Does the Misregulation of Codon-Biased Genes in the Anterior Pituitary Contribute to Familial Dysautonomia? (Poster)

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Familial Dysautonomia (FD) is a devastating neurodevelopmental and neurodegenerative childhood disease characterized by a diminished number of autonomic neurons. FD children suffer from a multitude of autonomic symptoms including cardiovascular instability, gastrointestinal incoordination, and respiratory dysfunction. FD patients also exhibit an abnormal autonomic stress response, tend to be small in stature, and have difficulty gaining and maintaining weight. FD results from a mutation in the IKBKAP gene and diminished levels of the corresponding protein IKAP, a scaffold that assembles the multi-subunit complex, Elongator. Elongator functions in the modification of tRNAs that mediate translation of AA- and AG-ending codons. IKAP is expressed throughout the autonomic nervous system and historically FD symptoms have been attributed to autonomic dysfunction. Here we show that IKAP is also robustly expressed in the pituitary gland, both during development and in the adult. We hypothesize that many FD symptoms may actually result from aberrant pituitary regulation of the autonomic nervous system. To test this hypothesis we are currently generating a conditional knockout mouse where Ikbkap will be selectively ablated in the anterior pituitary. While waiting for our mouse model, we have been optimizing techniques for quantifying pituitary specific genes that are likely candidates for Elongator regulation based on their content of AA- and AG-ending codons.