SURROGATE MARKERS IN ANIMAL MODELS OF ACQUIRED EPILEPSY: THE GOOD, THE BAD AND THE UGLY

F. Edward Dudek*, Tallie Z. Baram†, Edward H. Bertram‡ and Frances E. Jensen§

*Dept of Physiology, University of Utah School of Medicine, Salt Lake City, UT; †Dept of Pediatrics, University of California Irvine, Irvine, CA; ‡Dept of Neurology, University of Virginia, Charlottesville, VA and §Dept of Neurology, Harvard Medical School, Childrens Hospital/University of Virginia, Boston, MA

Summary: Acquired epilepsy is generally considered to be the time-dependent development of spontaneous recurrent seizures after an insult to the brain. To monitor for and confirm the presence of bona fide seizures can be technically demanding and resource-intensive, particularly when one considers the time required for the development of chronic epilepsy after a brain insult and the effort necessary to detect and validate the actual seizures, which have a range of specific electrical properties and typically last 10’s of seconds to minutes. The use of alternatives to these actual seizures, or surrogate markers, for epileptogenesis has a long history, but is founded on several unproven assumptions. Examples of surrogate markers for experimental epilepsy include (1) “hyperexcitability” to extracellular stimulation, (2) increased seizure susceptibility to challenges with chemo-convulsants (e.g., kainic acid and flurothyl), and (3) brief (i.e., <15 seconds) rhythmic activity in the EEG. Although each of these changes could be interpreted as being pro-excitatory and, by extension, pro-epileptogenic, the actual basis for each of these changes and their implications for the development of epilepsy are poorly understood. This workshop will debate the pros and cons of these different surrogate markers, which are often used to validate animal models of acquired epilepsy, to test hypotheses about mechanisms of epileptogenesis, and ultimately, to discover anti-epileptogenic therapies. We will present opposing positions, and invite the audience to comment on the potential utility and predictive value of each of the markers.