

AWARD NUMBER: W81XWH-19-1-0539

TITLE: Microvascular Barrier Biomarkers to Predict ICP Therapeutic Intensity After Severe TBI

PRINCIPAL INVESTIGATOR: Charles S. Cox, Jr., MD

CONTRACTING ORGANIZATION: University of Texas Health Science Center at Houston

REPORT DATE: OCTOBER 2022

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Development Command  
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;  
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

# REPORT DOCUMENTATION PAGE

Form Approved  
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.

<b>1. REPORT DATE</b> OCTOBER 2022		<b>2. REPORT TYPE</b> Annual		<b>3. DATES COVERED</b> 01-SEP-2021 to 31-AUG-2022	
<b>4. TITLE AND SUBTITLE</b>  Microvascular Barrier Biomarkers to Predict ICP Therapeutic Intensity After Severe TBI				<b>5a. CONTRACT NUMBER</b> W81XWH-19-1-0539	
				<b>5b. GRANT NUMBER</b>	
				<b>5c. PROGRAM ELEMENT NUMBER</b>	
<b>6. AUTHOR(S)</b> Charles S. Cox, Jr., MD  E-Mail: Charles.s.cox@uth.tmc.edu				<b>5d. PROJECT NUMBER</b>	
				<b>5e. TASK NUMBER</b>	
				<b>5f. WORK UNIT NUMBER</b>	
<b>7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)</b> University of Texas Health Science Center at Houston				<b>8. PERFORMING ORGANIZATION REPORT NUMBER</b>	
<b>9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)</b>  U.S. Army Medical Research and Development Command Fort Detrick, Maryland 21702-5012				<b>10. SPONSOR/MONITOR'S ACRONYM(S)</b>	
				<b>11. SPONSOR/MONITOR'S REPORT NUMBER(S)</b>	
<b>12. DISTRIBUTION / AVAILABILITY STATEMENT</b>  Approved for Public Release; Distribution Unlimited					
<b>13. SUPPLEMENTARY NOTES</b>					
<b>14. ABSTRACT</b> Severe traumatic brain injury (TBI) is a leading cause of death and disability that often occurs in conjunction with multiple other injuries, with and without hemorrhagic shock. Current guideline-based neurocritical care is designed to minimize intracranial hypertension using a tiered escalation in therapies, and seeks to avoid factors that aggravate the initial injury (hypotension and hypoxia). Our project seeks to measure the shed component of the microvascular barrier/glycocalyx (syndecan-1 and thrombomodulin) as a predictor of the edemagenic status of the post-TBI neurovascular unit. The ultimate goal is to be able to use a simple blood test that identifies the shed components of the microvascular barrier to rapidly identify the subset of severe TBI patients that require high intensity management—the “malignant ICP phenotype.” The global hypothesis for this project is syndecan-1 release predicts the cerebral edema/therapeutic intensity level for intracranial hypertension phenotype after TBI. The presence of hemorrhagic shock/resuscitation exacerbates the edemagenic phenotype. To date, Phase 1 of the study (n=25) has been completed. Phases 2/3 initiated enrollment in October 2021 (Year 3) and 10/50 patients have been enrolled through the end of Y3Q4. An additional patient has been enrolled in Y4.					
<b>15. SUBJECT TERMS</b> Traumatic brain injury, intracranial hypertension, syndecan-1					
<b>16. SECURITY CLASSIFICATION OF:</b>			<b>17. LIMITATION OF ABSTRACT</b>  Unclassified	<b>18. NUMBER OF PAGES</b>  36	<b>19a. NAME OF RESPONSIBLE PERSON</b> USAMRDC
<b>a. REPORT</b>  Unclassified	<b>b. ABSTRACT</b>  Unclassified	<b>c. THIS PAGE</b>  Unclassified			<b>19b. TELEPHONE NUMBER (include area code)</b>

## TABLE OF CONTENTS

	<u>Page</u>
1. Introduction	4
2. Keywords	4
3. Accomplishments	5
4. Impact	9
5. Changes/Problems	10
6. Products	12
7. Participants & Other Collaborating Organizations	15
8. Special Reporting Requirements	20
9. Appendices	20

**1. INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

Severe traumatic brain injury (TBI) is a leading cause of death and disability, and often occurs in conjunction with multiple other injuries and with and without hemorrhagic shock. Current guideline-based neurocritical care is designed to minimize intracranial hypertension using a tiered escalation in therapies, and seeks to avoid factors that aggravate the initial injury (hypotension and hypoxia). This project seeks to measure the shed component of the microvascular barrier/glycocalyx (syndecan-1 and thrombomodulin) as a predictor of the edemagenic status of the post-TBI neurovascular unit. Current neurocritical care treatment paradigms focus on hyperosmolar strategies to limit cerebral edema and the resultant intracranial hypertension/tissue ischemia. To be effective, an intact microvascular barrier is essential. The ultimate goal of this project is to be able to use a simple blood test that identifies the shed components of the microvascular barrier to rapidly identify the subset of severe TBI patients that require high intensity management—the “malignant ICP phenotype.” The global hypothesis for this project is syndecan-1 release predicts the cerebral edema/therapeutic intensity level for intracranial hypertension phenotype after TBI. The presence of hemorrhagic shock/resuscitation exacerbates the edemagenic phenotype. To accomplish this goal, we will employ continuous ICP waveform monitoring to define 3 tiers of ICP insults as defined by pressureXtime insults that predict poor outcomes, loss of autoregulation with a CPP<60 mm Hg, or high intensity interventions to reduce the ICP as quantified by the PILOTmod score>25. These data will be correlated with glycocalyx disruption in the early post-injury period. Cerebral edema imaging will be evaluated to quantify the tissue edema driving the ICP. These early data will be correlated with 6-month Glasgow Outcome Scores and DT-MRI based brain volumetric measurements to quantify injury related tissue loss. This project will enroll patients in two clinical prospective observational studies. Study 1 is a descriptive pilot study that will enroll 25 consecutive severe TBI patients and develop and validate the tools to define the tiers of the malignant ICP phenotype and represents phase 1 of this project. Study 2 is also a prospective observation study that will enroll 50 consecutive severe TBI patients and encompasses phases 2 and 3 of this project. Phase 2 is the physiological phase focused on the patient response to the ICP insults ascertained by serum albumin, syndecan-1, and thrombomodulin levels. Phase 3 will correlate these physiologic measures with structural endpoints defined by imaging. By being able to accurately and acutely predict severe TBI patients who may develop rapid progression to a malignant intracranial pressure phenotype, patients in Forward Surgical or En Route Critical Care could be rapidly triaged to facilities with neurosurgical capabilities, and/or aggressively monitored for complications of elevated ICP. We expect this project to produce a tool that rapidly predicts patients that will require high-intensity neurocritical care, and identify a cohort of more homogeneous patients for future aggressive interventions.

**2. KEYWORDS:** *Provide a brief list of keywords (limit to 20 words).*

traumatic brain injury, TBI, intracranial pressure, syndecan-1, intracranial hypertension

3. **ACCOMPLISHMENTS:** *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.*

**What were the major goals of the project?**

*List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.*

**Major Task 1: Clinical Study (Phase 1)**

Subtask 2: Prepare regulatory documents and research protocol

Milestone 1: Local IRB approval at UTHHealth for Study 1 (target month: 1, completed prior to month 1 on 09-AUG-2019 )

Milestone 2: HRPO approval for Study 1 (target month: 3, completed in month 2 on 11-OCT-2019)

Subtask 2: Finalize data management system and eCRFs

Milestone 3: Data management system completed (target month: 1, completed in month 4 on 15-DEC-2019)

Subtask 3: Perform clinical study

Milestone 4: Research staff trained (target month: 3, completed in month 4 on 15-DEC-2019)

Milestone 5: 1st participant consented, screened and enrolled (target month: 4, completed in month 9 on 26-MAY-2020, 100% completed)

Milestone 6: Enrollment and data collection completed for Study 1 (target month: 18, 25/25 patients consented and enrolled as of 19-JUN-2021, 100% completed in month 22)

Subtask 4: Report results from clinical study

Milestone 7: Report Study 1 results from data analyses (target month: 24, 100% completed in month 28)

**Major Task 2: Clinical Study (Phases 2-3)**

Subtask 1: Prepare for study

Milestone 8: Protocol for Study 2 developed and approved (target month: 15, 100% completed in month 25 on 30-SEP-2021)

Subtask 2: Conduct Study

Milestone 9: 1st participant consented, screened and enrolled in Study 2 (target month: 15, 100% completed in month 26 on 29-OCT-2021)

Milestone 10: Study 2 enrollment and data collection completed (target month: 36, 10/50 consented and enrolled by 31-AUG-2022, 20% completed)

Subtask 3: Report results from clinical study

Milestone 11: Report Study 2 results from data analyses (target month: 36, 0% completed)

**What was accomplished under these goals?**

*For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.*

Major activities during the past quarter were enrollment of patients into Study 2.

Screening for Study 2 began in Y3Q1 on 15-OCT-2021. Through 31-AUG-2022, all patients were screened in the STICU and Neuro ICU, 34 were determined to be eligible and 10 of those consented and were enrolled. No patients were enrolled in the past quarter. One additional patient was enrolled in early September, making the total enrolled 11. They will be listed on the next report.

	<b>During this Quarter</b>	<b>Overall</b>
Eligible N	7	34
Enrolled N (% of eligible)	0 (0)	10 (32.4)
Not enrolled N (% of eligible)	7 (100)	24 (67.6)
Withdrawn eligible N (% of eligible)	0	0
Withdrawn not eligible N*	0	1

\* One patient was initially consented in Y3Q1, but later determined to not be eligible due to their non-traumatic injury. That patient was withdrawn from the study prior to the baseline MRI and therefore was a minor deviation that resulted in no additional risk to the patient.

Reasons for non-enrollment for the 24 (7 in this quarter) who were eligible but not enrolled are found in the table below. The most common reason for not enrolling is that the consent window expired. Ten patients did not have their LAR identified or were not able to be consented within the 72 hour window, which is equivalent to the number of patients who have been enrolled. There were 4 patients/LARs who refused to date, which represents a 14.3% refusal rate overall (refusals/eligible).

<b>Reason for non-enrollment of eligible patient</b>	<b>During this Quarter N (%)</b>	<b>Overall N (%)</b>
Missed	0 (0)	2 (8.3)
No Moberg available at time of eligibility/equipment issue	0 (0)	1 (4.2)
LAR identified but consent window expired before LAR provided consent or was able to be contacted	4 (57.1)	9 (37.5)
LAR/patient refused	1 (14.2)	5 (20.8)
Patient or LAR not identified	1 (14.2)	5 (20.8)
Not notified of eligible patient	0 (0)	0 (0)
Enrolled in another study	0 (0)	1 (4.2)
Patient became DNR before consent	1 (14.2)	1 (4.2)
<b>TOTAL</b>	<b>7</b>	<b>24</b>

Once patients are enrolled in Cohort 2, the Moberg monitor collects data for at least 96 hours after ICP placement. Blood samples are taken at baseline (ED admission) and 2, 12, 24, 48, 96 hours after ICP placement in Phase 2. For Phase 3, the patient has a DT-MRI at baseline and another at 6 months after their enrollment. Enrollment delays are due to COVID-19 continuing to be a logistical barrier to getting patients consented and enrolled within the 72 hour window. As we are heading into the summer trauma season and COVID-19 hospitalizations have declined, we expect enrollment to pick up.

**What opportunities for training and professional development has the project provided?**

*If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. “Training” activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. “Professional development” activities result in increased knowledge or skill in one’s area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.*

Nothing to Report

**How were the results disseminated to communities of interest?**

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.*

Nothing to Report

**What do you plan to do during the next reporting period to accomplish the goals?**

*If this is the final report, state “Nothing to Report.”*

*Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.*

We will continue to enroll patients in Phases 2/3 in the next reporting period (Y4Q1).

4. **IMPACT:** Describe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:

**What was the impact on the development of the principal discipline(s) of the project?**

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).*

Nothing to Report

**What was the impact on other disciplines?**

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.*

Nothing to Report

**What was the impact on technology transfer?**

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:*

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to Report

**What was the impact on society beyond science and technology?**

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:*

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to Report

- 5. CHANGES/PROBLEMS:** *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, “Nothing to Report,” if applicable:*

Nothing to Report

**Actual or anticipated problems or delays and actions or plans to resolve them**

*Describe problems or delays encountered during the reporting period and actions or plans to resolve them.*

During Phase 1, we identified 3.2 eligible patients/month and enrolled 1.6 patients/month. Identification of eligible patients has been similar in Phase 2/3 at 3.1 patients/month, but enrollment seems to have slowed to 0.9 patients/month. Reasons for non-enrollment are similar with rate of not identifying an LAR decreasing from 20.4% to 14.7%, unable to consent within 72 hours increasing from 8.2% to 26.5% and rate of refusal increasing from 4.1% (2 of 49) to 14.7% (5 of 34). The decrease in not identifying LARs provides evidence that we have done a better job working with social workers and the clinical team. There are also fewer restrictions on visitation recently. However, we have been less able to obtain consent from LARs due to running out of time and refusals, representing a potential additional 3 and 1 additional patients respectively if we were experiencing the same rates as in Phase 1. We are currently exploring the reasons behind the increase in refusals, which anecdotally has affected enrollment in other studies as well. Once we complete the investigation of refusals across all studies, we will be better able to recommend a plan of action.

**Changes that had a significant impact on expenditures**

*Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.*

Due to the COVID-19 shutdown and not adding personnel effort until patient enrollment was about to begin, we have spent less than expected to date. We are utilizing those funds for the no cost extension.

**Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents**

*Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.*

**Significant changes in use or care of human subjects**

No significant changes have been made to the Human Use Regulatory Protocols. There have been updates to the consent form to better reflect the minor risks of general anesthesia and/or sedation for the research MRIs. The continuing review was approved by the UTHealth Houston CPHS on 18-APR-2022 and was submitted to HRPO for acknowledgement the following week. The revised consent form and CR approval are attached in Appendix A.

**Significant changes in use or care of vertebrate animals**

Not applicable

**Significant changes in use of biohazards and/or select agents**

Not applicable

**6. PRODUCTS:** *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state “Nothing to Report.”*

- **Publications, conference papers, and presentations**  
*Report only the major publication(s) resulting from the work under this award.*

**Journal publications.** *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume; year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report

**Books or other non-periodical, one-time publications.** *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report

**Other publications, conference papers and presentations.** *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (\*) if presentation produced a manuscript.*

Nothing to Report

- **Website(s) or other Internet site(s)**

*List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.*

Nothing to Report

- **Technologies or techniques**

*Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.*

Nothing to Report

- **Inventions, patent applications, and/or licenses**

*Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.*

Nothing to Report

- **Other Products**

*Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:*

- *data or databases;*
- *physical collections;*
- *audio or video products;*
- *software;*
- *models;*
- *educational aids or curricula;*
- *instruments or equipment;*
- *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
- *clinical interventions;*
- *new business creation; and*
- *other.*

Nothing to Report

## 7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

### **What individuals have worked on the project?**

*Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of*

compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate “no change”.

Example:

Name: Mary Smith  
Project Role: Graduate Student  
Researcher Identifier (e.g. ORCID ID): 1234567  
Nearest person month worked: 5  
Contribution to Project: Ms. Smith has performed work in the area of combined error-control and constrained coding.  
Funding Support: The Ford Foundation (Complete only if the funding support is provided from other than this award.)

Name: Charles Cox, MD  
Project Role: PI  
Researcher Identifier (e.g. ORCID ID): Unknown  
Nearest person month worked: 2  
Contribution to Project: Dr. Cox oversaw screening and enrollment for Phase 1 and analysis of the resulting data.

Name: Charles Wade, PhD  
Project Role: Co-I  
Researcher Identifier (e.g. ORCID ID): Unknown  
Nearest person month worked: 1  
Contribution to Project: Dr. Wade oversaw laboratory collect and analysis for Phase 1 and analysis of the resulting data.

Name: Ryan Kitagawa, MD  
Project Role: Co-I  
Researcher Identifier (e.g. ORCID ID): Unknown  
Nearest person month worked: 1  
Contribution to Project: Dr. Kitagawa is an expert in trauma-related neurosurgery and assisted the team with enrolling patients into Phase 1.

Name: HuiMahn “Alex” Choi, MD  
Project Role: Co-I  
Researcher Identifier (e.g. ORCID ID): Unknown  
Nearest person month worked: 1  
Contribution to Project: Dr. Choi is an expert in ICP monitoring, assisted the team with enrolling patients into Phase 1, and assisted with interpretation of the ICP data.

Name: Claudia Pedroza, PhD  
Project Role: Co-I  
Researcher Identifier (e.g. ORCID ID): Unknown  
Nearest person month worked: 1  
Contribution to Project: Dr. Pedroza is a biostatistician. She ran the data coordinating center and supervised the analysis of data.

Name: Erin Fox, PhD  
Project Role: Co-I  
Researcher Identifier (e.g. ORCID ID): Unknown  
Nearest person month worked: 1  
Contribution to Project: Dr. Fox is an epidemiologist and the Project Manager. She manages the day-to-day aspects of the projects, drafts all reports, and assists in data interpretation.

Name: Steve Kosmach, RN  
Project Role: Nurse Coordinator  
Researcher Identifier (e.g. ORCID ID): Unknown  
Nearest person month worked: 1  
Contribution to Project: Mr. Kosmach consented patients in the Neuro ICU for Study 1 and collected and entered all clinical research data.

Name: Yidao Cai  
Project Role: FITBIR Data Programmer  
Researcher Identifier (e.g. ORCID ID): Unknown  
Nearest person month worked: 2  
Contribution to Project: Mr. Cai is sending data to FITBIR.

Name: Jude Savarraj  
Project Role: FITBIR Data Programmer  
Researcher Identifier (e.g. ORCID ID): Unknown  
Nearest person month worked: 1  
Contribution to Project: Dr. Savarraj is responsible for downloading, managing, and analyzing the waveform data from the Moberg.

Name: Yao-Wei “Willa” Wang, MD  
Project Role: Laboratory Manager  
Researcher Identifier (e.g. ORCID ID): Unknown  
Nearest person month worked: 1  
Contribution to Project: Dr. Wang is the Laboratory Project Manager and oversees the day-to-day operations of the research laboratory.

Name: Symantha Lopez, Veda Pa, Garrett Woodruff, Selina Gonzalez, Kalea Dixon, Daisy Lopez  
Project Role: Laboratory Research Assistants  
Researcher Identifier (e.g. ORCID ID): Unknown  
Nearest person month worked: 1 month each  
Contribution to Project: Laboratory Research Assistants back up clinical RAs to provide 24/7 screening and enrollment coverage and perform all laboratory analyses

Name: Subin Alexander, Natolie Hamilton, Victoria Herrick, Kendra Tyner  
Project Role: Clinical Research Assistants  
Researcher Identifier (e.g. ORCID ID): Unknown  
Nearest person month worked: 1 month each  
Contribution to Project: Clinical Research Assistants screen patients and hook up the Moberg ICP monitoring data capture device with 24/7 coverage.

**Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?**

*If there is nothing significant to report during this reporting period, state “Nothing to Report.”*

*If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.*

**Previously active grants that have closed:**

For Erin Fox, PhD

Title: Linking Investigations in Trauma and Emergency Services (LITES)  
Time Commitment: 15%  
Supporting Agency: University of Pittsburgh (DoD Federal Pass Through)  
Agency PoC: DJ Swank, [d.j.swank@pitt.edu](mailto:d.j.swank@pitt.edu)  
Performance Period: 10/16-12/21  
Role: Co-Principal Investigator

Title: Linking Investigations in Trauma and Emergency Services LITES Task Order 0002: Task Order 2: Shock, Whole blood and Assessment of TBI (SWAT)  
Time Commitment: 5%  
Supporting Agency: University of Pittsburgh (DoD Federal Pass Through)  
Agency PoC: DJ Swank, [d.j.swank@pitt.edu](mailto:d.j.swank@pitt.edu)  
Performance Period: 09/2017-04/2022  
Role: Co-Investigator

For Charles Wade, PhD

Title: Linking Investigations in Trauma and Emergency Services (LITES)  
Time Commitment: 5%

Title: Linking Investigations in Trauma and Emergency Services LITES Task Order 0002: Task Order 2: Shock, Whole blood and Assessment of TBI (SWAT)  
Time Commitment: 10%

**New Active Grants:**

For Charles Wade, PhD

Title: Platelet-Derived Extracellular Vesicles for Hemorrhage Control and Prevention of Hemorrhagic Shock

Major Goals: The overall goal of this proposal is to test the efficacy of human platelet-derived extracellular vesicles (PEVs) in providing pro-hemostatic support, maintaining hemodynamic stability and attenuating the development of multiple organ failure associated with hemorrhagic shock.

Status of Support: Active

Project Number: W81XWH-21-1-10683

Name of PD/PI: Jessica Cardenas, PhD

Source of Support: Department of Defense

Primary Place of Performance: The University of Texas Health Science Center at Houston

Project/Proposal Start and End Date: 09/2021-08/2025

Total Amount Awarded:

*Describe partner organizations – academic institutions, other non-profits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.*

*Provide the following information for each partnership:*

*Organization Name:*

*Location of Organization: (if foreign location list country)*

*Partner's contribution to the project (identify one or more)*

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

Nothing to Report
-------------------

## **8. SPECIAL REPORTING REQUIREMENTS**

**COLLABORATIVE AWARDS:** *For collaborative awards, independent reports are required from BOTH the Initiating Principal Investigator (PI) and the Collaborating/Partnering PI. A duplicative report is acceptable; however, tasks shall be clearly marked with the responsible PI and research site. A report shall be submitted to <https://ers.amedd.army.mil> for each unique award.*

**QUAD CHARTS:** *If applicable, the Quad Chart (available on <https://www.usamraa.army.mil>) should be updated and submitted with attachments.*

- 9. APPENDICES:** *Attach all appendices that contain information that supplements, clarifies or supports the text. Examples include original copies of journal articles, reprints of manuscripts and abstracts, a curriculum vitae, patent applications, study questionnaires, and surveys, etc.*

## Appendix A. Regulatory documents

**NOTICE OF APPROVAL TO IMPLEMENT REQUESTED CHANGES**

DATE: June 02, 2022

**HSC-MS-19-0628** - *Microvascular Barrier Biomarkers to Predict ICP Therapeutic Intensity after Severe TBI (Phase I)*

PI: Dr. Charles Cox Jr

Reference Number: 231083

**PROVISIONS;** Unless otherwise noted, this approval relates to the research to be conducted under the above referenced title and/or to any associated materials considered at this meeting, e.g. study documents, informed consent, etc.

APPROVED: By Expedited Review and Approval

**CHANGE APPROVED:**

- TBI ICP Consent Version 3 Spanish (5/24/2022) update (risk: general anesthesia/sedation)
- TBI ICP Consent Version 3 English (5/24/2022) update (risk: general anesthesia/sedation)

REVIEW DATE: 06/02/2022

APPROVAL DATE: 06/02/2022



CHAIRPERSON: Charles C. Miller, III, Ph.D.

Upon receipt of this letter, and subject to any provisions noted above, you may now implement the changes approved.

**CHANGES:** The principal investigator (PI) must receive approval from the CPHS before initiating any changes, including those required by the sponsor, which would affect human subjects, e.g. changes in methods or procedures, numbers or kinds of human subjects, or revisions to the informed consent document or procedures. The addition of co-investigators must also receive approval from the CPHS. ALL PROTOCOL REVISIONS MUST BE SUBMITTED TO THE SPONSOR OF THE RESEARCH.

**INFORMED CONSENT:** Informed consent must be obtained by the PI or designee(s), using the format and procedures approved by the CPHS. The PI is responsible to instruct the designee in the methods approved by the CPHS for the consent process. The individual obtaining informed consent must also sign the consent document. **Please note that if revisions to the informed consent form were made and approved, then old blank copies of the ICF MUST be destroyed. Only copies of the appropriately dated, stamped approved informed consent form can be used when obtaining consent.**

**UNANTICIPATED RISK OR HARM, OR ADVERSE DRUG REACTIONS:** The PI will immediately inform the CPHS of any unanticipated problems involving risks to subjects or others, of any serious harm to subjects, and of any adverse drug reactions.

**RECORDS:** The PI will maintain adequate records, including signed consent documents if required, in a manner that ensures subject confidentiality.

## CONSENT TO TAKE PART IN RESEARCH

**Simple Study Title:** TBI ICP and Biomarker Study (Phase 2/3)

**Full Study Title:** Microvascular Barrier Biomarkers to Predict ICP Therapeutic Intensity after Severe TBI (Phase 2/3)

**Study Sponsor:** Department of Defense

**Principal Investigator:** Charles Cox, MD

**Study Contact:** Steven Kosmach, MSN, RN, CCRC (713) 500-7328

The purpose of this study is to better understand the relationship of intracranial pressure (ICP) values and blood samples that measure inflammation in individuals who have experienced a traumatic brain injury (TBI) that may be useful in predicting recovery.

If you choose to participate in this study, you will be asked to allow us to collect blood samples over the first 4 days of your hospital stay, have one brain MRI before discharge, and complete a brief disability assessment questionnaire at time of discharge and by telephone 6 months after the TBI. The total amount of time you will be in this study is 6 months.

This is an observational study therefore the risks are minimal however there is also the potential risk of breach of confidentiality. The only alternative is to not participate in this observational study.

Participation in this research study is voluntary. 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), and/or Memorial Hermann Healthcare System.

If you are interested in participating, please continue to read below.

If you are unable to provide written informed consent, or have legally transferred authority to consent for health care decisions to another person, a Legally Authorized Representative may consent on your behalf to participate in this study. "You" refers to the patient in this consent form.

### **What is the purpose of this research study?**

Severe head injuries can cause the brain to swell. The expanding tissue increases the pressure within the skull and can result in further brain injuries. Intracranial pressure (ICP) monitoring is standard of care for patients with severe traumatic brain injuries. Bedside monitors continuously display ICP values but this information is usually only recorded in the medical record at hourly intervals. The purpose of this study is to better understand ICP changes immediately following severe TBI by collect very detailed information on ICP values, (recorded every 5 seconds). Research blood samples will be tested for proteins linked to inflammation and brain swelling. This study is observational so there will be no study treatment, medication or procedure.

The Department of Defense is paying UTHealth for their work on this study.

**Who is being asked to take part in this study?**

You are being asked to take part in this research study because you have experienced a traumatic brain injury. This study is being conducted at UTHealth. About 50 people will take part in the study at UTHealth, and Memorial Health System.

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

If you agree to participate, blood samples (about 1 ½ tablespoons) will be collected at the time of emergency department admission, and at 2, 12, 24, 48 and 96 hours after the ICP monitor was placed as standard of care. The total amount of blood withdrawn during your participation will be about 9 tablespoons.

You will also have a brain MRI scan once the ICP monitor is removed.

We will also complete a brief disability assessment called the Glasgow Outcome Scale (GOSE) at the time you leave the hospital and again by telephone at 6 months after your TBI. The GOSE is routinely used to measure an individual's recovery following TBI and should take no more than 10 minutes to complete. In addition we will also collect information from your medical records during your hospital stay.

The results of these research tests will not have an effect on your care. You will not receive results of these research tests, nor will the results be put in your health record. Your leftover blood samples, if any, will be stored in a secure lab at the UTHealth Medical School for future research and for an indefinite period of time.

**How long will you be in the study?**

If you agree to take part, your participation will last for 6 months and will involve the time you are in the hospital and then a phone call approximately 6 months from the time you were admitted to the hospital.

**What choices do you have other than this study?**

The only option is to not take part in this study. You will continue to receive the standard care for traumatic brain injury.

**What are the risks of taking part in this study?**

Because this is an observational study, the risks are minimal. One potential risk is the possibility of breach of confidentiality. All measures are taken to protect your personal identity. The information collected will be de-identified and identified only by a unique study ID number.

MRI Scans: MRI scans are very safe procedures, and there is no radiation or contrast media involved. The MRI does involve the use of a large magnet that 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. Some people are uncomfortable in the scanner, as it is an enclosed space. You may require sedation or general anesthesia to complete the MRI. The risks associated with sedation and general anesthesia include respiratory depression and low heart rate and blood pressure. An Anesthesiologist will monitor you closely during the MRI to prevent complications from the sedation or general anesthesia.

**GINA**

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. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this Federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

**What are the benefits to taking part in this study?**

You may not directly benefit from participating in the study, but the knowledge gained from your participation may, in the future, help others with traumatic brain injury.

**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 Charles Cox, MD at 713-500-7329.

Your doctor or the sponsor can stop the study at any time. Your doctor or the sponsor may stop your participation in the study if your condition worsens, the study is stopped, you do not meet all the requirements of the study, 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 suffer an injury as a result of taking part in this research study, please understand that nothing has been arranged to provide free treatment of the injury or any other type of payment. However, necessary facilities, emergency treatment, and professional services will be available to you, just as they are to the general community. You should report any such injury to Charles Cox, MD at 713-500-7300. You will not give up any of your legal rights by signing this consent form.

**What are the costs of taking part in this study?**

The sponsor will pay for the special tests and examinations that are required by this study and not otherwise part of your standard medical care. If you receive a bill that you believe is related to your taking part in this research study, please contact Charles Cox, MD or his research staff at 713-500-7300 with any questions.

**How will privacy and confidentiality be protected?**

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

If you sign this document, you give permission to UTHealth, 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; prehospital information, vital signs, lab reports, procedure and diagnostic reports, lab results, discharge notes, and physician notes.

Personal identifiers such as your name and medical record number will be removed from the information and samples collected in this study. After we remove all identifiers, the information or samples may be used for future research or shared with other researchers without your additional informed consent.

People 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 from the U.S. Food and Drug Administration (FDA)
- Representatives of Department of Defense

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.

**Federal Interagency Traumatic Brain Injury Information System**

Data from this study may be submitted to the Federal Interagency Traumatic Brain Injury (FITBIR) informatics system. FITBIR is a computer system run by the National Institutes of Health that allows researchers studying traumatic brain injury to collect and share information with each other. With an easier way to share, researchers hope to learn new and important things about traumatic brain injury more quickly than before.

During and after the study, the researchers will send information about your health and behavior and in some cases, your genetic information, to FITBIR. However, before they send it to FITBIR, they will remove information such as name, date of birth, and city of birth, and replace that information with a code number. Other researchers nationwide can then file an application to obtain access to your study data for research purposes. Experts who know how to protect health and science information will look at every request carefully to minimize risks to your privacy.

You will not benefit directly from allowing your information to be shared with FITBIR. The information provided to FITBIR might help researchers around the world treat future children and adults with traumatic brain injury so that they have better outcomes. FITBIR will report on its website about the different studies that researchers are conducting using FITBIR data; however, FITBIR will not be able to contact you about specific studies.

You may decide now or later that you do not want to share your information using FITBIR. If so, contact the researchers who conducted this study, and they will tell FITBIR, which can stop sharing the research information. However, FITBIR cannot take back information that was shared before you changed your mind. If you would like more information about FITBIR, this is available on-line at <http://fitbir.nih.gov>

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 Charles Cox, MD in writing at UTHealth, 6431 Fannin MSB 5.324, Houston, TX 77030

This Authorization will expire 6 years after the end of the study.

**Whom can you contact if you have questions about the study?**

If you have questions at any time about this research study, please feel free to contact the Charles Cox, MD or study staff at 713-500-7300, as they 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



**CONSENTIMIENTO INFORMADO PARA PARTICIPAR EN UN ENSAYO DE INVESTIGACION MÉDICA**

**Titulo Simple de la Investigación:** Lesión Cerebral Traumática (LCT), Presión IntraCraneal (PIC) y Estudio de Biomarcadores (Fase 2/3)

**Titulo Completo del Estudio:** Biomarcadores de barreras microvasculares para predecir la intensidad terapéutica de la PIC después de una LCT grave (Fase 2/3)

**Patrocinador del Estudio:** Departamento de Defensa

**Investigador Principal:** Dr. Charles Cox

**Contacto de Estudio:** Steven Kosmach, MSN, RN, CCRC (713) 500-7328

El propósito de este estudio es para entender mejor la relación de los valores de la presión intracraneal y las muestras de sangre que miden la inflamación en individuos que han sufrido una lesión cerebral traumática (LCT) y que pueden ser útiles para predecir la recuperación.

Si elige participar en este estudio, se le pedirá que nos permita tomar muestras de sangre durante los primeros 4 días de su estancia en el hospital, hacerle una imagen del cerebro por resonancia magnética (MRI, por sus siglas en ingles) y completar una breve evaluación de la incapacidad al momento de ser dado de alta y por teléfono 6 meses después de la LCT. Usted estará participando en el estudio por seis meses en total.

Este es un estudio observacional, por lo tanto, los riesgos son mínimos, sin embargo, también existe el riesgo potencial de que su participación o sus datos personales puedan ser descubiertos. La única alternativa es no participar en este estudio observacional.

La participación en este estudio de investigación es voluntaria. Puede optar por no participar en este estudio de investigación o puede optar por abandonar el estudio de investigación en cualquier momento. Su decisión no afectara la atención clínica que recibe en la Universidad of Texas Health Science Center (UTHealth) y / o Memorial Hermann Health System.

Si está interesado en participar, siga leyendo a continuación.

Si no puede proporcionar un consentimiento (permiso) informado por escrito, o si ha transferido legalmente la autoridad para consentir las decisiones de atención médica a otra persona, un Representante Legal Autorizado puede dar el consentimiento en su nombre para participar en este estudio. “Usted” se refiere al paciente en este formulario de consentimiento.

### **¿Cuál es el propósito de este estudio de investigación?**

Las lesiones graves en la cabeza pueden hacer que el cerebro se hinche. El tejido al hincharse puede aumentar la presión dentro del cráneo y puede provocar más lesiones cerebrales. La monitorización de la Presión Intracraneal (PIC) es la atención estándar para pacientes con lesiones cerebrales traumáticas graves. Los monitores utilizados en el cuarto del paciente muestran continuamente los niveles de presión intracraneal (PIC) pero ésta información generalmente solo se registra en el expediente médico a intervalos de una hora. El propósito de este estudio es comprender mejor los cambios en la (PIC) inmediatamente después de una Lesión Cerebral Traumática (LCT) grave mediante la recopilación de información muy detallada sobre los niveles de la (PIC) (registrados cada 5 segundos). Se analizarán muestras de sangre de investigación para detectar proteínas vinculadas a la inflamación e hinchazón del cerebro. Este estudio es de observación, por lo que no habrá tratamiento, medicamento o procedimiento del estudio.

El Departamento de Defensa está pagando a la Universidad UTHealth por el trabajo en este estudio.

### **¿A quién se le pide que participe en este estudio?**

Se le invita que participe en este estudio de investigación porque ha experimentado una lesión cerebral traumática. Este estudio se está realizando en la Universidad UTHealth. Alrededor de 50 personas participarán en el estudio en la Universidad UTHealth, y Memorial Health System.

### **¿Qué pasará si participo en este estudio?**

Si acepta participar, se tomarán muestras de sangre en el momento de la admisión en el departamento de urgencias, y a las 2, 12, 24, 48 y 96 horas después de que el monitor PIC se haya colocado como estándar de atención médica. También le pediremos que complete una evaluación breve llamada Escala de Coma de Glasgow (GCS, por sus siglas en inglés) al momento de salir del hospital y nuevamente a los 6 meses. El GCS se usa habitualmente para medir la recuperación de un individuo después de una LCT y no debe demorar más de 10 minutos en completarse. Además, también recopilaremos información de sus expedientes médicos durante su estadía en el hospital.

Se obtendrá aproximadamente 23 cc (aproximadamente 1 ½ cucharadas) de sangre extraída de una vena de su brazo al momento de la admisión en el departamento de urgencias (ED), y a las 2, 12, 24, 28 y 96 horas después de que se coloque el monitor PIC. La cantidad total de sangre extraída durante su participación será de aproximadamente 9 cucharadas. Los resultados de estas pruebas de investigación no afectarán su atención. No recibirá los resultados de estas pruebas de investigación, ni los resultados se incluirán en su registro de salud. Las muestras de sangre sobrantes, si las hay, se almacenarán en un laboratorio seguro en la Escuela de Medicina de la Universidad UTHealth para investigaciones futuras y por un período de tiempo indefinido.

### **¿Cuánto tiempo estará en el estudio?**

Si acepta participar, su participación durara 6 meses e implicara el tiempo que permanezca en el hospital de hasta 30 días y luego una llamada telefónica aproximadamente 6 meses desde el momento en que ingreso en el hospital.

### **¿Qué opciones tienes aparte de este estudio?**

La única opción es no participar en este estudio. Continuará recibiendo la atención estándar para lesiones cerebrales traumáticas.

### **¿Cuáles son los riesgos de participar en este estudio?**

Debido a que este es un estudio observacional, los riesgos son mínimos. Un riesgo potencial es la posibilidad de la perdida de la confidencialidad. Se toman todas las medidas para proteger si identidad personal. La información recopilada será des identificada e identificada solo por un número de identificación de estudio único.

Escaneo de Imagen por Resonancia Magnética: La Imagen por Resonancia Magnética es un procedimiento muy seguro, y no hay radiación ni medios de contraste involucrados. La Imagen por Resonancia Magnética implica el uso de un imán grande que puede interactuar con objetos metálicos como aparatos ortodonticos (dentales) o dispositivos implantados. Antes de la resonancia por magnética se le examinara cuidadosamente para detectar la presencia de objetos metálicos en su cuerpo. Algunas personas se sienten incomodas en el escáner, ya que es un espacio cerrado. Es posible que necesite sedación o anestesia general para realizar la Imagen por Resonancia Magnética (MRI, conocida por sus siglas en inglés). Los riesgos asociados a la sedación y a la anestesia general incluyen la depresión respiratoria y la disminución de la frecuencia cardiaca y de la presión arterial. Un anestesista le vigilara de cerca durante el escaneo para evitar complicaciones derivadas de la sedación o la anestesia general.

### **GINA**

Una ley federal, llamada Ley de No Discriminación de Información Genética (GINA, por sus siglas en ingles), generalmente hace ilegal que las compañías de seguros de salud, los planes de salud grupales y la mayoría de los empleadores lo discriminen en base a su información genética. Esta ley generalmente lo protegerá de las siguientes maneras:

Las compañías de seguros de salud y los planes de salud grupales no pueden solicitar la información genética que obtenemos de esta investigación.

Las compañías de seguros de salud y los planes de salud grupales no pueden usar su información genética al tomar decisiones con respecto a su elegibilidad o primas.

Los empleadores con 15 o más empleados no pueden usar su información genética que obtenemos de esta investigación al tomar la decisión de contratarlo, promoverlo o despedirlo o al establecer los términos de su empleo.

Tenga en cuenta que esta ley federal no lo protege contra la discriminación genética de las compañías que venden seguros de vida, seguros por discapacidad o seguros de atención a largo plazo.

### **¿Cuáles son los beneficios de participar en este estudio?**

Es posible que no se beneficie directamente al participar en el estudio, pero el conocimiento obtenido de su participación puede, en el futuro, ayudar a otros con lesiones cerebrales traumáticas.

### **¿Puedes dejar de participar en este estudio?**

Puede decidir dejar de participar en el estudio en cualquier momento. Para retirarse del estudio, llame al Dr. Charles Cox, al 713-500-7329.

Su médico o el patrocinador pueden detener el estudio en cualquier momento. Su médico o el patrocinador pueden detener su participación en el estudio si su condición empeora, el estudio se detiene, no reúne con todos los requisitos del estudio o si el estudio no es lo mejor para usted. Si se interrumpe su participación en el estudio, su médico discutirá otras opciones para su tratamiento.

Si deja de participar en este estudio, la información ya recopilada sobre usted se utilizará en el análisis de datos. Sin embargo, no se recopilará más información sin su permiso.

Mientras participa en este estudio, el equipo del estudio le notificará sobre información nueva que pueda estar disponible y que pueda afectar su disposición en permanecer en el estudio.

### **¿Qué sucede si se lesiona durante el estudio?**

Si sufre una lesión como resultado de participar en este estudio de investigación, comprenda que no se han hecho arreglos para proporcionar un tratamiento gratuito de la lesión o cualquier otro tipo de pago. Sin embargo, las instalaciones necesarias, el tratamiento de urgencia y los servicios profesionales estarán disponibles para usted, tal como lo están para la comunidad en general. Debe informar cualquier tipo de lesión al Dr. Charles Cox, al 713-500-7300. No renunciará a ninguno de sus derechos legales al firmar este formulario de consentimiento.

### **¿Cómo se protegerán la privacidad y la confidencialidad?**

Su privacidad es importante y su participación en este estudio se mantendrá confidencial. Sin embargo, no se puede garantizar la confidencialidad absoluta.

Su firma en este documento, autoriza al UTHealth, Memorial Hermann Healthcare System a usar y revelar (divulgar) su información de salud. La información de salud que nosotros

podemos usar o divulgar para esta investigación incluye; información pre hospitalaria, signos vitales, informes de laboratorio, procedimientos e informes de diagnóstico, resultados de laboratorio, resumen de la visita y las anotaciones del médico.

Los identificadores personales tales como su nombre y número de expediente médico se eliminarán de la información y de las muestras recolectadas en este estudio. Después de que eliminemos todos los identificadores, la información o las muestras pueden usarse para investigaciones futuras o compartirse con otros investigadores sin su consentimiento informado adicional.

Es posible que algunas personas que reciben su información no serán obligados a seguir las leyes federales de privacidad (como la Regla de Privacidad), si lo permiten las leyes que las rigen. No será identificado personalmente en ningún informe o publicación que pueda resultar de este estudio. Si toda la información que lo identifica o puede identificarlo se elimina de su información de salud, la información restante ya no estará sujeta a esta autorización y puede usarse o divulgarse para otros fines.

Los representantes de las organizaciones enumeradas a continuación verán su nombre y otros identificadores personales cuando revisen sus registros de investigación y registros médicos con el fin de verificar los datos del estudio:

- Representantes de la Universidad UTHealth y / o Memorial Hermann Health System
- Representantes de la Administración de alimentos y fármacos de los Estados Unidos (FDA por sus siglas en ingles).
- Representantes del Departamento de Defensa.

Tenga en cuenta que no tiene que firmar esta Autorización, pero si no lo hace, no podrá participar en este estudio de investigación. UTHealth y Memorial Hermann Health System no pueden retener el tratamiento o negarse a tratarlo si no firma esta Autorización.

### **Sistema de información federal inter-agencial sobre las lesiones cerebrales traumáticas**

Los datos de este estudio pueden enviarse al sistema informático Federal Inter-agencial de Lesiones Cerebrales Traumáticas (FITBIR, por sus siglas en ingles). FITBIR es un sistema informático administrado por los Institutos Nacionales de Salud que permite a los investigadores que estudian las lesiones cerebrales traumáticas a recopilar y compartir información entre ellos. Con una forma más fácil de compartir, los investigadores esperan aprender cosas nuevas e importantes sobre las lesiones

cerebrales traumáticas más rápido que antes.

Durante y después del estudio, los investigadores enviarán información sobre su salud y comportamiento y, en algunos casos, su información genética, a FITBIR. Sin embargo, antes de enviarla a FITBIR, eliminarán información tales como el nombre, la fecha de nacimiento y la ciudad de nacimiento, y reemplazarán esa información con un número de código. Otros investigadores de todo el país pueden presentar una solicitud para obtener acceso a los datos del estudio con fines de investigación. Los expertos que saben cómo proteger la información científica y de salud analizarán cada solicitud detenidamente para minimizar los riesgos para su privacidad.

No se beneficiará directamente al permitir que su información se comparta con FITBIR. La información proporcionada a FITBIR podría ayudar a los investigadores de todo el mundo a ayudar a futuros niños y adultos con lesiones cerebrales traumáticas para que tengan mejores resultados. FITBIR informará en su sitio web sobre los diferentes estudios que los investigadores están llevando a cabo y utilizando datos de FITBIR; sin embargo, FITBIR no podrá contactarlo sobre estudios específicos.

Puede decidir ahora o después que no desea compartir su información usando FITBIR. Si es así, comuníquese con los investigadores que realizaron este estudio y le dirán a FITBIR, que puede dejar de compartir la información de la investigación. Sin embargo, FITBIR no puede recuperar la información que se compartió antes de cambiar de opinión. Si desea obtener más información sobre FITBIR, puede obtenerla en línea en <http://fitbir.nih.gov>.

Puede cambiar de opinión y revocar (retirar) esta Autorización en cualquier momento. Incluso si revoca esta Autorización, los investigadores aún pueden usar o divulgar información de salud que ya hayan obtenido sobre usted según sea necesario para mantener la integridad o confiabilidad de la investigación actual. Para revocar esta autorización, debe comunicarse con el Dr. Charles Cox, por escrito a la Universidad de UTHealth, 6431 Fannin MSB 5.324, Houston, TX 77030

Esta autorización se vencerá 6 años después del final del estudio.

### **¿A quién puede contactar si tiene preguntas sobre el estudio?**

Si tiene preguntas en cualquier momento sobre este estudio de investigación, no dude en comunicarse con el Dr. Charles Cox, o el personal del estudio al 713-500-7300, ya que estarán encantados de responder sus preguntas. Puede ponerse en contacto con el equipo del estudio para analizar problemas, informar lesiones, expresar sus inquietudes, obtener información además de hacer preguntas sobre la investigación.

El Comité para la Protección de Sujetos Humanos (*Committee for the Protection of Human Subjects*) de la University of Texas Health Science Center ha revisado este estudio de investigación. Puede contactarlos para cualquier pregunta sobre sus derechos como sujeto de investigación y para discutir cualquier duda, comentario o queja sobre participando en un estudio de investigación al (713) 500-7943.

### FIRMAS

Firme a continuación solamente si entiende la información que se le ha proporcionado sobre la investigación y elige participar en este estudio de investigación. Asegúrese de que todas sus preguntas hayan sido respondidas. Si decide participar en este estudio de investigación, se le entregará una copia de este formulario de consentimiento firmado.

_____ Nombre Impreso del Participante	_____ Firma del Participante	_____ Fecha	_____ Hora
--	---------------------------------	----------------	---------------

_____ Nombre Impreso del Representante Legal Autorizado	_____ Firma del Representante Legal Autorizado	_____ Fecha	_____ Hora
--	---	----------------	---------------

_____ Nombre Impreso de la Persona que Obtiene el Consentimiento	_____ Firma de la Persona que Obtiene el Consentimiento	_____ Fecha	_____ Hora
---	--	----------------	---------------

Dr. Charles Cox  
UT-H-MS- Department of Pediatric Surgery

**NOTICE OF CONTINUING REVIEW APPROVAL**

**April 18, 2022**

**HSC-MS-19-0628** - *Microvascular Barrier Biomarkers to Predict ICP Therapeutic Intensity after Severe TBI (Phase I)*

PI: Charles Cox

**PROVISOS:** Unless otherwise noted, this approval relates to the research to be conducted under the above referenced title and/or to any associated materials considered at this meeting, e.g. study documents, informed consents, etc.

APPROVED: At a convened meeting

MEETING DATE: 04/08/2022

**EXPIRATION DATE:** 03/31/2023



CHAIRPERSON: Charles C. Miller, III, PhD

Upon review, the CPHS finds that this research is being conducted in accord with its guidelines and with the methods agreed upon by the principal investigator (PI) and approved by the Committee. This approval, subject to any listed provisions and contingent upon compliance with the following stipulations, will expire as noted above:

**CHANGES:** The PI must receive approval from the CPHS before initiating any changes, including those required by the sponsor, which would affect human subjects, e.g. changes in methods or procedures, numbers or kinds of human subjects, or revisions to the informed consent document or procedures. The addition of co-investigators must also receive approval from the CPHS. **ALL PROTOCOL REVISIONS MUST BE SUBMITTED TO THE SPONSOR OF THE RESEARCH.**

**INFORMED CONSENT:** Informed consent must be obtained by the PI or designee(s), using the format and procedures approved by the CPHS. The PI is responsible to instruct the designee in the methods approved by the CPHS for the consent process. The individual obtaining informed consent must also sign the consent document. **Please note that only copies of the appropriately dated, stamped approved informed consent form can be used when obtaining consent.**

**UNANTICIPATED RISK OR HARM, OR ADVERSE DRUG REACTIONS:** The PI will immediately inform the CPHS of any unanticipated problems involving risks to subjects or others, of any serious harm to

subjects, and of any adverse drug reactions.

**RECORDS:** The PI will maintain adequate records, including signed consent documents if required, in a manner which ensures subject confidentiality.