

## Author's Accepted Manuscript

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

Shuai Zhang, Zhibin Fan, Ping Qiao, Yinsuo Zhao, Yanan Wang, Da Jiang, Xiangming Wang, Xiaojuan Zhu, Yu Zhang, Baiqu Huang, Jun Lu, Xiaoxue Li



PII: S0012-1606(17)30509-2  
DOI: <https://doi.org/10.1016/j.ydbio.2018.02.009>  
Reference: YDBIO7692

To appear in: *Developmental Biology*

Received date: 28 July 2017  
Revised date: 30 January 2018  
Accepted date: 17 February 2018

Cite this article as: Shuai Zhang, Zhibin Fan, Ping Qiao, Yinsuo Zhao, Yanan Wang, Da Jiang, Xiangming Wang, Xiaojuan Zhu, Yu Zhang, Baiqu Huang, Jun Lu and Xiaoxue Li, miR-51 regulates GABAergic synapses by targeting Rab GEF GLO-4 and lysosomal trafficking-related GLO/AP-3 pathway in *Caenorhabditis elegans*, *Developmental Biology*, <https://doi.org/10.1016/j.ydbio.2018.02.009>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting galley proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

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

Shuai Zhang<sup>1</sup>, Zhibin Fan<sup>2</sup>, Ping Qiao<sup>2</sup>, Yinsuo Zhao<sup>3</sup>, Yanan Wang<sup>4</sup>, Da Jiang<sup>1</sup>, Xiangming Wang<sup>3</sup>, Xiaojuan Zhu<sup>1</sup>, Yu Zhang<sup>4</sup>, Baiqu Huang<sup>4</sup>, Jun Lu<sup>4\*</sup>, Xiaoxue Li<sup>1\*</sup>

<sup>1</sup>The Key Laboratory of Molecular Epigenetics of the Ministry of Education, Northeast Normal University, Changchun 130024, China;

<sup>2</sup>The Department of Cell Biology, College of Basic Medical Sciences, Jilin University, Changchun 130021, China;

<sup>3</sup>National Laboratory of Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences, 15 Datun Road, Chaoyang District, Beijing 100101, China.

<sup>4</sup>The Institute of Genetics and Cytology, Northeast Normal University, Changchun 130024, China; luj809@nenu.edu.cn.

lix956@nenu.edu.cn

\*Corresponding authors.

**Abstract**

A deficit of GABA ( $\gamma$ -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 (Pentylentetrazole) and aldicarb hypersensitivities, and decreased the number of GABAergic synapses and abundance of GABA<sub>A</sub> 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,  $\gamma$ -aminobutyric acid; PTZ, pentylentetrazole; SNB-1, Synaptobrevin 1; GEF, guaninenucleotide exchange factor; SVs, synaptic vesicles; Ach, acetylcholine; NMJs, neuromuscular junctions; miRNAs, microRNAs; GluR, glutamate receptor; nAChR: neuronal

Download English Version:

<https://daneshyari.com/en/article/8467405>

Download Persian Version:

<https://daneshyari.com/article/8467405>

[Daneshyari.com](https://daneshyari.com)