**ABSTRACT / PROJECT SUMMARY – PROJECT 3 – BIOMARKERS OF HUMAN EPILEPTOGENESIS AFTER TRAUMATIC BRAIN INJURY**

The mechanisms underlying human acquired epileptogenesis remain poorly understood and a novel multimodal approach to study the process from inception to manifest clinical epilepsy is needed. We have selected Post-Traumatic Epilepsy (PTE) as a model to pursue this understanding because the timing of the potential epileptogenic insult is known and the period of epileptogenesis can be determined. **The EpiBioS4Rx Scientific Premise is Epileptogenesis after TBI can be prevented with specific treatments; the identification of relevant biomarkers and performance or rigorous preclinical trials will permit the future design and performance of economically feasible full-scale clinical trials of antiepileptogenic therapies.** In Project 3, we plan to perform a multicenter, multidisciplinary observational study of early epileptogenesis after moderate-severe TBI in 300 subjects with the specific injury phenotype of temporal and/or frontal lobe hemorrhagic contusional injury that matches the experimental injury models in animal *Projects 1 and 2*. We plan four specific aims that feature determining measuring the presence of early electroencephalographic, MRI and blood biomarkers of epileptogenesis. In aim 4, we plan to create the ideal clinical trial network and trial design informed by our animal Project 2 as well as shared data from large biomarkers trials in both adults (TRACK, CENTER) and children (ADAPT) with TBI. In the *Public Engagement Core*, we have recruited an outstanding multidisciplinary team of consumers, consumer advocates and key opinion leaders in TBI, PTE, and Epilepsy Clinical Trials to work in this project. We plan a highly integrated and adaptive study design across all 3 Projects and 3 Cores of EpiBioS4Rx to enable a rigorous experimental design for robust and unbiased results. Integration is demonstrated by injury type, methodology, mechanistic investigation, shared analysis and methods, shared public engagement core, and shared DSMB The ultimate goal is to develop a personalized medicine approach for a future definitive clinical trial for an antiepileptogenic drug for PTE.