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ROLE OF CALCIUM BINDING PROTEINS IN THE EARLY DEVELOPMENT OF THE ZEBRAFISH CNS

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Ionic Calcium (Ca^{+2}) plays an important role in controlling many physiological processes, such as muscle contractions, nerve signaling, membrane permeability, cell division and hormone release. It is well known that in nerve cells, the excess intracellular concentration of Ca^{+2} causes cell death. In recent years, many studies have reported that certain intracellular calcium binding proteins (CaBPs) act as calcium buffers, endogenous neuroprotectants to prevent neuronal death from excess Ca^{+2} influx, plays role in neuronal Ca^{2+} signaling and Ca^{+2} homeostasis, prevent or delay Ca^{+2} related excitotoxicity and are involved in neurotransmission. Besides, they are excellent markers for the neuroanatomical studies to identify unknown neuronal populations and pathways in CNS. We have investigated the role of calb2a and calb2b genes that are expressed in the CNS and multiple other tissues during early embryonic development of zebrafish. We have adopted individual and combined morpholino mediated inactivation approach to investigate the functions of calb2a and calb2b. Morpholino inactivation of *calb2a/calb2b* alone failed to generate an obvious phenotype. Morphological inspection of *calb2a/calb2b* combined knockdown morphants showed abnormal neural plate folding in midbrain-hindbrain region. The loss of mRNA leads to severe hydrocephalus, axial curvature defect, and yolk sac edema. Knockdown of *calb2a/calb2b* showed an impaired touchdown and swimming performance. Co-injection of the *calb2a/calb2b* morpholino oligonucleotide cocktail with human mRNA leads to the rescue of the strong morphant phenotype. This study provided the first comprehensive analyses of the zebrafish Calb2a and Calb2b proteins that are highly conserved and are originated from the same ancestral gene in evolution. Homology modeling and docking with the similar structure and Ca^{2+} binding sites for both proteins provide the evidence that they may have similar function and one can compensate for the loss of other. It confirms the unique and essential functions of *calb2a /calb2b* genes in the early development of the zebrafish.

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