Kairns Solutions: Stacking Molecular Insights for Epilepsy Control

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Like the *rock cairns* one might see on a trail in Moab that guide your path, we propose a novel way to explore the genetic landscape of epilepsy by staking the outputs of multiple spatial technologies. We have chosen to research a compelling disease with an unmet clinical need–epilepsy. The U.S. Center for Disease Control and Prevention estimates that 1.2% of the total US population has active epilepsy, with most instances occurring in the very young or very old. The epilepsy foundation also estimates that 1 in 26 persons will develop epilepsy in their lifetime. Of these, 10% will progress to an aggressive form of epilepsy called status epilepticus (SE), characterized by its extended duration. Mortality rates of individuals with SE are high–20%. Furthermore, epilepsy remains a significant side effect of many drugs that treat cancer, bacterial infections, and even antidepressants. To date, there are few drugs to treat or provide long-term remedies for SE, and little is known about how the body naturally (through genetics) responds to seizures (especially in space and time).

We outline our research to “stack” the data we collect from spatial electrophysiological readouts and spatial transcriptomics to “visualize” the genes that differentially express during SE, self regulating seizures, and regions with no epileptic activity, providing a roadmap of how different patterns of epileptiform activity alter gene expression. Layering spatial technologies is necessary to further our understanding of SE and provide greater insight into potential drug and gene therapies. We hypothesize that significant transcriptomic differences between progressive SE, phasic seizures, and different brain regions will provide novel insights into the etiology and progression of seizures. In turn, our findings may lead to developing a gene therapy or drug therapy capable of altering epileptiform activity on the transcriptomic landscape.