Секция «Нейрофизиология и физиология ВНД»

Axonal intrinsic survival mechanisms in Drosophila melanogaster

Научный руководитель – Neukomm Lukas Jakob

Гаврилова Виктория Андреевна
Студент (бакалавр)
Московский государственный университет имени М.В.Ломоносова, Биологический факультет, Кафедра биоорганической химии, Москва, Россия
E-mail: vi.rilova@gmail.com

The morphological integrity of neurons and their axons is essential for sustained nervous system function [1]. Most of the volume of a neuron is taken by its axon. Therefore, axonal and synaptic maintenance is a major challenge for the neuron, however, the underlying molecular mechanisms are poorely understood.

Wallerian degeneration (WD) is a well-established system to study how injured axons execute their self-destruction. WD consists of two molecularly distinct processes: 1. From the soma separated axons execute their own destruction within 1 day through an evolutionarily conserved axon death signaling cascade; 2. Surrounding glia clear the resulting debris within 5 days. Several axon death genes have been identified in *Drosophila*, and the modification thereof potently attenuates axon death signaling. Axons with attenuated axon death signaling stay functionally and morphologically preserved for weeks without support coming from the soma[2]. The mechanism of self-preservation in the absence of soma remains unknown.

Here, we present our newly established model in *Drosophila* to identify which of the genes of our interest (GOI) have the strongest effect on axonal and synaptic preservation. We take advantage of Johnston's organ (JO) neurons, where neuronal soma are housed in antenna, and their axons project into the CNS. Optogenetic activation of JO neurons elicits antennal grooming as a simple behavior, which serves as a proxy for preservation of axonal and synaptic structures over time. Upon antennal ablation (e.g. removal of JO soma), wild-type axons and their synapses degenerate within 7 days, whereas axons with attenuated axon death signaling remain preserved. Likewise, optogenetics fails to elicit antennal grooming in wild-type flies, while mutants continue to groom. Fly crosses were performed to generate wild type and mutants with attenuated axon death signaling. After GOI achivied the highest level of expression, nonlethal surgical removal of JO soma was performed to induce degeneration of JO neurons. Seven days after the ablation the optogenetic analysis combined with a behavioral readout was performed to assay the neurons' ability to drive grooming behavior in adult *Drosophila*. Grooming frequency was measured. We established the significance of one GOI for axonal and synaptic preservation.

The above preliminary results form the basis for assessing the promising candidates for their requirement for the maintenance of structure or function specifically in axons and synapses. The established model serves as an excellent tool to tackle the biology underlying axonal intrinsic maintenance mechanisms, which will thus help to define targets for therapeutic intervention in a broad range of axonopathies.

Источники и литература

1) Mariano, et al. Maintaince mechanics of circuit-integrated axons. Curr Opin Neurobiol, 2018
2) Neukomm, et al. Axon Death Pathways Converge on Axundead to Promote Functional and Structural Axon Disassembly. Neuron, 2017