Our laboratory uses the model organism *Drosophila* in order to define mechanisms and pathways associated with human neurodegenerative disease. We have defined a number of pathways that impact disease progression; in particular, we have found that stress pathways are integral to disease mechanisms, and the dysfunction or lack of sufficient protection from stress pathways may contribute to degeneration. Mechanistic studies indicate that epigenetic impacts on the ability of the stress response to function with age may be an important factor that impacts susceptibility to brain disease. We are also pursuing mechanisms of ALS/FTD, in particular genes that influence TDP-43 toxicity and the toxicity of the GGGGCC RNA repeat, of C9orf72. Our findings highlight the strength of fly studies to reveal new understanding.

**Abstract:**

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