University of California, Los Angeles

CONSENT TO PARTICIPATE IN RESEARCH

Type 2 Diabetes Mellitus and Blood Brain Barrier Improvement – A Randomized Clinical Trial

Rajesh Kumar, PhD, Department of Anesthesiology, University of California, Los Angeles (UCLA) is conducting a research study.

You are selected as a possible participant in this study because you are 40-65 years of age, have been diagnosed with Type 2 Diabetes Mellitus, and do not have contraindications to the MR procedures. Your participation in this research study is voluntary.

Why is this study being done?

This study will examine patients with T2DM through brain MRI scans, cognition assessments, blood tests, and questionnaires. Our goal is to see if a thiamine supplement (taking vitamin B1 capsules) can improve function. Patients will be asked to come to UCLA two times three months apart and each visit will last about 2.5-3 hours.

What will happen if I take part in this research study?

If you volunteer to participate in this study, the researcher will ask you to do and understand the following:

- You will be asked to arrive at the Department of Radiological Sciences, MRI suite (300 Medical Plaza, UCLA) at your scheduled time and be met by the Principal investigators (Dr. Choi or Dr. Kumar), who will review the procedures and obtain your consent.
- All T2DM adults will be escorted for blood draw at the Department of Pathology and Medicine. Once the subject is back, the participant will be taken to the MRI scanner room.
- We will perform various non-invasive MR procedures during the same visit, and you will require a second visit to UCLA (3 months after first visit) to complete the study.
- You will not have any caffeine (coffee, soda etc) or alcohol 10 hours before the scheduled MRI.
- You may opt out at any time, even if you have not completed all the procedures.
- Prior to the study, Dr. Kumar or a research team member will review your medical history relevant to the current study (e.g., myocardial infarction).
- Dr. Kumar or a research team member will also review the MRI safety questionnaire to ensure you can safely participate in a MRI scan. If we determine that you cannot safely enter into the scanner, you will be excluded from the study.
- The imaging examinations performed as part of this research will not be reviewed by

a UCLA radiologist and no formal interpretation will be rendered. All questions concerning the findings (normal or abnormal) from this exam should be referred to the principal investigator.

- **Procedure 1, medical history, questionnaires and blood test:** You will complete a questionnaire regarding your safety in the MRI scanner machine and provide consent to participate in this study. You will then complete a number of questionnaires regarding your mood, feelings of anxiousness and other emotions, diabetes severity and self-care abilities, and cognitive tests. We will measure A1C levels by a finger prick blood test using the point-of-care A1CNow instrument. All T2DM adults will then be escorted for blood draw at the Department of Pathology and Medicine. Once subject is back, the participant will be taken to the MRI scanner room.
- **Procedure 2, MRI scanning:** After completing the medical history and assessments, we will take you in the MRI suite to familiarize you with the scanner environment. You will have a device attached to your finger to measure oxygen saturation levels in the blood (no needles required), electrodes attached to your chest to record your heart activity, a band placed around your chest to record breathing, and be given ear plugs to decrease the MRI scanner sounds and protect your hearing. You will then be placed in the MRI scanner, lying flat and as still as possible. You will lie without doing anything for about 1.5 hours while we obtain MRI scans. If you wish to come out from the scanner, you may do so at any time by signaling the scanner operator, who will be talking with you regularly.

- After the scanning session, we will remove recording devices and answer any questions you may have which will take approximately 10 minutes.

- After an independent departmental statistician responsible for randomly assigning the patients into two groups, we will place an electronic order to the pharmacy to get ready the study specific drug. The study drug will be prepared as capsule with thiamine (Thiamine Hydrochloride) 500 mg for the treatment group and a placebo capsule for the non-treatment group. Since thiamine is without color and odor and capsule will be with same color, this drug cannot be identified between placebo and treatment. Both groups will take one capsule daily for 3-months (in the morning) after baseline studies.

- These same procedures will be repeated at your 3-month follow up visit: you will fill out the same questionnaires, have your A1C and blood levels tested, and repeat the same MRI scans.

How long will I be in the research study?

Participation will take between 2.5 to 3 hours per visit to UCLA, and involves two visits (3 months apart).

Are there any potential risks or discomforts that I can expect from this study?

- The device attached to your finger to record blood oxygen levels may cause a slight pressure on your finger; however, it should not cause long-lasting discomfort. Rarely, people develop an itchy skin rash at the places where the electrodes are attached to the body. Such reactions can be treated with a cortisone-type cream, but frequently

disappear without treatment.

- Being asked about your medical history or health-related issues may bring up feelings of sadness, anxiety, despair or tiredness. You only need to answer questions that you are comfortable with, and you are free to stop the procedures at any time. If we believe you are unduly distressed or otherwise uncomfortable, we will stop the experiment.
- While lying in the MRI scanner, you may feel anxious because of the close confines of the space. However, you will be in communication with the operators at all times while in the scanner, and if you wish to be removed from the scanner, you will be taken out instantly. There are no known additional risks from the MRI scanner**;** however, the procedure may involve risks that are currently unforeseeable.
- The imaging examinations performed as part of this study will not be reviewed by a UCLA radiologist and no formal interpretation will be rendered. Because of this, there is a small chance that clinical findings on the images would not be identified or communicated to you.
- You may feel a little local discomfort from the fingerstick blood test for A1C and mild bruising from the blood draw, which can be rapidly and effectively treated using ice and bandages, if necessary.
- Side effects from thiamine are rare, but may involve allergic reactions such as: rash, redness, soreness, swelling, nausea, restlessness, feeling of warmth, sweating, or weakness, but the proposed thiamine dose should be safe.

Are there any potential benefits if I participate?

- You will not directly benefit from your participating in the research.
- The results of the research may have benefits to society such as possibly better outcomes for those diagnosed with T2DM and/or maybe overall improved quality of life and daily activities. This clinical trial study will provide data needed to implement a large-scale clinical trial.

What other choices do I have if I choose not to participate?

The alternative to participation is to not participate.

Will I be paid for participating?

- You will receive up to $300 per visit for participating in this study, and you will be reimbursed for parking costs.
- If you finish interviews, questionnaires, test, and medical history and are not eligible for the remaining MRI procedures, or if you wish to terminate the study before completion, you will be paid for the parts of the study completed according to the following schedule:

  Procedure 1 – Questionnaires, cognitive test, and medical history $50
  Procedure 2 – MRI scanning $100 (or $15 per scan if not all completed)

- If the investigators stop your participation during the MRI scanning procedures because of study inclusion/exclusion protocol (such as significant changes in heart rate, oxygen saturation, or blood pressure) you will receive full payment of $150.
- You will receive your payment as a check in the mail from UCLA, typically within 1-2 months of the study date.
- You will be required to provide your social security number (SSN) or individual tax payer identification number (ITIN) and mailing address in order to be paid for your participation. Your SSN/ITIN will be retained in a locked cabinet behind locked doors under the control of the investigator. Your SSN will be destroyed once you have cashed your payment check.
- If you are a non-resident alien, you will be required to register with the UCLA GLACIER system in order for payments to be processed. As a non-resident alien, you may be subject to tax withholdings.
- Personal information about you, including your name, address, and social security number or individual tax payer identification number, will be released to the UCLA Accounting Office for the purpose of payment and for tax reporting to the Internal Revenue Service (IRS).
- If you complete and receive payment for more than one study visit, your information must be uploaded into UCLA's payment system. Because of this, your name and address will be accessible to UCLA personnel that have access to the payment system.

Will information about me and my participation be kept confidential?

- The researchers will do their best to make sure that your private information is kept confidential. Information about you will be handled as confidentially as possible, but participating in research may involve a loss of privacy and the potential for a breach in confidentiality. Study data will be physically and electronically secured. As with any use of electronic means to store data, there is a risk of breach of data security. Confidentiality will be maintained as best possible by means of storing cognitive and mood evaluations data and any medical history using a code number (instead of your name), with no personal information, and only authorized researchers will have access to the code sheets (that link the code with your name). The information from the MRI studies is of two kinds, 1) the signals that tell the oxygen level in your body, heart rate and breathing rate, and 2) the brain images which show brain structural integrity. All of this information is stored with only numbers (not with your name) to identify them. All other information collected about you has only a code.
- It is possible that other investigators conducting other research might request that data collected for this study be shared for further research. Even if you agree that your data may be shared with other investigators, your name or other personal identifying information would not be revealed. Though your privacy is very important to us and we will use many safety measures to protect your privacy, it is possible that there may be unforeseen privacy risks. For example, although we would not put any personal identifying information about you in a shared database, someone in the future might find some way to link your medical information or other information collected for this study back to you even in the absence of your name or other personal identifying

information. Alternatively, there could be violations to the security of the separate computer systems used to store the codes linking your information to you.

- All codes and code sheets will be kept in a locked file cabinet in one of the PI's office (56-132 CHS) so that your privacy is protected. Also, all brain MRI and physiology data (oxygen level in your body, heart rate and breathing rate) will be stored in a computer protected with password, with access to authorized personal only.
- When the results of the research are published or discussed in conferences, no information will be included that would reveal your identity. Only the investigators listed in this consent form will have access to the results of the research; no information will be included that would reveal your identity.

- The research team may not be able to keep confidential any disclosure or endorsement of thoughts to harm yourself. In the event that you tell Dr. Lavretsky (or any of the research staff) that you are thinking about killing yourself or you answer yes to a question about having thoughts about suicide, you will be asked more questions about the thoughts. Depending on how intense your thoughts are or how much you feel like hurting yourself, the research staff may provide you with referrals for treatment, work with you to contact your personal physician, trusted family member, or therapist to discuss your thoughts of harming yourself; or work with you on a plan that may include getting you to a hospital for safety.

Information about you is protected by a federal Certificate of Confidentiality. This means that we can't be forced to release information about you for any legal proceeding, even if a court of law asks.

The Certificate allows us to use information about you for purposes of this research, or to disclose it for other research when allowed by law. The Certificate requires other researchers to also protect information we share with them.

There are limits to this protection. The Certificate does not protect your information when:

- You or your family voluntarily release information about yourselves.
- You consent to release of information (for example, the uses described in this form, or if you sign release forms for employment, insurance or medical care).
- A federal agency audits or evaluates research that it funds.
- Researchers are required to report possible intent to harm yourself or others, child abuse, elder abuse, or infectious disease cases.

Are there any costs for taking part in this study?

- The study will pay for the cost of all required study items and services as described in this consent form.

What other things should I consider before participation?

- Any specimens (e.g., tissue, blood, urine) obtained for routine lab testing will be discarded or destroyed once they have been used for the purposes described in the protocol.

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

- You can choose whether or not you want to be in this study, and you may withdraw your consent and discontinue participation at any time.
- Whatever decision you make, there will be no penalty to you, and no loss of benefits to which you were otherwise entitled.
- You may refuse to answer any questions that you do not want to answer and still remain in the study.

Who can I contact if I have questions about this study?

- **The research team member:**
  If you have any questions, comments or concerns about the research, you can talk to one of the study's principal investigator. Please contact:

  Rajesh Kumar, PhD, Co-Principal Investigador
  Associate Professor In-Residence
  Department of Anesthesiology
  Room 56-141, Center for the Health Sciences
  University of California at Los Angeles
  Los Angeles, CA 90095-1763
  Tel: 310.206.1679; 310.206.6133
  Email: rkumar@mednet.ucla.edu

- **UCLA Office of the Human Research Protection Program (OHRPP):**
  If you have questions about your rights while taking part in this study, or you have concerns or suggestions and you want to talk to someone other than the researchers about the study, please call the OHRPP at (310) 206-2040; by email: participants@research.ucla.edu or U.S. mail:
  UCLA OHRPP
  Box 951406
  Los Angeles, CA 90095-1406.

You will be given a copy of this information to keep for your records.

CONTACT FOR FUTURE RESEARCH

- UCLA researchers may contact me in the future to ask me to take part in other brain research studies.

YES **NO**

SIGNATURE OF STUDY PARTICIPANT

Name of Participant

Signature of Participant | Date

SIGNATURE OF PERSON OBTAINING CONSENT

Name of Person Obtaining Consent | Contact Number

Signature of Person Obtaining Consent | Date