

Familial Dysautonomia (FD)

Written by Administrator

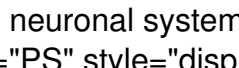
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Familial dysautonomia (FD) is an autosomal recessive congenital neuropathy which results from poor development and progressive degeneration of the nervous system. The mutation responsible for FD was found at the 5' splice site of intron 20 of the IKBKAP gene, encoding the I β B kinase complex-associated protein (IKAP). The mutation results in exon 20 shifting from constitutive inclusion in normal individuals to alternative splicing in the patients, causing a frameshift and a stop codon in the skipped isoform, which leads to reduced IKAP expression.

The ultimate goal of our research is to improve the quality of life for patients that suffer from FD through developing new therapies and by better understanding of underlying molecular cause of the disease and the role of *IKBKAP* gene regulation in neurons. To accomplish this objective we developed reliable *in vitro* and *in vivo* models of FD.

As was shown in our laboratory, the mutation reduces the binding affinity between the splicing factor U1 and the 5' splice site of exon 20. We also screened a battery of therapies to restore normal *IKBKAP* synthesis. Phosphatidylserine (PS) has been identified to be an efficient treatment, which elevates the expression levels of the *IKBKAP* gene, both in cell lines from FD patients cells and in the humanized FD mice generated in our lab. PS is currently under a clinical trial in FD patients and the initial results are very promising. PS treatment releases treated cells from cell cycle arrest, and also affects genes involved in Parkinson's disease.

Our group established very productive research focusing on the underlying molecular cause of FD. We are currently studying the importance of exon 20 of the *IKBKAP* gene in neuronal development and functionality, the ability of our drug therapy to improve their function, and increase our drug permeability to the neuronal systems.

The image is a placeholder for a photograph of Phosphatidylserine (PS) treatment. The alt text is "PS".