Public Abstract
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Title:REGULATION OF CALCIUM SIGNALING BY p130PH IN ASTROCYTES

Ca2+ signaling is a characteristic form of astrocyte excitability and has been suggested to mediate chemical transmitter release, including glutamate, but its role in ischemia is not clearly understood. Our previous study (Ding et al., 2009) demonstrated that astrocytes exhibit enhanced Ca2+ signaling following photothrombosis-induced ischemia. Given that astrocytes intimately contact neurons to form tripartite synapses and can release glutamate in response to Ca2+ elevation, we hypothesize that astrocytes contribute to brain damage through glutamate release. The goal of this thesis is to test this hypothesis by selectively inhibiting astrocytic Ca2+ signaling in vivo using a Ca2+ chelator BAPTA-AM and a molecular approach. Our study has demonstrated that BAPTA-AM significantly reduces ischemia-induced brain damage, suggesting a protective role of BAPTA in ischemia. We introduced an inositol 1, 4, 5-trisphosphate (IP3) binding protein p130PH into astrocytes to selectively disrupt IP3-dependent Ca2+ signaling pathway. Results from an in vitro study demonstrated that expression of p130PH in cultured astrocytes significantly reduced ATP stimulated Ca2+ signals. To introduce p130PH in vivo, we developed recombinant adeno-associated virus (rAAV) vectors, which encode astrocyte-specific promoter ABC1D and p130PH. Viral vectors were injected into the cerebral cortexes of mice to test the gene expression pattern. Immunohistochemistry staining has shown that p130PH was specifically expressed in astrocytes, not in neuron or microglia. Further study will be focusing on determining whether p130PH will have a protective effect on brain damage and neuronal death after photothrombosis induced cerebral ischemia.