Characterizing Biomarkers of Epileptogenesis in Rett Syndrome

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Epilepsy is highly prevalent in Rett syndrome (RTT) and is quite challenging to manage. The significant variability in epilepsy onset, frequent behaviors in RTT that mimic seizures, and anti-seizure medication side effects capable of exacerbating common RTT symptoms necessitate development objectively measured clinical criteria capable of predicting epilepsy onset. Such biomarkers of epileptogenesis would permit development of risk-based management strategies and also support future trials of potential new therapies. We hypothesize that the process of epileptogenesis in RTT will be associated with measurable differences in cognitive, neurophysiologic and/or molecular phenotype arising after initial RTT diagnosis which could serve as predictive biomarkers. For this clinical fellowship proposal we will begin developing a predictive algorithm for RTT-related epilepsy using longitudinally collected clinical data on girls with classic RTT and MECP2 mouse models to determine patient phenotype and EEG characeristics predicting epilepsy in classic RTT and neuronal gene expression changes associated with seizure development in Mecp2 mutant mice. The results of this proposal will have an important impact on patient care decisions and also provide insight into molecular mechanisms warranting further study as potential targets for future anti-epileptogenesis therapies.