

PROTECTION OF HUMAN SUBJECTS – INFORMATICS AND ANALYTICS CORE (IAC)

Traumatic brain injury (TBI) represents a leading cause of death and disability worldwide, resulting in major social, economic, and health problems such as physical, cognitive, emotional, and behavioral sequelae. Approximately 3–5% of moderate and 25–50% of severe TBI cases develop post-traumatic epilepsy (PTE), defined as recurring seizures that develop more than 7 days after injury.

PTE accounts for approximately 4% of focal epilepsies in the general population and is the leading cause of epilepsy with onset in young adulthood. Many of these patients do not respond to antiepileptic drugs and are considered medically intractable. Despite representing an important public health problem, the mechanisms through which PTE develops have not been well studied. Identifying the underlying cellular and molecular substrates responsible for the establishment of PTE is urgently needed to develop hypotheses about its pathogenesis and potential means of prevention and treatment of this devastating disease.

This study is part of a Center without Walls (CWOW) multicenter collaborative effort to identify and validate markers and mechanisms of epileptogenesis after TBI and involves collection, analysis, and banking of human blood, CSF, and brain tissue samples. The specimens will be from multiple sources.

1. Human Subjects Involvement and Characteristics:

1.1. Epilepsy patients

Tissues are removed in a manner completely independent from any research study to treat the patient's epileptic disorder. However, in many cases large resections contain regions with varying degrees of epileptic activity that forms the basis for an internally-controlled study design. Additional control brain specimens will be collected each time when an autopsy is performed in patients with normal neurologic history. The population will consist of adults and will range in age from 18 to 60 years old. All tissues from these subjects will be coded and de-identified immediately after collection. Only the coded and de-identified information will be provided to the EpiBioS4Rx collaborators and/or will be sent to the EpiBioS4Rx Biobank. All clinical information will be held strictly confidential.

1.2. Archival tissue samples

All samples within the archive have been deidentified and are coded by a 6 digit number. All specimens and analyses will be performed at each center; data obtained will be kept at the center. Dr. Denes Agoston at the Uniformed Services University will be responsible for analysis, data entry into the EpiBioS4Rx IAC, and safeguarding of data. Data will be in digital and paper form and will be stored at each center where they are collected.

2. Risks to participants:

The primary risk to participants is loss of confidentiality due to inadequate de-identification of data. We believe this risk will be very small, as numerous precautions will be instituted to mitigate the risk at all participating institutions.

3. Protection against risks:

TBI and epilepsy patients will be enrolled in this study only if written consent is obtained. No patients will be excluded based on age, sex, race, or social status. There should be no adverse events related to the research and no discomforts or risks for injury related to this study. The tissue being used for research is excess/discarded tissue, derived from autopsy and biopsy tissue removed to treat TBI and epilepsy/ seizure disorder. Tissue collection will not interfere with surgical procedure, neuropathological diagnostic and clinical care. However, there is a minimal discomfort, pain, or bruising during venipuncture, but only trained personnel will perform this procedure to ensure safety. The risks to the confidentiality of research subjects and their families are eliminated by the use of randomly generated numbers to code specimens throughout their processing and analysis. All clinicopathological information, even though retrievable by the randomly assigned

code number, is held in the strictest confidence. A list of patient names and any identifying information will be kept in a separate offline document to ensure patient confidentiality. All printed records will be kept in a locked file cabinet. No research results will be placed in the medical records and no information will ever be released or published in a way that will identify a specific individual.

4. Potential Benefits

There is no direct benefit to participating subjects. However, there is the indirect benefit to society as a whole of the scientific knowledge gained from the investigational/research use of collected tissue and data. The research will have broad ramifications for all TBI patients with and without seizures if the involved fundamental regulatory pathways can be defined and used to develop new diagnostic tools and treatment strategies. In addition, specific cellular and molecular biomarkers may be discovered that could predict epilepsy in TBI patients.

5. Importance of the Knowledge to be gained

We have already gained important knowledge pointing to important regulatory pathways in human epilepsy. As discussed above in point 3, the risks of performing these studies on tissue that would otherwise be discarded are low compared to the potential benefit of the new knowledge gained.