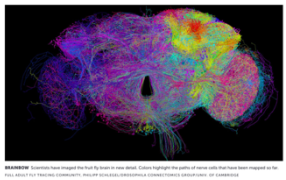
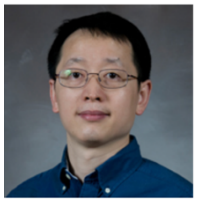
SCIENCE at the Edge



Probing the molecular mechanisms of neurodegenerative disorders in fruit flies



Dr. Sheng Zhang

Center for Metabolic and Degenerative Diseases
Department of Neurobiology and Anatomy
The University of Texas Health Science Center at Houston (UTHealth)

Friday, May 21st
11:30 a.m. EDT

https://msu.zoom.us/j/99778771280
Meeting ID: 997 7877 1280
Passcode: SATE

Why do neurons die early in neurodegenerative diseases? Why are distinct groups of neurons are more specifically affected in each of the diseases? The classical genetic model of Drosophila, the fruit fly, yields novel insights into human brain diseases.

In this model system, we found that both the function and regulation of Huntington's disease gene Huntingtin are highly conserved; the wild-type Huntingtin protein plays a role in selective autophagy, a critical cellular homeostasis pathway.

In Parkinson's disease (PD), one puzzle is why the disease mainly affects a subset of dopaminergic neurons. As in mammals, dopaminergic neurons in the fly brain are clustered into different functional groups, each occupying stereotypic positions with distinct projection patterns. We observed that different dopaminergic clusters had differential vulnerability to PD-related stresses, likely due to intrinsic differences in their handling of intracellular dopamine. Therefore, perturbation of disease genes' normal function might be an important factor in selective neuronal losses in neurodegenerative disorders.

Rui et al, "Huntingtin functions as a Scaffold for Macroautophagy". (2015) *Nature Cell Biology* 17(3) (PMCID: PMC4509454)

Tito et al *"A simple one-step dissection protocol for whole-mount preparation of adult Drosophila brains*". (2016) *The Journal of Visualized Experiments* (118). (doi: 10.3791/55128).

Xu et al, "HAP40 is a conserved central regulator of Huntingtin and a specific modulator of mutant Huntingtin toxicity". *BioRxiv* (https://doi.org/10.1101/2020.05.27.119552)