are at risk of having a condition or disease for which there is currently not effective treatment. Such information could lead you to experience additional stress.

There may be privacy risks involved with your participation in the study, which are discussed in detail within the Confidentiality and Data Protection Section.

The research may involve risks that are unforeseeable.

Will being in this research benefit me?

You may not derive any benefit from participating in this study. We cannot promise any benefits to you or others from your taking part in this research. Potential benefit to you may include the identification of variation or changes from your baseline profile that may be worthy of further evaluation and testing by your primary care physician. Possible benefits to others include identifying methods of medical monitoring over time that may lead to enhanced detection of deviations.

What other choices do I have besides taking part in this research?

Your alternative is to not take part in this research. You may continue to participate in your standard of care procedures like maintaining generally accepted intervals of testing, as suggested by your current primary care physician.

What happens to the information collected for this research? Confidentiality and Data Protection

Your privacy is very important to the Sponsor and the study researchers, and they will expend every reasonable effort to protect your privacy in accordance with applicable law. During the study, the study Investigator and study staff will collect and record in your study record sensitive information about you such as: birthdate, gender, ethnicity, health data, information derived from samples collected from you and results of study procedures. Further, samples, such as urine, stool, blood, and saliva samples may be collected from you as described in this informed consent form. Except as required by law, your study samples and study records will not include your name or other direct personal identifiers. Rather, your study samples and records will be identified by an assigned code number (the "Patient ID Code"). This code can only be tracked back to you via a master list linking the code numbers to names, which will be held by the study Investigator and kept separate from the study samples and study records. Only your coded study samples and data will be forwarded to Sponsor. The master list linking your name to your Patient ID Code will not be provided to Sponsor. Although procedures are in place to protect your privacy, absolute confidentiality cannot be guaranteed.

The coded data received by the Sponsor and its service providers will be stored, processed and compiled, including by manual and electronic methods. The coded data and your study samples may be transferred within the United States and to other countries. The coded data from this study, including that obtained from your study samples, may be used by or for Sponsor to carry out the study, for product development and marketing, including marketing and development of the PUER research Program, to meet legal obligations and requirements in connection with the study and to make publications or presentations. Your name and identify will not be included in any such publications or presentations. Additionally, coded data and samples may be used for future research as described later in this informed consent form. By signing this informed consent form you are agreeing that your coded data and samples may be used and disclosed as described in this informed consent form.

Coded data collected in this research might be used for future research or distributed to another investigator for future research without your consent.

Certain medical information collected during the study, including the results of some tests and procedures (excluding genetic testing) may be included in your medical record by your Provider. Your medical record may include your name and other information that directly identifies you.

The information included in your medical record will be available to the study Investigator and study staff, study monitors and other parties authorized by Sponsor, regulatory agencies such as the FDA, the institutional review board (IRB) (an oversight committee that looks out for the rights and welfare of research subjects), health care providers other than study staff and your insurance company. Your medical records and other personal information will be protected in accordance with U.S. law and any other applicable data protection laws. Your study records and samples will likewise be stored and kept according to applicable legal requirements.

Your private information and your medical record will be shared with individuals and organizations that conduct or watch over this research, including:

- The study investigator, study staff and those working for or with them
- The research Sponsor
- People who work with the research sponsor, its affiliates, persons and organizations working with sponsor and its affiliates
- Government agencies with human research oversight authority WCG IRB, the Institutional Review Board (IRB) that reviewed this research

By signing this consent form, you authorize the above organizations and individuals to access your study and medical records for the purposes provided in this informed consent form and further agree that the IRB and regulatory authorities may make copies of such records, including those with your name on them.

The Sponsor may publish the results of this research. However, your name and other identifying information will be kept confidential.

The Sponsor will protect your information from disclosure to others to the extent required by law. The Sponsor cannot promise complete secrecy.

Samples

Samples will be collected from you by the study staff as described in this informed consent form. Some samples will be tested immediately and then destroyed. Other samples will be stored for later testing (including future research as described in this informed consent) and may be sent to Sponsor and/or those working with sponsor for this purpose. Such samples will not include your name, but will be identified by a Patient ID Code. Sponsor and those working with sponsor will keep your samples securely until they are destroyed. Sponsor and those working with Sponsor may keep and use your coded samples for the purposes described in this informed consent for up to ten (10) years following the issuance of a final study report by the Sponsor (a report discussing the study at all participating institutions. After this ten-year period such samples will be destroyed.

Samples collected in this research might be deidentified and used for future research or distributed to another investigator for future research without your consent.

In addition to the above, representatives of regulatory authorities may have access to your samples.

Some of your blood samples may be used for genetic testing. There are laws that protect you from discrimination based on your genetic information. 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. 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. In some cases, employers could use your genetic information to decide whether to hire or fire you. However, there is a risk that someone could get access to your genetic information and identify you by name.

You may still participate in this research study if you do not agree to your blood samples being used for genetic testing.

Do you consent to genetic testing of your blood samples?

☐ **YES** ☐ **NO**

Who can answer my questions about this research?

If you have questions, concerns, or complaints, or think this research has hurt you or made you sick, talk to the research team at the phone number listed above on the first page.
This research is being overseen by WCG IRB. An IRB is a group of people who perform independent review of research studies. You may talk to them at 855-818-2289 or researchquestions@wcgirb.com if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

What if I am injured because of taking part in this research?

If you are injured or get sick because of being in this research, you need to seek medical attention immediately, as you normally would. Your insurance may be billed for this treatment. The sponsor will pay any charges that are not covered by insurance policy or the government, provided the injury was not due to an underlying illness or condition and was not caused by you or some other third party. No other payment is routinely available from the study Investigator or sponsor. If you are injured as a result of this study, you do not give up your right to pursue a claim through the legal system.

Can I be removed from this research without my approval?

The person in charge of this research can remove you from this research without your approval. Possible reasons for removal include:

- It is in your best interest
- You are pregnant at any visit
- You have a side effect that requires stopping the research
- The research is canceled by a government agency with human clinical research oversight authority or the sponsor
- You are unable to keep your scheduled appointments

We will tell you about any new information that may affect your health, welfare, or choice to stay in this research.

What happens if I agree to be in this research, but I change my mind later?

You may decide at any time to leave the study. Simply contact the research team and asked to be withdrawn. Your research data will continue to be used up to the date of withdrawal.

There is no penalty to you for withdrawing from the study. You can continue to receive medical care from your physicians.

Will I be paid for taking part in this research?

You will not be paid for taking part in this research.

Your specimens and data (even if identifiers are removed) may be used for commercial profit. You will not share in this commercial profit.

Statement of Consent:

Your signature documents your consent to take part in this research.

Signature of adult subject capable of consent	Date

Signature of person obtaining consent	Date

The study patient has indicated that he/she is unable to read. The consent document has been read to the patient by a member of the study staff, discussed with the patient by a member of the study staff, and the patient has been given an opportunity to ask questions of the study staff.

Printed Name of Impartial Witness

Signature of Impartial Witness* Date

*Impartial Witness: A person, who is independent of the study, who cannot be unfairly influenced by people involved with the study, who attends the informed consent process if the patient or the patient's legally acceptable representative cannot read, and who reads the informed consent and any other written information supplied to the patient. Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

During your participation in this study, the study doctor and study staff will collect or create personal health information about you (for example, medical histories and results of any tests, examinations, or procedures you undergo while in the study) and record it on study documents. The study doctor will keep this personal health information (other than genetic testing results) in your study-related records (that we will refer to as "your study records"). In addition, the study doctor may obtain, and include in your study records, information regarding your past, present and/or future physical or mental health and/or condition. Your study doctor may ask you to sign a separate authorization to obtain some or all of your medical records from your doctor. Your study records may include other personal information (such as Social Security number, hospital medical record numbers, date of birth, etc.), which could be used to identify you. Health information that could identify you is called "Protected Health Information" (or "PHI").

Under federal law (the HIPAA "Privacy Rule"), your PHI that is created or obtained during this research study cannot be used to conduct the research or disclosed (given to anyone) for research purposes without your permission. This permission is called an "Authorization." **You may not participate in this study unless you sign this Authorization. By signing, you are agreeing to allow the study doctor and staff to use your PHI to conduct this study.**

By signing this Authorization, you also are agreeing to allow the study doctor to disclose PHI to the following entities and bodies:

- The Sponsor of this study and its affiliates and anyone working on behalf of the Sponsor to conduct this study. The Sponsor will analyze and evaluate the PHI and may use it to develop new tests, procedures, and commercial products. The Sponsor may, however, look at your study records that identify you. In addition, the Sponsor may visit the study site to oversee the way the study is being conducted and may review your PHI during these visits to make sure the information is correct.
- The Institutional Review Board ("IRB") may have access to your PHI in connection with its responsibilities.
- The United States Food and Drug Administration (“FDA”) and/or other public health regulatory agencies in the United States or foreign countries.

These disclosures help ensure that the information related to the study is available to all parties who may need it for research purposes.

Except for the disclosures described above, your PHI will not be shared with others unless required by law. If your PHI is given to the parties listed above and/or to others who are not required to comply with the federal law (including the HIPAA Privacy Rule), your PHI will no longer be protected by this law and could possibly be used or disclosed without your permission.

By signing this document, you agree that you will not be able to see or copy, and will not be able to correct, some or all of your PHI until the Sponsor has completed all work related to this study. At that time, you may ask to see your records**.**

This Authorization will remain in effect until December 31, 2037.

You have a right to revoke your Authorization at any time. If you revoke it, your PHI will no longer be used for this study, except to the extent the parties to the research have already taken action based upon your Authorization or need the information to maintain the integrity or reliability of the current research. To revoke your Authorization, you must write to the study doctor, stating that you are revoking this Authorization to Use and Disclose Protected Health Information. If you revoke this Authorization, you will not be allowed to continue to be in this study.

You will receive a copy of this Authorization after you have signed it.

_____ _____
Signature of Patient Date

_____
Printed Name of Patient

_____ _____
Signature of the Person Obtaining the Authorization Date

_____
Printed Name of the Person Obtaining the Authorization