



Fengquan Zhou, Ph.D.

Assistant Professor

CONTACT INFORMATION:

Ross 215, 720 Rutland Avenue, Baltimore, MD 21287

443-2875649 (phone), 410-5026414 (fax)

Email: fzhou4@jhmi.edu

RESEARCH GOALS: *Molecular mechanisms of neuronal morphogenesis during development and regeneration* - The overall goal of our research is to understand the molecular mechanisms underlying development of the mammalian nervous system. Specifically, we are interested in understanding how neurons generate their complex morphology and form proper circuitries during development and how neurons regenerate to restore connections after brain, spinal cord, or peripheral nerve injuries.

RESEARCH SUMMARY AND CURRENT PROJECTS:

1. *Role of GSK-3 signaling in neural development and regeneration:* The complicated behaviors of an animal arise from intrinsic neural networks, which include the precise connections between neurons in the form of circuits. During development of the nervous system, axon growth guided by a myriad of extracellular cues is one of the major events that contribute to the formation of such neural circuits. Mistakes in these processes are believed to underlie many neurodevelopmental disorders, such as autism and schizophrenia. Recent studies have linked Glycogen Synthase Kinase-3s (GSK-3s) and their associated signaling molecules with these psychiatric disorders. For instance, many autism associated genes are known to regulate GSK-3 activities, such as Pten, TSC-1/2, serotonin, and DISC1. In addition, two GSK-3 substrates, APC and CLASP, both of which are microtubule binding proteins, are also associated with autism. Thus, we think that GSK-3s and their mediators may form an important signaling module to control neuronal morphogenesis downstream of genes that control neural circuitry formation. Recently, we also showed that inhibition of GSK-3s could promote axon regeneration after spinal cord injuries. Therefore, the overall goal of this project is to understand the role of GSK-3 signaling in key events of neural development and regeneration. The results of the study will help us elucidate the molecular mechanism underlying these diseases and identify potential therapeutic targets.
2. *Engineering the growth cone machinery to promote axon regeneration:* Another major interest of the lab is to find ways to promote axon regeneration after brain and spinal cord injuries. The failure of axon regeneration in the CNS is due to reduced ability of adult CNS neurons to support axon growth, as well as the hostile environment of adult CNS contributed by inhibitory molecules, such as myelin based inhibitors and inhibitory chondroitin sulfate proteoglycans (CSPGs). The growth cone at the tip of the growing axon is not only the machinery that drives axon growth, but also the final target of the inhibitory molecules that prevent axon growth. We believe that directly targeting the growth cone machinery will be a novel approach to enhance axon regeneration. The overall goal of this project is to use genetic or pharmacological approaches to manipulate the growth cone cytoskeleton and determine if it can promote axon growth in either permissive or inhibitory environment. Several neural injury models in the spinal cord or the peripheral nerves are used in this study.
3. *Experimental approaches:* In these studies, we take multi-stepped experimental approaches: 1) in vitro culture of dissociated primary neurons or brain slices 2) high-resolution microscopy and live

cell imaging of mammalian neurons 3) in vivo gene electroporation to manipulate embryonic (in utero) and adult neurons.

RECENT PUBLICATIONS:

1. Zhou F-Q and Cohan CS. (2001) Growth cone collapse through coincident loss of actin bundles and leading edge actin without actin depolymerization. *Journal of Cell Biology*, 153 (5): 1071-1084.
2. Zhou F-Q, Waterman-Storer CM, and Cohan CS. (2002) Focal loss of actin bundles causes microtubule redistribution and growth cone turning. *Journal of Cell Biology*, 157 (5): 839-849. (Cover figure and highlighted article)
3. Snider WD, Zhou F-Q, Zhong J, and Markus A. (2002) Signaling the pathway to regeneration. *Neuron*, 35 (1): 13-16.
4. Zhou F-Q, Zhong J, and Snider WD. (2003) Extracellular crosstalk: when GDNF meets N-CAM. *Cell*, 113 (7): 814-815.
5. Zhou F-Q and Cohan CS. (2004) How actin filaments and microtubules steer growth cones to their targets. *Journal of Neurobiology*, 58(1): 84-91.
6. Zhou F-Q, Zhou J, Dedhar S, Wu Y-H, and Snider WD. (2004) NGF-induced axon growth is mediated by localized inactivation of GSK-3 β and functions of the microtubule plus end binding protein, APC. *Neuron*, 42(6): 897-912. (Highlighted article with preview)
7. Zhou F-Q, Walzer MA and Snider WD. (2004) Turning on the machine: genetic control of axon regeneration by c-Jun. *Neuron*, 43(1):1-2.
8. Zhou F-Q and Snider WD. (2005) GSK-3 β and microtubule assembly in axons. *Science*, 308: 211-214.
9. Zhou F-Q and Snider WD. (2006) Intracellular control of developmental and regenerative axon growth. *Phil. Trans. R. Soc B*, 361(1473): 1575-92. (Review)
10. Kim W-Y, Zhou F-Q, Zhou J, Yokota Y, Wang Y-M, Yoshimura T, Kaibuchi K, Woodgett JR, Anton ES, and Snider WD. (2006) Essential roles for GSK-3 β in Neurotrophin-induced and hippocampal axon growth. *Neuron*, 52(6): 981-996
11. Dill J, Wang H, Zhou F-Q and Li S. (2008) Inactivation of Glycogen Synthase Kinase 3 promotes axonal growth and recovery in the CNS. *Journal of Neuroscience*, 28(36): 8914-28.