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Angiotensin II confers ischemic neuroprotection *in vitro* through inhibiting miR-497 maturation

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MicroRNAs (miRNAs) are important molecular players involved in regulation of numerous signaling pathways in cerebral ischemia reperfusion injury. Recent experimental evidences demonstrated that miR-497 promotes ischemic neuronal death by negatively regulating anti-apoptotic proteins. Therefore, small molecule mediated inhibition of miR-497 was suggested as a potential neurotherapeutic strategy to limit ischemic brain injury. In the present study, we adopted a concrete in silico method, which included 3D modeling of pre-miR-497, virtual screening of chemical database to retrieve small molecules that can inhibit miR-497 maturation. A novel hit, Angiotensin II, being peptide and lack of pre-miRphilic antibiotic structure in it made an interesting entry as miR-497 inhibitor candidate. The neuroprotective efficacy of angiotensin II was evaluated against oxygen-glucose deprivation (OGD) and reoxygenation-induced neuronal cell death in N2A cells. To confirm the inhibitory potential of angiotensin II on miR-497 maturation, expression levels of miR-497 were checked using TaqMan® MiRNA Assay Kit. Angiotensin II treatment effectively reduced OGD-induced neuronal cell death. Further, it also decreased the levels of miR-497 in N2A cells, demonstrating its miRNA inhibitory potential. The present study for the first time reports the pre-miR-497 inhibitory potential of angiotensin II through which it could elicit neuroprotection against OGD insult. Prospective studies of elucidating neuroprotective efficiency of angiotensin II and in combination with angiotensin II receptor antagonists may provide effective therapeutic strategy against ischemic stroke.

Recent Publications

1. Sinoy S, Fayaz S M, Charles K D, Suvanish V K, Kapfhammer J P, Rajanikant G K (2017) Amikacin inhibits mir-497 maturation and exerts post-ischemic neuroprotection. Molecular Neurobiology. 54(5):3683-3694.
2. Yin K J, Deng Z, Huang H, Hamblin M, Xie C, Zhang J, Chen YE (2010) miR-497 regulates neuronal death in mouse brain after transient focal cerebral ischemia. Neurobiology of Disease. 38(1):17-26.

Biography

Rajanikant G K is an Associate Professor and former Head of the School of Biotechnology, National Institute of Technology Calicut, India. He is also the Coordinator of the Bioinformatics Infrastructure Facility, the Department of Biotechnology, Govt. of India sponsored Bioinformatics center. He has been an active Teacher and Mentor, and has been the recipient of numerous grants, funded by the Department of Biotechnology (DBT), Department of Science & Technology (DST), Indian Council of Medical Research (ICMR) and Kerala State Council for Science, Technology & Environment (KSCSTE). He has expertise in wide range of research areas such as cerebral ischemia, multiple sclerosis, cutaneous wound healing and radiation protection. His research is focused on exploiting sophisticated computational drug design strategies for the identification of novel target specific small molecule neurotherapeutics against ischemic stroke. His work has been published in prestigious scientific journals such as *Journal of Neuroscience, Stroke, PLOS One, Molecular Neurobiology, Cell Death & Disease, Neuroscience & Biobehavioral Reviews, Physiology & Behavior, Journal of Chemical Information & Modeling, Current Drug Targets, CNS & Neurological Disorders-Drug Targets, Current Pharmaceutical Design, Current Medicinal Chemistry, Plastic & Reconstructive Surgery and Radiation Research.* He received Postdoctoral training in Neurobiology at the University of California at Davis, California and the Michigan State University, East Lansing, Michigan. He graduated with PhD degree from the Manipal University, India and received Senior Research Fellowship from ICMR for his dissertation work.

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