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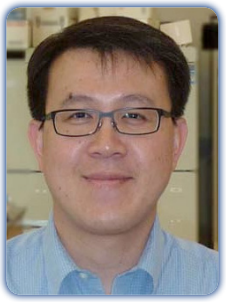

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PKCε-ATF2 signaling in ischemia-induced neurodegeneration

Cardiac arrest continues to be the leading cause of death worldwide. Global cerebral ischemia that accompanies cardiac arrest is one of the major causes of morbidity and mortality. Out of many therapeutic approaches investigated, one of them is ischemic preconditioning, which is sufficient to protect brain tissues from subsequent lethal ischemic insult. PKCε peptide activator administered before, but not after, ischemia mediates preconditioning and confers neuro protection. However, the use of preconditioning as a therapeutic approach has not become standard clinical practice because the occurrence of cardiac arrest and cerebral ischemia is sudden and unpredictable. Thus, post-ischemic therapeutic targets have to be unraveled. The beneficial effects of PKCε peptide activators in ischemic preconditioning stimulate interests in understanding the molecular and cellular actions of PKCε after global cerebral ischemia. A detailed understanding of PKCε signaling pathways requires identification of its downstream targets. This study is to determine the downstream mediators of PKCε, so that novel therapeutic targets can be developed. We found that PKCε mediated the phosphorylation of Activating Transcription Factor 2 (ATF2) at threonine 52 in the hippocampus. ATF2 is a member of the Activator Protein 1 (AP1) transcription factor superfamily regulating normal growth and development as well as response to cellular stress. In response to global cerebral ischemia, PKCε expression was gradually decreased. This resulted in leakage of nuclear ATF2 to the mitochondria and subsequent ischemia-induced neurodegeneration. This study not only provides the first insight into the neuronal cell death regulated by PKCε and ATF2, but also establishes a strong base to develop new classes of therapeutic molecules to inhibit the leakage of ATF2 and reduce brain injury after cardiac arrest.

Biography

Wen-Hai Chou has completed his PhD from Department of Molecular Medicine, University of Texas Health Science Center, San Antonio and Post-Doctoral studies from University of California, San Francisco. He is an Assistant Investigator of National Health Research Institutes, Taiwan. He has published more than 22 papers in reputed journals including *Neuron, Journal of Clinical Investigation, Journal of Neuroscience* and *Journal of Biological Chemistry*.

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