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Investigation of the nervous system in a mouse model for Familial Dysautonomia

Familial dysautonomia (FD) is a genetic disorder affecting the development and maintenance of the nervous system, and is prevalent in those of Ashkenazi Jewish descent. FD is caused by a point mutation in the *Ikbkap* gene, resulting in a decreased amount of the IKAP protein. FD patients experience symptoms such as decreased sensitivity to pain or temperature, dysfunction of the autonomic nervous system, incoordination, hypotonia, various dysfunctions of the organs, and even death. In addition, FD patients experience progressive blindness due to the loss of retinal nerve fiber layer. In order to study the role of IKAP in the retina, we developed the retina-specific *Ikbkap* conditional knockout (CKO) mouse model. We used this model to quantify retinal ganglion cells in the retinal nerve fiber and found decreased cell numbers in the mutant mouse at different ages. Data from our lab has revealed evidence of CNS deficits in mice with FD, such as behavioral alteration, a reduction in specific neuronal populations, reduction in spinal motor neuron innervation, and alteration in cortical morphology. In order to further investigate the implications of FD on the CNS, we generated another mouse model (*Tuba1 α*) in which *Ikbkap* is deleted in all neurons. Our data show that both adult and embryonic *Tuba1 α* mice have enlarged lateral ventricles in the brain, a symptom occurring in other degenerative and developmental disorders. We used this mouse model to investigate proprioceptive and nociceptive neurons in the embryonic DRG in order to compare development in the DRG to the brain. Neither population was altered in the mutant mouse, suggesting that these cell types are resilient to the disease during embryogenesis.

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