Subject Research ID#: _____

This consent form is not valid without a TTUHSC El Paso IRB stamp in the lower left corner of each page.

CONSENT TO TAKE PART IN A RESEARCH STUDY

This is a research study for people who voluntarily choose to take part. Please take your time to make a decision, and discuss the study with your personal doctor, family and friends if you wish.

STUDY TITLE: Cerebral Cavernous Malformations (**C**CMs) among **Hi**spanic **P**opulation **S**tudy group (CHIPS)

INVESTIGATOR(s): Jun Zhang, PhD, ScD, Anantha-Ramana.Vellipuram, MD

CO-INVESTIGATOR(s): Richard Brower, M.D. (Neurology), Jonathan Lavezo, M.D. (Pathology), Claudia Prospero-Ponce, M.D. (Neurology), Jose Gavito, M.D. (Radiology), Vikas Gupta, M.D. (Neurology)

CONTACT TELEPHONE NUMBERS:

915-215-6562 (Monday-Friday 8am-5pm) ***or*** 915-309-4619 (after normal business hours)

(You may contact the investigator(s) at the number(s) listed above at any time if you develop any of the conditions listed in #5 or if you have any unexpected complications.

INSTITUTIONS:

Texas Tech University Health Sciences Center El Paso, 4801 Alberta Ave. El Paso, TX 79905

University Medical Center of El Paso, 4315 Alameda, El Paso TX 79905

KEY INFORMATION

1. **What am I being asked to do?**
   We are asking you to take part in a research study about cerebral cavernous malformations (CCMs). The purpose of the study is to try to identify genetic factors that cause CCMs.

   This key information is being provided to you to help you decide whether or not you should participate. Additional information is provided to you in the '**Detailed Information**' section of the document.

2. **Do I have to take part in this study?**
   You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or

give up any legal rights or benefits. If you are a student or employee, your participation in this study will have no effect on your grades or employment status.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered.

3. What is this study about? How long will it last?

This study is being done to answer the following question: What are the genetic factors that cause cerebral cavernous malformations (CCMs)?

If you agree to be in this study, you will have blood taken from one of the arm veins, as part of your standard of care, with an additional one and a half tablespoons (2 vials, one for serum collection and one for plasma) being drawn for this study. Blood draw will take approximately 30 minutes or less. The genetic material (DNA) and proteins will be obtained from this blood sample, for genetic testing and biomarker validation.

In the unique circumstances where blood draws are not required for standard of care, one-and-a-half tablespoons of blood (2 vials, one for serum collection and one for plasma) will be extracted for genetic testing and validation analysis by research co-PI for this study with the following modifications from the standard procedure.

1. You will initially be asked if you would like to participate in this study by your physician if you meet the inclusion criteria.
2. Primary care physicians on this protocol will be able to perform an electronic medical search of their patients to identify patients that were previously diagnosed with CCMs in the past 10 years (1/1/2011-1/1/2021). Primary Care physicians may ask currently approved research personnel to assist them with this task. Medical records will only be assessed to confirm ICD9/10 codes for their patients to confirm eligibility requirements, and to obtain electronic mail addresses, phone numbers, and/or mailing address to contact/present their patients with the currently approved IRB recruitment flyer/letter so they can decide if they would like to participate.
3. Any Patients that qualify to participate, upon a medical search review by their primary care physician, will still be contacted and presented with our IRB approved recruitment flyer so that they can decide on whether they would like to participate. If these patients are interested in participating, they will be consented, as normal, and blood draw performed, as normal.
4. Alternatively, patients may contact either Dr. Johnathan Abou-Fadel or Dr. Jun Zhang to see if they qualify to participate in the study (based off the inclusion criteria) from posted notices of solicitation and recruitment flyers posted at the following websites:
    1. https://www.angioma.org/biomarker-development-project-in-el-paso-seeking-participants/
    2. https://elpaso.ttuhsc.edu/research/ccm-survey.aspx
    3. https://elpaso.ttuhsc.edu/research/ccm-survey-spanish.aspx
5. Patients participating in blood draw for research purposes only that were not recruited involving a UMC/TTUHSCEP physician may provide their medical records to either Dr. Johnathan Abou-

Fadel or Dr. Jun Zhang at their discretion to help make the analysis of their blood donation more meaningful in terms of clinical symptoms associated with the scope of this study. All medical records will be stored according to the same HIPAA compliance and regulations as if those records were obtained from their direct PCP.

6. If you agree to provide medical records, additional demographic information that will be obtained includes affected individuals, age of onset, ethnicity, gender, type of stroke, date of birth, treatments received. An assessment of the patient's current condition will be made by asking if the patient shows any signs of gait apraxia, cognitive deficiency, and seizures. Specific questions will be asked in order to evaluate physical, social, cognitive, and overall health.
7. Consent/blood draws will be in the PFS and Laboratory suite located at University Medical Center of El Paso, 1st floor UMC main building, 4815 Alameda Ave, El Paso, TX 79905. Alternatively, if this location is not available for consenting patients, we will consent patients in private, closed-door conference rooms that can be reserved for CONSENTING ONLY. These rooms are located in MSBI rooms #2106, 3106 and 4106 located at 5001 El Paso Drive, El Paso, TX 79905. No other research procedures pertaining to this study will occur in these rooms other than consenting patients
8. You will be walked over to the PFS and Laboratory suite by Dr. Johnathan Abou-Fadel or Dr. Jun Zhang where informed consent and/or assent will be conducted (if consenting was not already completed in MSBI 2106, 3106 or 4106) by either Dr. Johnathan Abou-Fadel or Dr. Jun Zhang, followed by blood draw for research purposes only which will be handled by a phlebotomists working in the PFS and laboratory suite.
9. The PFS and Laboratory suite is both a research lab as well as having equipped stations where phlebotomy work can be safely performed. Having one site for both processes eases our workflow and limits the number of coordinators that need to be added to this study by using different locations for each process. As stated in the procedure section for "blood draw for research purposes only" in the study application, the patients/subjects will be personally escorted by Dr. Johnathan Abou-Fadel or Dr. Jun Zhang and will stay with the subjects until all assents/consents have been performed as well as completion of the blood draws. Once complete, Dr. Johnathan Abou-Fadel or Dr. Jun Zhang will transport the samples back to the lab where they will be processed, and Biological molecules obtained from this sample (Nucleic acid and proteins) will be stored in MSBI in our -80 freezers until ready for analysis. All samples provided will be coded for confidentiality and privacy. Completion of the questionnaire and the blood draw should take less than 30 minutes of the subject's time and will be completed in one visit.

You might have/had a Magnetic Resonance Angiography (MRA) exam performed, as part of your standard of care, and will be asked if the PI can review these images/reports with your physician to get as much information as possible to understand CCM disease progression. This is a test that helps us find blood vessel diseases in the brain.

With your consent, your medical record will also be reviewed to collect demographic and physical exam information to pair with your blood sample to get as much information as possible to understand CCM disease progression.

4. **What are the key reasons I might choose to take part in this study?**
   We hope to learn information that may help others with similar conditions in the future.

   For a complete description of the benefits, refer to the '**Detailed Information'** section of the consent form.

5. **What are the key reasons I might choose <u>not</u> to take part in this study?**
   It is very unlikely, but the most common risks of drawing blood include pain and bruising, and very rarely infection at the site of draw. The risks of blood draw are similar in males and females. Having your blood drawn by a physician greatly reduces these risks/discomforts. There may be some risks that the study doctors do not yet know about.

   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 a research subject based on genetic information. This law generally will protect research subjects by prohibiting health insurance companies and group health insurance plans from requesting genetic information that is collected in a research study. Health insurance companies and group health plans are also prohibited from using genetic information when making decisions regarding eligibility or premiums. Employers with 15 or more employees may not use genetic information obtained from research when making a decision to hire, promote or fire an employee or in setting conditions of employment.

   All health insurance companies and group health plans must follow this law by May 21, 2010. All employers with 15 or more employees must follow this law as of November 21, 2009.

   This Federal law does not protect against genetic discrimination by companies that sell life, disability, or long-term care insurance. More information about the impact of GINA on research can be found in the following OHRP Guidance document: <u>http://www.hhs.gov/ohrp/policy/gina.pdf</u>.

   For a complete description of the risks, refer to the '**Detailed Information'** section of the consent form.

   For a complete description of the alternative treatment/procedures, refer to the '**Detailed Information'** section of the consent form.

6. **What if I have questions?**
   For questions about this study, contact the Investigator, Dr. Jun Zhang, at 915-215-4197.

   If you would like to speak to someone who is not involved in the study about your rights as a participant, research-related injuries, or any other matter related to the study, you can call the TTUHSC EthicsPoint Hotline: 1-866-294-9352.

   Or, you can file an EthicsPoint report online: <u>https://secure.ethicspoint.com/domain/media/en/gui/44534/index.html</u>. Please choose the

"Regulatory Compliance" option when making an online report.

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask your study doctor or nurse.

DETAILED INFORMATION

7. What is the purpose of this study?

The purpose of the study is to try to identify the genetic factors that cause cerebral cavernous malformations (CCMs). Such information may allow the development of better treatments for this brain disorder which has relatively high prevalence in the Hispanic population. It is well known that, strokes associated with several different genetic disorders, can be caused by different genes in different types of stroke, such as cerebral cavernous malformations (CCMs). In research conducted with human subjects, several genes that possibly cause strokes from CCMs, have been reported, but need further validation.

We expect approximately 100-900 participants to enroll in this study in the El Paso borderland area.

8. What will happen during this study?

If you agree to be in this study, we will extract an additional one and a half tablespoons of blood (2 vials, one for serum collection and one for plasma), that is already being drawn as part of your standard of care, from one of your arm veins. Blood draw will take approximately 30 minutes or less. The genetic material (DNA) and proteins will be obtained from this blood sample, for genetic testing and biomarker validation. Genetic research looks at diseases that are passed on through generations within the same families. Genes are inherited from your parents and determine your physical features such as the color of your hair and eyes, etc. We will make every effort to keep a stock of these cells alive in our laboratory for a short time, to allow additional tests to be done if we need it, without having to ask for another blood sample from you. The samples will be coded in such a way as to keep your identity private.

In the unique circumstances where blood draws are not required for standard of care, one-and-a-half tablespoons of blood (2 vials, one for serum collection and one for plasma) will be extracted for genetic testing and validation analysis by research co-PI for this study. These samples will be frozen and stored identical to samples obtained through standard of care blood draws for future use. All samples provided will be coded for confidentiality and privacy. Completion of the questionnaire and the blood draw should take less than 30 minutes of the subject's time and will be completed in one visit.

You might have/had a Magnetic Resonance Angiography (MRA) exam performed, as part of your standard of care, and will be asked if the PI can review these images/reports with your physician to get as much information as possible to understand CCM disease progression. This is a test that helps us find blood vessel diseases in the brain.

With your consent, your medical record will also be reviewed to collect demographic and physical exam information to pair with your blood sample to get as much information as possible to understand CCM disease progression.

9. What will be done that is different from my usual care?

There will be no difference in your standard clinical care if you decide to participate in this study.

10. Will there be any added risks to me from this study if I am a female/male?
The risks of blood draw are similar in males and females.

11. What other choices do I have if I do not take part in the research study?
This study does not involve treatment. You do not have to be in this research study. If you do not participate, your clinical care at UMC/TTUHSC will not be affected whatsoever.

12. What about confidentiality and the privacy of my records?
We will keep your involvement in this research study confidential to the extent permitted by law. In addition to the staff carrying out this study, others may learn that you are in the study. This might include federal regulatory agencies such as the Food and Drug Administration (FDA) and the Office for Human Research Protection (OHRP), Texas Tech University Health Sciences Center El Paso (TTUHSC EP) representatives, representatives from any hospital or site where the research takes place, and the TTUHSC EP Institutional Review Board (a committee that reviews and approves research). These people may review and copy records involving your participation in this research. A copy of this document may be placed in your medical record.

Study results that are used in publications or presentations will not use your name.

13. Who is funding this study?
TTUHSC EP (Molecular and Translational Medicine, Neurology, Radiology) and Neurosurgery (UMC) Department is providing the space and supplies for this study. No one on the research staff will receive anything of value from other agencies, organizations, or companies to carry out this research.

14. Will it cost me anything to take part in this research study?
Any procedures that are considered standard of care are your or your insurance provider's responsibility.

You and/or your insurance provider will not have to pay for exams, tests, and procedures done for research purposes only or that are covered by the study.

Talk to your insurance provider and the study staff to make sure that you understand what your insurance pays for and what it does not pay for if you take part in this study. Also, find out if you need approval from your plan before you can take part in the study.

Ask your doctor or nurse for help finding the right person to talk to if you are unsure which costs will be billed to you or your insurance provider.

Any additional testing/counseling desired, including additional genetic testing or genetic counseling services provided in the additional resources document, will be at your own cost either through insurance or self-pay, and is not part of this study.

15. Will I receive anything for taking part in this research study?
You will not be paid for participating in this study.

16. Does anyone on the research staff have a personal financial interest in this study?
No one on the research staff has a financial interest in this study.

17. What if I am hurt by participating in this study?
Texas Tech University Health Sciences Center El Paso (and UMC EP) does not offer to pay for or cover the cost of medical treatment for research related illness or injury. No funds have been set aside to pay or reimburse you in the event of such injury or illness unless specifically stated.

If you have a research related illness or injury, care will be available to you as usual, but you and/or your medical or hospital insurance company will be responsible for the cost of treatment. Before entering this study, you should check whether your insurance company might limit your insurance coverage if you take part in a research study.

18. Can I stop being in the study?
Yes, you may decide to stop taking part in the study at any time. If you leave the study, we cannot remove any information we have collected to that point. If you leave the study, your right to standard medical care will continue.

If you decide to stop, let your study doctor know as soon as possible. It's important that you stop safely. If you stop, you can decide if you want to keep letting the study doctor know how you are doing.

Your study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

19. Can someone else end my participation in the study?
Under certain circumstances, the investigators, TTUHSC El Paso, or the study sponsor may decide to end your participation in this research study earlier than planned. This might happen because:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- The study is stopped by the Institutional Review Board (a committee that reviews and approves research) or the Food and Drug Administration.

20. What will happen to my blood sample when the research study is over?
In this study, we will be collecting some of your blood. When the study is done, we will make sure that this blood sample is appropriately discarded and cannot be identified as belonging to you. We will keep biological molecules (DNA and proteins) obtained from your blood sample to use in our future research, or in research done by our colleagues. If your unidentifiable sample is used in future studies, we will not ask for your consent again before using it. You will not know when or if those samples are used for research, and no one will be able to tell you any results of research that used your samples.

(1) It is highly unlikely, but it is possible that these samples will be used in research that could profit the investigator or others. If the sample is used in that way, you will not share in any of the potential profit.
(2) The future research might include "whole genome sequencing." Sequencing allows researchers

to identify your genetic code. Changes in your genetic code may be passed down through your family. For example, these genetic changes may be passed down to your children in the same way that eye and hair color are passed down. These are called germline changes.

There are implications related to knowledge of possible genetic information that may be obtained as a result of this study. These include knowledge of genetic mutations which may be shared with you, as well as significant risk factors for those who test positive for these gene mutations. Because of the potential of a genetic basis for genetic inheritance of CCMs, resources have been provided in a separate document for additional genetic screening, if desired, as well as resources for genetic counselling. All additional resources are your financial responsibility and are not associated with this study.

Your signature indicates that:

- **this research study has been explained to you;**
- **you have been given the opportunity to ask questions and have received answers;**
- **you accept your responsibility to follow the instructions given to you by the research team regarding study participation and, if applicable, research medication;**
- **you agree to take part in this study.**

You will be given a signed and dated copy of this form.

_____
Printed Name of Subject

		AM/PM
Signature of Subject	Date	Time
If applicable, Signature of Authorized Representative	Date	Time

I have discussed this research study with the subject [and/or his or her authorized representative] using language that is understandable and appropriate. I believe I have fully informed the subject of the possible risks and benefits, and I believe the subject understands this explanation. I have given a copy of this form to the subject.

_____
Printed name of authorized research personnel who conducted the informed consent discussion

		AM/PM
Signature of authorized research personnel who conducted the informed consent discussion	Date	Time

[For research personnel use only, if applicable] Subject Research ID#: _____

TEXAS TECH UNIVERSITY HEALTH SCIENCES CENTER EL PASO
AUTHORIZATION TO USE AND/OR DISCLOSE YOUR PROTECTED HEALTH INFORMATION for a RESEARCH STUDY

STUDY TITLE: **C**CMs among **Hi**spanic **P**opulation **S**tudy group (CHIPS)

This form is intended to tell you about the use and/or disclosure (sharing) of your personal **Protected Health Information** (PHI) if you decide to participate in the research study described on the previous pages. The health information about you that may be used or disclosed is described below. This information is usually found in your medical records. Only the health information about you that is needed for this research study will be used or disclosed. When you consider taking part in this research study, you are also being asked to give your permission for your Protected Health Information to be released from your doctors, clinics, and hospitals to the research personnel approved for this research study. This Authorization specifically relates to the research study described in the attached Informed Consent document.

1. This Authorization is valid indefinitely or until such time as legal requirements will allow this Authorization to be destroyed.

2. If you choose to cancel this Authorization, please give notice in writing to:

TTUHSC-El Paso Privacy Officer
Office of Institutional Compliance
5001 El Paso Drive
El Paso, TX 79905

If you sign this Authorization, the following persons, groups or organizations may rely on this Authorization to disclose your Protected Health Information to the Principal Investigator and other research personnel who are conducting this Study:

- your treating physicians and healthcare providers and their staff,
- associated healthcare institutions and hospitals where you have or may receive care.

While this research study is in progress, the Principal Investigator or research personnel working on this study will inform you whether or not you will be allowed to see the research related health information that is created about you or collected by the research personnel prior to the end of the study. After the study is finished you may request this information as allowed by the TTUHSC EP Notice of Privacy Practices.
The Protected Health Information that you authorize to be used or disclosed for research purposes may include your current or future health information from some or all of your health records, including:

• hospital records and reports • admission history, and physical examination • X-ray films and reports; operative reports • laboratory reports, treatment and test results (including sexually transmitted diseases, HIV or AIDS) • any other Protected Health Information needed by the research personnel listed above. (* use separate form for disclosure of psychotherapy notes)	• immunizations • allergy reports • prescriptions • consultations • clinic notes • mental health records • alcohol / substance abuse records

For the purposes of this study, your Protected Health Information may need to be reviewed or disclosed to individuals or organizations within and/or outside of TTUHSC EP who sponsor, approve, assist with, monitor or oversee the conduct of research studies. This includes, but is not limited to, the TTUHSC EP Institutional Review Board, TTUHSC EP compliance reviews, the US Food and Drug Administration (FDA) or governmental agencies in other countries. Some of these individuals or organizations may share your health information further, and your health information may not be protected by the same privacy standards that TTUHSC EP is required to meet.

If you choose to sign this Authorization form, you can change your mind about this later. If you change your mind, send a letter to the person identified above telling us to stop collecting and sharing your Protected Health Information. When we receive your request, you may be asked to leave the research study if all the necessary information has not been collected. We may still use the information about you that we have already collected. We need to know what happens to everyone who starts a research study, not just those people who stay in it.

You have the right to refuse to sign this form. If you choose not to sign this form, your regular health care will not be affected. However, not signing this form will prevent you from participating in this research study and prevent you from receiving research related health care services provided under this study.

I have had the opportunity to review and ask questions regarding this Authorization to use or disclose my personal health information, and I will receive a copy of this form. By signing this Authorization, I am confirming that it reflects my wishes.

_____
Printed Name of Subject

_____ _____
Signature of Subject Date

_____ _____
If applicable, Signature of Authorized Representative Date