28 | O r a l

NEUROPROTECTIVE AND REGENERATIVE ROLES OF INTRANASAL WNT-3A ADMINISTRATION AFTER FOCAL ISCHEMIC STROKE IN MICE

Zheng Zachory[1], Wei[1], James Ya Zhang[1], Tammi M Taylor[1,2], Xiaohuan Gu, Yingying Zhao[1] and Ling Wei[1]

[1]Department of Anesthesiology Emory University School of Medicine, 617 Pierce Drive Atlanta, GA 30284, USA
[2]Department of Biology, College of Science, Engineering and Technology, Jackson State University, 1400 Lynch Street, P.O. Box 18540, Jackson, Mississippi, USA

Abstract: 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 h 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 seven 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 peri-infarct zone. Both the molecular and cellular effects of Wnt-3a were blocked by the Wnt specific inhibitors XAV-939 or Dkk-1. In functional assays, Wnt-3a treatment enhanced the local cerebral blood flow (LCBF) in the peri-infarct, as well as improved sensorimotor functions in a battery of behavioral tests. Together, our data demonstrates that the Wnt-3a signaling can act as a dual neuroprotective and regenerative factor for the treatment of ischemic stroke.

Key words: Stroke, Wnt3a, neuroblast, proliferation,

Acknowledgements: This research supported by a grant from the National Institutes of Health (Grant N0.1G12RR13459), through the NCRR-RCMI Center for Environmental Health at Jackson State University (JSU) and NINDS at Emory University