Neuroprotective and Regenerative Roles of the Wnt-3a Pathway after Focal Ischemic Stroke in Mice

Wei, Zheng; Emory University, Department of Anesthesiology/Neurology, Atlanta, GA USA
Zhang, James; Emory University, Department of Anesthesiology/Neurology, Atlanta, GA USA
Taylor, Tammi; Jackson State University, Department of Biology, Jackson, MS USA and Emory University, Department of Anesthesiology/Neurology, Atlanta, GA USA
Gu, Xiaohuan; Emory University, Department of Anesthesiology/Neurology, Atlanta, GA USA
Wei, Ling; Emory University, Department of Anesthesiology/Neurology, Atlanta, GA USA

Abstract (300 word limit)

Wnt signaling is a conserved pathway involved in expansion of neural progenitors and lineage specification during development. However, the role of Wnt signaling in the post-stroke brain has not been well-elucidated. We hypothesized that Wnt-3a would play an important role for neurogenesis and brain repair. Adult male mice were subjected to a focal ischemic stroke targeting the sensorimotor cortex. Mice that received Wnt-3a (2 µg/kg/day, 1 hr after stroke and once a day for the next 2 days, intranasal delivery) had reduced infarct volume compared to stroke controls. Wnt-3a intranasal treatment of 7-days upregulated the expression of brain-derived growth factor (BDNF), increased the proliferation and migration of neuroblasts from the subventricular zone (SVZ), resulting in increased numbers of newly formed neurons and endothelial cells in the penumbra. Both the molecular and cellular effects of Wnt-3a were blocked by the Wnt specific inhibitors XAV-939 and Dkk-1. In functional assays, Wnt-3a treatment enhanced the local cerebral blood flow (LCBF) in the penumbra, as well as improved sensorimotor functions in a battery of behavioral tests. Together, our data demonstrates that Wnt-3a signaling can act as a dual neuroprotective and regenerative factor for the treatment of ischemic stroke.

Image

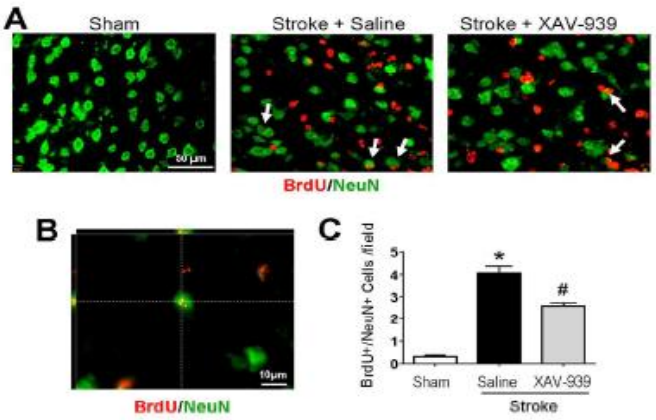


Figure 3. Downregulation of Wnt activity downregulated endogenous neurogenesis after stroke. **A.** Representative immunofluorescence images for NeuN+ (green), BrdU+ (red), and NeuN+/BrdU+ colabeled cells (white arrows) among different treatment groups. **B.** Representative confocal 3-dimensional image (Z-stack thickness = 10 Bm) confirming colocalization of BrdU and NeuN fluorescence. **C.** Quantification of neurogenesis by NeuN+/BrdU+ colabeled cells in the penumbra following administration of either saline (negative control) or the Wnt-signaling inhibitor, XAV-939. All data represented as mean • } SEM; *: p<0.05 compared to sham; #: p<0.05 compared to saline. N = 4-10/group.

Recent Publications (minimum 5)

1. Wei, N., Yu, S.-P., **Taylor, T.M.**, Gu, X., Liu, X-F., Wei, L. 2012 Delayed of Hypoxic-Preconditioned Bone Marrow Mesenchymal Stem Cells Showed Enhanced Cell Homing and Therapeutic Benefits in Ischemic Stroke Mice. Cell Transplantation

2. Wei ZZ, Yu SP, Lee JH, Chen D, **Taylor TM**, Deveau TC, Yu AC, Wei L. 2014. Regulatory role of the JNKSTAT1/3 signaling in neuronal differentiation of cultured mouse embryonic stem cells. Cell Mol Neurobiol.

3. Wei ZZ, Zhang JY, **Taylor TM**, Gu X, Zhao Y, Wei L. Neuroprotective and regenerative roles of intranasal Wnt-3a Administration after focal ischemic stroke in mice. J Cereb Blood Flow Metab. 2017 Jan 1:271678X17702669.doi: 10.1177/0271678X17702669. [Epub ahead of print]

Photograph



Biography (150 word limit)

Dr. Taylor joined the faculty as an Assistant Professor of Genetics in the Department of Biology in the College of Science, Engineering, and Technology at Jackson State University. While at JSU, Dr. Taylor is a Research Center for Minority Investigators (RCMI) faculty member, a graduate and undergraduate student advisor, mentor, and professor. She obtained her PhD in Microbiology from Indiana University, a Masters of Science degree in Biology, from Jackson State University, and her Bachelors of Science degree in Biology from Tougaloo College. She was a Fellowship in Research and Science Teaching (FIRST) postdoctoral fellowship at Emory University in the Departments of Anesthesiology and Neurology. Her current research focus is determining the role of signal transducer activator of transcription 3 (STAT-3) on the regeneration of nerve tissue and functional recovery after focal ischemic stroke.

Email: tammi.m.taylor@jsums.edu

Notes/Comments: