UTHealth
The University of Texas
Health Science Center at Houston

CONSENT TO TAKE PART IN RESEARCH

Simple Study Title:	HB-adMSC's for Neurological Injury
Full Study Title:	A Clinical Trial to Determine the Safety and Efficacy of Hope Biosciences Autologous Mesenchymal Stem Cell Therapy for the Treatment of Traumatic Brain Injury and / or Hypoxic-Ischemic Encephalopathy
Study Sponsor:	Hope Biosciences
Principal Investigator:	Charles S. Cox, Jr, MD, Professor, Department of Pediatric Surgery UTHealth McGovern Medical School
Study Contact:	Steven Kosmach, MSN, RN, CCRC, Clinical Trial Program Manager 713-500-7329

The purpose of this research study is to test the safety and benefit of autologous adipose derived mesenchymal stem cell infusions, (here after referred to as HB-adMSC's) as a treatment for individuals with brain injuries. "Autologous" refers to an individual's cells or tissues, or coming from self. "Adipose" refers to fat cells.

If you agree to participate in the study, you will have 7 clinic visits over a 14 month period with each visit lasting 2 to 6 hours. We will also contact you by telephone 2 years after your last stem cell infusion for a brief assessment of your health. There will be one additional visit for adipose tissue (fat cells) to be taken from a small incision on your stomach and processed into HB-adMSC's. You will receive 3 HB-adMSC infusions over a 6 week period with 14 days separating the infusion visits. We will evaluate the safety and benefit of the cell infusions at the 6 and 12 month post-infusion study visits and at the 2 year follow-up telephone call. The study visits will be conducted at Memorial Hermann Hospital-Texas Medical Center (MHH-TMC) and the Houston Methodist Research Institute (HMRI). The fat extraction will be done at a local physician clinic partnered with Hope Biosciences.

The risks of being in this study include pain and scarring from the abdominal incision, possible infection, pain and bruising from blood samples. The remote (extremely unlikely) risks include organ damage from the cell infusion and death. You may not directly benefit from participating in the study. The knowledge gained from this study may help doctors develop better treatments for individuals with brain injuries.

Your participation is voluntary; the only alternative is to not participate in this research study and continue with standard therapies.

You may choose not to take part in this research study or may choose to leave the research study at any time. Your decision will not affect the clinical care you receive at the University of Texas Health Science Center at Houston (UTHealth) or Memorial Hermann Healthcare System

If you are interested in learning more about the study, please continue reading below.

You are invited to take part in the in the protocol titled "A Clinical Trial to Determine the Safety and Efficacy of Hope Biosciences Autologous Mesenchymal Stem Cell Therapy for the Treatment of Traumatic Brain Injury and Hypoxic-Ischemic Encephalopathy". This consent form has important information about this study to help you decide whether or not to take part in this study. Your decision to take part is voluntary. You may refuse to take part or choose to stop

taking part, at any time. A decision not to take part or to stop being a part of the research project will not change the services available to you from the University of Texas Health Science Center at Houston (UTHealth) and Memorial Hermann Healthcare System.

What is the purpose of this research study?
The purpose of this study is to investigate the safety and benefit of HB-adMSC's as a treatment for sub-acute or chronic neurological injuries. HB-adMSC's are an investigational biological product and not Food and Drug Administration (FDA) approved as a treatment for neurological injuries. Hope Biosciences is paying UTHealth for their work on the study.

Who is being asked to take part in this study?
You are being invited to take part in the study because you have been diagnosed with a sub-acute or chronic neurological injury that is unlikely to improve with the present standard of care approaches. The study is being conducted at UTHealth and will enroll 24 individuals.

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

What will happen if I take part in this study?
Pre-Screening Call:
Our screening procedures start with a telephone call to provide a general overview of the study and discuss eligibility requirements. You're receiving this informed consent document because you have already spoken with the study coordinator and, after discussing the study, have expressed interest in continuing the screening procedures. If, after reviewing this consent you're still interested in participating in the study, you or your legally authorized representative (LAR) will need to sign and return the consent by secure e-mail or in the pre-paid envelope provided. The authorization for release of health information will allow us to request medical records related to your neurological injury and determine your eligibility to participate in the study.

We will schedule a conference call with you to review your medical history and the study consent to ensure all your questions have been answered and you understand and agree to visits and procedures. The baseline visit will be scheduled at a time convenient for you. You will be provided with information on the clinic locations and parking options for each visit.

Visit 1: Screening
The first study visit will be conducted in the Clinical Research Unit (CRU) at MHH and is expected to take about 4 hours to complete. The visit will begin with a review of this consent document to ensure all your questions have been answered and to verify your willingness to continue with the study.
You will undergo the following assessments/procedures:

- Review of any interval changes in your health since the conference call.
- Physical and neuro exam.
- You will be asked about your medical history, your family medical history, any over the counter or prescription medications taken within the last 30 days, and demographic information like race, ethnicity, employment and marital status.
- Vital signs including blood pressure, heart rate, temperature, respiratory rate, and oxygen saturation.

- Blood sample collection (about 4 tbsp.) for routine clinical lab tests measuring your general health (CBC with diff, metabolic, coagulation, and renal function panels), research lab tests, and a pregnancy test for women of childbearing potential.
- Chest x-ray.
- Standardized tests and assessments to measure your degree of disability from the brain injury.

The research team will review the test results from the procedures listed above. Abnormal test results like a chest x-ray suggesting a respiratory infection may require the visit to be cancelled and rescheduled for a later time. There is always the potential that new information from the test results might prevent your further participation in the study. A study coordinator will call you within 24 hours of the visit to schedule the next study procedures or discuss the test results preventing your continued participation in the study.

If you are eligible to continue in the study, we will schedule the fat extraction visit with Hope Biosciences. At the visit, a local anesthetic will be used to numb the skin on your abdomen, flank, or hip area. A small incision will then be made to collect about 2 tbsp. of adipose tissue, and then closed and covered with a sterile dressing. You will be monitored closely during the short procedure. The study coordinator will contact you the day after the fat extraction to assess your recovery.

Hope Biosciences will process your fat cells into HB-adMSC's over a 5 to 7 week period. There is the remote possibility that the HB-adMSC infusion may not meet Hope Biosciences strict release criteria. Reasons include an insufficient quantity of stem cells to deliver the target dose or product contamination. If an unlikely event like this occurs, you will be contacted immediately and given the choice of repeating the fat extraction visit or withdrawing from the study.

Visit 2: Baseline Imaging

The baseline imaging visit will be conducted at the HMRI and scheduled within 10 days of your screening visit. The visit is expected to take about 5 hours to complete.
You will undergo the following assessments/procedures:

- Review of any interval changes in your health since the last visit.
- Physical and neuro exam.
- Vital signs including blood pressure, heart rate, temperature, respiratory rate, and oxygen saturation.
- A repeat pregnancy test for women of child bearing potential.
- Insertion of an intravenous (IV) needle into a vein on your hand or forearm.
- A brain PET/MRI scan.
- Instructions on administering Lovenox by injection for 7 day beginning the day before each infusion visit and completing the Lovenox medication log.

A positron emission tomography (PET) scan is an imaging technique that uses a radio tracer designed to bind or "stick" to specific types of cells in the human body. Radio tracers contain a very small amount of radioactivity and are given by IV injection immediately before the PET scan. The PET scan then measures the location and the amount of radio tracer. [^{11}C]ER-176 is radio tracer designed to bind with a type of brain cells called microglia. Microglia cells play an important role in brain healing after injury.

Magnetic resonance imaging (MRI) uses a large magnet and radio frequency waves to create pictures of internal body structures; no radiation exposure is involved.

For both scans, you will be positioned on a padded table and asked to lie on your back. You will be able to communicate with the imaging staff during the scans and they will be able to see and hear you. At various time points you will be asked to lie perfectly still while the machine is scanning. Radiology staff routinely contact patients 24hr. after imaging exams for a brief assessment of the patient's health.

Visits 3 thru 5: HB-adMSC Infusions

You will have three infusion visits over a 6 week period with 14 days (+/- 2 days) separating the infusions. Each visit will be conducted in the CRU at MHH and will take about 6 hours to complete. You will receive a reminder call from the study team to begin the Lovenox injections the day before the visit.

You will undergo the following assessments/procedures:

- Review of any interval changes in your health since the last study visit,
- Review of the Lovenox medication log,
- Vital signs including blood pressure, heart rate, temperature, respiratory rate, and oxygen saturation.
- Blood sample collection (about 2 tbsp.) for routine clinical labs assessing your general health (CBC with diff, metabolic, coagulation, and renal function panels), and pregnancy test for women of childbearing potential.
- An intravenous needle will be inserted in a vein on your hand or forearm for infusion of the autologous HB-adMSC's.

We will monitor your vital signs closely during the infusion and for the next 4 hours after the infusion. The research team will contact you by telephone the day after the infusion for a brief assessment of your health since leaving the hospital.

Visit 6: Six Months Post-Infusion:

You will be asked to return six months after the last HB-adMSC infusion. The visit will be conducted at both the CRU and HMRI and is expected to take about 8 hours to complete. The visit may be scheduled over a two day period.

You will undergo the following assessments/procedures:

- Review of any interval changes in your health since the last study visit,
- Physical and neuro exam,
- Vital signs including blood pressure, heart rate, temperature, respiratory rate, and oxygen saturation,
- Blood sample collection (about 2 tbsp.) for routine clinical lab tests measuring your general health (CBC with diff, metabolic, coagulation, and renal function panels), and a repeat pregnancy test for women of child bearing potential.
- Blood sample collection (about 1 tbsp.) for research lab tests.
- A brain PET/MRI scan.
- Standardized tests and assessments to measure your degree of disability from the brain injury.

Visit 7: One Year Post Infusion

The study visit will be conducted in the CRU and is expected to take about 2 hours to complete.

You will undergo the following assessments/procedures:

- Review of any interval changes in your health since the last study visit,
- Physical and neuro exam,

- Vital signs including blood pressure, heart rate, temperature, respiratory rate, and oxygen saturation,
- Blood sample collection (about 2 tbsp.) for routine clinical lab tests measuring your general health (CBC with diff, metabolic, coagulation, and renal function panels), and a repeat pregnancy test for women of child bearing potential.
- Blood sample collection (about 1 tbsp.) for research lab tests.
- A chest x-ray.
- Standardized tests and assessments to measure your degree of disability from the brain injury.

Two Year Follow-Up Telephone Call
A member of the research team will contact you by telephone 2 years after your last stem cell infusion to determine if you 've had any health problems since your last study visit. The brief telephone call will take no more than 10 min. to complete.

How long will you be in the study?
If you agree to take part in this study, your participation will last about 14 months and will involve 7 study visits at MHH and or HMRI and 1 visit at a clinic partnered with Hope Biosciences.

What choices do you have other than this study?
You may continue with conventional therapies, and/or identify other clinical trials for which you may be eligible.

What are the risks of taking part in this study?

Blood Draws:
Obtaining blood samples may cause minor discomfort, feeling lightheaded, fainting, bruising, clotting, and bleeding from the site of the needle stick and, in rare cases, infection.

Fat Extraction & HB-adMSC Infusions:
The procedure to collect fat from your stomach will leave a small scar, and you may experience discomfort from the surgical procedure. The area around the incision will be numbed with local anesthetic to minimize discomfort and the procedure will be performed using sterile technique to minimize the risk of infection. Because the stem cell infusion is a product from your body, we do not expect any bad reactions that can sometimes occur when stem cells are obtained from another individual. To minimize any potential reactions, you will be given two medications (Benadryl and Solumedrol) before the infusion. Both drugs are FDA approved. Potential risks of the IV infusion of HB-adMSC's include blood clots, infection, respiratory distress/failure, liver injury, neurologic injury, tumor growth, organ failure, and death.

Lovenox:
To minimize the potential risk of blood clots, you will be given Lovenox. Potential risks of Lovenox include irritation, pain, bruising, redness or swelling at the injection site.

PET Imaging:
During the scan you will receive the amount of radioactivity that you have been exposed to over the last 15 months from natural background sources. Safe levels of radiation exposure for humans is estimated to be approximately 50 milliSieverts (mSv) over the course of 1 year. The radiation exposure from PET Imaging is approximately 20 mSv for both scans and well within the safety limit.

MRI Imaging:
No radiation or contrast media is required for the brain MRI scan. Some people find the narrow space of the scanner uncomfortable. Medication is available for individuals with claustrophobia. MRI machines make loud banging and clicking noises during scans. Headphones will be available for your comfort. The large magnets used for MRI imaging can interact with metal objects like dental braces or implanted devices. You will be carefully screened for the presence of metal objects in or on your body before the MRI.

We may come across unexpected and unforeseen problems related to the HB-adMSC infusion.

COVID-19 Vaccinations During Study Participation:
We strongly encourage subjects to receive the COVID-19 vaccinations. However, vaccinations in general are known to cause a temporary inflammatory response that may alter the study test results and stem cell infusions. We will ask you to not receive a COVID-19 vaccination or booster shot two weeks before the brain imaging visits and two weeks before and after the stem cell infusion visit.

Pregnancy/Birth Control:
The effects of HB-adMCS's on human reproductive organs and unborn babies has not been studied and may be harmful in ways we do not currently know.

For Women: If you are pregnant, planning to become pregnant, or are breastfeeding a child, you cannot participate in this study.

For Women & Men:
You must use at least one highly effective method of birth control during the study. If you are already using birth control, the research team let you know if your current method of birth control is acceptable during the study. Acceptable methods of birth control include the following highly effective methods:

- Hormonal birth control.
- Intrauterine device (IUD).
- Surgical sterilization (tying or blocking the fallopian tubes, vasectomy).
- True sexual abstinence (not having heterosexual intercourse during the study if this is in line with your preferred and usual lifestyle).

You should notify the study team immediately if you, or for males, your partner becomes pregnant during the study.

What are the benefits to taking part in this study?
You may not directly benefit from participating in the study. The knowledge gained from this study may help doctors develop better treatments for individuals with brain injuries.

Can you stop taking part in this study?
You may decide to stop taking part in the study at any time. To withdraw from the study, please contact Dr. Cox at 713-500-7300.

Your doctor or Hope Biosciences can stop the study at any time. Your doctor may stop your participation in the study if your condition worsens, or you do not meet all the requirements of the study, and/or the study is not in your best interest. If your participation in the study is stopped, your doctor will discuss other options for your treatment.

If you stop participating in this study, the information already collected about you will still be used in the data analysis. However, no further information will be collected without your permission.

While taking part in this study, the study team will notify you of new information that may become available and could affect your willingness to stay in the study.

What happens if you are injured during the study?
If you require medical treatment for an illness or injury that is a direct result of taking the study product, Hope Biosciences will pay for reasonable and routine costs of such treatments if the following conditions are met:

- The illness or injury was a result from participation in the study.
- The cost of treatment or any part of the costs is not covered by any other health insurance, government health program, or others providing coverage for health care.

Neither payment nor reimbursement for such things as pre-existing conditions, illnesses or diseases totally unrelated to the study, lost wages, property damage, disability, or discomfort is available. You or your insurance company will be responsible for payment for any tests or care done outside of the scope of the study.

If you suffer any injury as a result of taking part in this research study the sponsor of this study, Hope Biosciences, will pay for reasonable and necessary medical expenses if the injury is a direct result of taking the study medicine or undergoing study procedures, and not due to the natural course of any underlying disease or treatment process.

You should report any such injury to Dr. Cox at 713-500-7300 and to the Committee for the Protection of Human Subjects at 713-500-7943. You will not give up any of your legal rights by signing this consent form.

If you are treated for a research injury that is paid for by Hope Biosciences, Hope Biosciences or its representative will collect your name, date of birth, gender, and Medicare Health Insurance Claim Number or Social Security Number to determine your Medicare status. If you are a Medicare beneficiary, Hope Biosciences will report the payment and information about the study you are in to the Centers for Medicare & Medicaid Services, in accordance with CMS reporting requirements. Hope Biosciences will not use this information for any other purpose.

What are the costs of taking part in this study?
The study sponsor will pay for all study related visits and procedures.

If you receive a bill that you believe is related to your taking part in this research study, please contact Dr. Cox at 713-500-7300 or the study coordinator at 713-500-7329.

You will receive $20 for each study visit to cover the cost of parking.

What will happen with my blood and fat tissue samples?
Your blood and fat tissue samples will only be used for specific tests that are required for this study. All samples will be destroyed after testing unless you give permission for future use.

☐ **Yes** ☐ **No** I give my consent for leftover tissue samples to be used for future research conducted by Hope Biosciences.

Can we contact you in the future?
Can we contact you in the future regarding other research studies you may be interested in?

☐ **Yes** ☐ **No** I give my consent for future contact.

How will privacy and confidentiality be protected?
Your privacy is important and your participation in this study will be kept confidential. However, absolute confidentiality cannot be guaranteed.

If you sign this document, you give permission to UTHealth and Memorial Hermann Healthcare System to use and disclose (release) your health information. The health information that we may use or disclose for this research includes all information in your medical record, results of physical examinations, medical history, and lab and diagnostic test results. Please understand that health information used and disclosed may include information relating to HIV infection, drug abuse, alcohol abuse, behavioral health, and psychiatric care. The identifying information we release to Hope Biosciences will be limited to the extent possible as required by regulations and laws governing stem cell lab facilities.

Coordinators, researchers, and administrative staff who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect your health information and may share your information with others without your permission, if permitted by laws governing them. You will not be personally identified in any reports or publications that may result from this study. If all information that does or can identify you is removed from your health information, the remaining information will no longer be subject to this authorization and may be used or disclosed for other purposes.

Representatives of the organizations listed below will see your name and other personal identifiers when they review your research records and medical records for the purposes of verifying study data:

- Representatives of UTHealth and/or Memorial Hermann Health System
- Representatives of the sponsor of this research including the physician performing the fat extraction procedure, contract research organizations and the Medical Safety Monitor
- Members of the Data and Safety Monitoring Board (an independent group of experts that reviews this study's data to make sure participants are safe and the research data is reliable)
- Representatives from the U.S. Food and Drug Administration (FDA)

Please note that you do not have to sign this Authorization, but if you do not, you may not participate in this research study. UTHealth and Memorial Hermann Health System may not withhold treatment or refuse treating you if you do not sign this Authorization.

You may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, researchers may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current

research. To revoke this Authorization, you must contact Dr. Cox in writing at: UTHealth, 6431 Fannin Street, MSB 5.324, Houston, TX 77030.

This Authorization will expire 15 years after the end of the study.

Whom can I contact if I have questions about the study?
If you have questions at any time about this research study, please feel free to contact Dr. Cox at 713-500-7300, as he will be glad to answer your questions. You can contact the study team to discuss problems, report injuries, voice concerns, obtain information in addition to asking questions about the research.

The Committee for Protection of Human Subjects at the University of Texas Health Science Center has reviewed this research study. You may contact them for any questions about your rights as a research subject, and to discuss any concerns, comments, or complaints about taking part in a research study at (713) 500-7943.

SIGNATURES

Sign below only if you understand the information given to you about the research and you choose to take part in this research study. Make sure that all your questions have been answered. If you decide to take part in this research study, a copy of this signed consent form will be given to you.

Printed Name of Subject	Signature of Subject	Date	Time

Printed Name of Legally Authorized Representative	Signature of Legally Authorized Representative	Date	Time

Printed Name of Person Obtaining Informed Consent	Signature of Person Obtaining Informed Consent	Date	Time