

REGULATION OF CALCIUM SIGNALING BY p130PH IN ASTROCYTES

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ABSTRACT

Ca²⁺ signaling is a characteristic form of astrocyte excitability, 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. Our goal 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 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 showed that p130PH was specifically expressed in astrocytes. 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.