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Poorva Jain Washington University in St. Louis

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### A Role for the Potassium Channel Seizure in Regulating Intrinsic Neuronal Stress Response in Drosophila Melanogaster Poorva Jain

#### Mentors: Yehuda Ben-Shahar and Alexis Hill

The human ether a go-go related potassium channel (hERG) has been previously implicated as a major contributor to the cardiac disorder Long QT Syndrome (LQTS). Patients with mutations in hERG also present higher rates of seizures than patients with mutations in other genes. This seizure phenotype has long been assumed to be an indirect consequence of defective heart physiology, therefore more extensive research has been done on the cardiac function of hERG and its homologs than on the neuronal functions. However, hERG is also expressed in the brain and there is evidence in Drosophila melanogaster (fruit fly) that mutations in the homolog of hERG, seizure (sei), elicit heat based seizure phenotypes. This suggests that the seizures associated with LQTS could be a direct consequence of disrupted hERG function in neurons. We wanted to use behavioral paradigms in D. melanogaster studying sei to better understand how hERG directly impacts seizure behaviors. We saw sei to be widely expressed in the nervous system of flies. By screening available potassium channel mutant lines, and downregulating their neuronal expression, we characterized sei mutants as unique in increasing seizure behavior in flies during heat stress. Changing our behavioral paradigm, our experiments using a cold stress assay support a model where SEI function is only relevant after a neuron reaches a threshold activity level. While our experiments demonstrate that sei impacts neuronal function, our initial behavioral experiments using hERG expressing transgenic flies do not indicate that hERG functions properly when expressed in Drosophila. Further studies must be performed to in order to understand how to better model hERG in flies especially as the fly model recapitulates some but not all human biology in providing essential proteins or correct trafficking for this ion channel to function correctly.