Precision Imaging and Histological Phenotyping for RNA Profiling of Human Epilepsy Tissue

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Background: Up to 40% of persons with epilepsy are not controlled by available medications. Our understanding of mechanisms of seizure genesis is limited by animal models that may not adequately reflect human epilepsy. RNA profiling of human surgical epilepsy tissue may provide unique insights into pathological processes for development of novel interventions.

Methods: In a collaborative investigation with the Penn State Institute of Personalized Medicine, we have biobanked surgical tissue from 37 epilepsy patients that have been evaluated with high-resolution MRI, FDG-PET, and detailed cortical EEG mapping. After classifying the regions of each specimen based on severity of epileptiform EEG abnormalities, and also performing quantitative neuroimaging (FreeSurfer) and histopathological analysis (CellProfiler), we utilize differential RNA expression analysis to determine significant associations of specific biochemical pathway up regulation and down regulation with neuroimaging, glial, and neuronal pathologies.

Results: We present the differential RNA expression correlations with: 1) most and least electrically abnormal regions of the resected temporal lobe, 2) normal versus atrophic hippocampi based on presurgical MRI, and 3) quantified glial and neuronal cell counts and volumes in normal versus epileptic tissue.

Discussion: Differential RNA profiling of quantified phenotyping of imaging and histopathological abnormalities allows the potential to identify novel mechanisms of pathological processes and seizure genesis in human epilepsy.