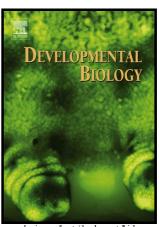
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miR-51 regulates GABAergic synapses by targeting Rab GEF GLO-4 and lysosomal trafficking-related GLO/AP-3 pathway in *Caenorhabditis elegans*

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Abstract

A deficit of GABA (γ-aminobutyric acid) transmission will lead to epilepsy and other cognitive disorders. Recent evidence has shown that neuronal miRNAs affect various synapses, including GABAergic synapses. However, the miRNAs that control GABAergic synapses remain not fully understood. Here, we identified miR-51, a member of *Caenorhabditis elegans* miR-99/100 family, as a key regulator of GABAergic synapses. Loss of *mir-51* increased PTZ (Pentylenetetrazole) and aldicarb hypersensitivities, and decreased the number of GABAergic synapses and abundance of GABA_A receptors. A Rab guaninenucleotide exchange factor (GEF) GLO-4, a well-known component in lysosomal trafficking-related GLO-4/GLO-1/AP-3 (GLO/AP-3) pathway, was discovered to be the direct target of miR-51. Rescue experiments showed that GLO-4 expressed in GABAergic motor neurons functioned as a suppressor of miR-51. Disruption of *glo-1* or AP-3 gene *apm-3* attenuated the defects of GABAergic synapse in *mir-51* mutants, suggesting miR-51 regulated GABAergic synapses through GLO/AP-3 pathway. The present study implies the essential roles of miRNAs on the nervous pathologies characterized by mis-regulated GABA signaling, such as epilepsy.

Abbreviations

GABA, γ-aminobutyric acid; PTZ, pentylenetetrazole; SNB-1, Synaptobrevin 1; GEF, guaninenucleotide exchange factor; SVs, synaptic vesicles; Ach, acetylcholine; NMJs, neuromuscular junctions; miRNAs, microRNAs; GluR, glutamate receptor; nAChR: neuronal

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