J Cancer Sci Ther 2018, Volume 10
DOI: 10.4172/1948-5956-C11-154

MicroRNA-122 Therapeutic for ischemic stroke

Da Zhi Liu
University of California at Davis, USA

Based upon our previous findings that microRNA-122 (miR-122) were decreased in peripheral blood of both humans and rats after ischemic stroke, we hypothesized that elevating miR-122 in blood might improve outcomes after ischemic stroke. Using the in vivo polyethylene glycol 2000 (PEG)-liposome based miRNA transfection system and the rat middle cerebral artery occlusion (MCAO) model, we recently demonstrated that intravenous (i.v.) miR-122 mimic, given immediately after MCAO, elevated miR-122 in peripheral blood, prevented neurological impairments, and reduced brain infarction volume by 90% after MCAO in rats. Moreover, the results showed that miR-122 mimic, given 6 hr after MCAO, attenuates neurological impairments and reduced brain infarction volume by 54% after MCAO in rats. Using Taqman PCR based assays, we demonstrate fourteen direct miR-122 target genes (e.g. Pla2g2a, Nos2, Vcam1, Clic4, Ucp2, Dlg2, and others) decrease in blood leukocytes following miR-122 mimic treatment after MCAO in rats. Focusing on ONE miR-122 target gene (Pla2g2a), we demonstrate that miR-122 mimic decreases Pla2g2a expression in brain microvascular endothelial cells (BMVECs) after MCAO in rats. Luciferase reporter assays confirmed that miR-122 bound to wild-type but not mutated 3'UTR of Pla2g2a. These results show that Pla2g2a is decreased in leukocytes and BMVECs following miR-122 mimic treatment after MCAO, which likely contributes to the therapeutic effects of miR-122 mimic on ischemic stroke.

Acknowledgments: This study was supported by the UC Davis Innovative Development Award and NIH grants R01NS089901 (DZL) and RO1NS101718 (FRS). There were no conflicts of interest.

dzliu@ucdavis.edu

Notes: