

**MicroRNA-9 induces defective trafficking of Nav1.1 and Nav1.2 by targeting Navβ2 protein coding region in rat with chronic brain hypoperfusion**

Lihua Sun, Xueling Hu, Hui Che, Yanan Bao, Fei Guo and Jing Ai  
Harbin Medical University, China

Previous studies have demonstrated that the trafficking defects of Nav1.1/Nav1.2 are involved in the dementia pathophysiology. However, the detailed mechanisms are not fully understood. Moreover, whether the impaired miRNAs regulation linked to dementia is a key player in sodium channel trafficking disturbance remains unclear. The cognitive impairment induced by chronic cerebral ischemia through chronic brain hypoperfusion (CBH) by bilateral common carotid artery occlusion (2VO) is likely reason to precede dementia. Our results found the impairment of Nav1.1/Nav1.2 trafficking and decreased expression of Navβ2 and increased miR-9 in the hippocampus and cortex of rats following CBH generated by bilateral 2VO. Intriguingly, MiR-9 suppressed, while AMO-miR-9 enhanced, the trafficking of Nav1.1/Nav1.2 from cytoplasm to cell membrane. Further study showed that overexpression of miR-9 inhibited the expression of Navβ2 by targeting on its coding sequence (CDS) domain by dual luciferase assay. However, binding-site mutation or miR-masks failed to influence Navβ2 expression as well as Nav1.1/Nav1.2 trafficking process, indicating that Navβ2 is a potential target for miR-9. Lentivirus-mediated miR-9 overexpression also inhibited Navβ2 expression and elicited translocation deficits to cell membrane of Nav1.1/Nav1.2 in rats, whereas injection of lentivirus-mediated miR-9 knockdown could reverse the impaired trafficking of Nav1.1/Nav1.2 triggered by 2VO. We conclude that miR-9 may play a key role in regulating the process of Nav1.1/Nav1.2 trafficking via targeting on Navβ2 protein in 2VO rats at post-transcriptional level, and inhibition of miR-9 level may be a potentially valuable approach to prevent Nav1.1/Nav1.2 trafficking disturbance induced by CBH.

**Biography**

Lihua Sun, Associate Professor of Pharmacology, has completed her PhD at the age of 29 years from Harbin Medical University and postdoctoral studies from Harbin Medical University. She is working on the research and teaching of Pharmacology, the research interest focuses on Cardio-Cerebral Vascular pharmacology. She has published more than 35 papers in international peer-reviewed journals and has been supported by series of national scientific foundations and has been serving as a Reviewer for PLOS ONE and Gene. She obtained the rewards from Ministry of Education of China due to her success in researches.

[azhrbmu@126.com](mailto:azhrbmu@126.com)

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