# FOREIGN JUSTIFICATION *-* Project 1 – BIOMARKERS OF EPILEPTOGENESIS AFTER EXPERIMENTAL TRAUMATIC BRAIN INJURY

## Why the two foreign sites (Kuopio, Finland; Melbourne, Australia) are necessary for the project success

The aim of **Project 1** is to identify sensitive and specific plasma molecular, electrophysiological, and MRI biomarkers for post-traumatic epileptogenesis in a clinically relevant animal model within a three-year study period. Statistical power demands a prohibitively large number of animals for the study to be conducted at any one laboratory, because of throughput limitations imposed by long-term video-EEG and its analysis.

Moreover, experiments will need to be cost-effective, to abide by 3R animal experimentation principles, and to be designed rigorously for robust and unbiased results. Because of these needs, a laboratory suitable for **Project 1** will require: (1) experience in using TBI/PTE animal models, (2) a facility and experience in using state-of-the art magnetic resonance imaging in rodents, (3) facility for and experience in conducting long-term video-EEG monitoring, and (4) experience in molecular studies. Importantly, all these will need to be available in the same study site,as the same animal undergoes multiple tests. There are few laboratories in the world with such capacity, expertise and track record. UCLA has an R01 (NS33310) that includes studies of rat TBI and has recently completely two electrophysiological studies in TBI animals. The first found cortical pHFOs and a new paroxysmal event consisting of repetitive pHFOs and EEG spikes or “rHFOSs” that only occurred in TBI rats that later developed seizures (Epilepsia, in press). These data are included in the preliminary studies of this project. The other study quantified the progressive electrophysiological abnormalities after TBI in rats that later developed seizures and those rats that did not, and the study is under review as of the submission of this application. In addition, there are two other sites in the world which have proven track records, including multiple published papers and competitive grant funding, in such studies: University of Eastern Finland (Kuopio, Finland) and University of Melbourne (Melbourne, Australia). This is the reason why **Project 1** has two foreign study sites, Finland and Australia.