# The Characterization of Dravet Syndrome using a Drosophila Melanogaster Model

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Mutations in the SCN1A sodium channel gene are often associated with a variety of epileptic disorders, necessitating efficient model systems to investigate cellular mechanisms and analyze potential therapeutic targets. Through my experimentation, I established that Drosophila knock-in flies with the K1270T SCN1A mutation known to result in a form of genetic epilepsy characterized by febrile seizures demonstrate a heat-induced increase in sodium current activity and seizure phenotype as well as a reduction in exploratory activity. In order to assess whether specific SCN1A mutations lead to distinct phenotypes in Drosophila as they do in humans, this study utilizes a knock-in line Drosophila model bearing a mutation that induces a severe epileptic disorder known as Dravet Syndrome (DS). The introduction of the SCN1A mutation (S1231R) into the voltage-gated sodium channel resulted in flies exhibiting spontaneous and heat-induced seizures with distinct characteristics and lower onset temperature than the Canton-S flies. In addition, it was discovered through electrophysiological studies of GABAergic interneurons in the brains of adult paraDS flies in an in-vivo model system, that the missense paraDS mutation results in a conditional reduction in sodium current activity and repeated firing. Furthermore, feeding Drosophila with the serotonin precursor 5-HTP causes a suppression of heat-induced seizures in paraDS but not Canton-S flies. Differences in sodium currents in paraDS and Canton-S GABAergic interneurons shows that repetitive firing and seizure phenotype is induced by both loss- and gain-of-function alterations in sodium currents. The positive effect of 5-HTP on heat-induced (febrile) seizures identifies the serotonin pathway as a potential therapeutic target for DS.

**Awards Won:**