PLENARY SPEAKER

Roles of Phosphoinositide-Specific Phospholipase C Isozymes

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ABSTRACT
Phosphoinositide-specific phospholipase C (PLC) hydrolyzes phosphatidylinositol-4, 5-bisphosphate (PIP2) to generate s econd messengers, inositsol-1,4, 5-triphosphate(IP3) and diacylglycerol (DAG), in ligand-mediated signal transduction. DAG activates protein kinase C (PKC) of IP3 binding to its receptor triggers the release of calcium ions from intracellular stores. The roles of phosphoinositide-specific phospholipase C (PLC) have been extensively investigated in diverse cell li nes and pathological conditions. Up to date, 13 mammal PLC isozymes have been identified and are divided into six su btypes: PLCb(1-4), g(1-2), d(1,3,4), e, x, and h(1-2).
PLC isozymes commonly have highly conserved X and Y domains which is responsible for PIP2 hydrolysis. Each PLCs con tain diverse regulatory domains including the C2 domain, the EF-hand motif, and the pleckstrin homology (PH) domain. Notably, each PLC subtype has a unique domain and PLC isozymes are differentially expressed in different tissues. Thes e unique domains and different expression patterns contribute to the specific regulatory mechanisms and functional di versity of PLC isozymes.
PLC is being extensively investigated on PLCb-mediated GPCR and receptor tyrosine kinase signaling in brain, and their important functions have been discovered. Neurotrophin factors activate PLC g1 through Trk receptors, a family of three receptor kinases that have been implicated in the regulation of cell survival, proliferation, the fate of neural precursors, axon and dendrite growth and patterning, and membrane channels. Correlatively, PLC g1 has been implicated in brain diseases, such as Parkinson's disease, epilepsy, limbic epileptogenesis, and bipolar disorder. However, the in vivo role of PLC g1 has not been clearly demonstrated. We used conditional gene targeting in mice to eliminate the PLC g1 in forebrain. Forebrain-PLC g1 knockout mice display hyper-locomotor activity. In addition, these mice show autism-like behaviors including reduced social interaction and decreased social communication. They also exhibit impaired context-dependent spatial memory. Deletion of PLC g1 results in impaired LTP dependently on TrK B receptor activation. In mEPSC and mIPSCs recording, PLC g1 deletion has no effect on excitatory synaptic transmission. However, mIPSC frequency, but now amplitude, is substantially decreased. These results suggest that the imbalance between excitation and inhibition in PLC g1 deleted hippocampus contributes to autism-like behaviors. These results demonstrate a critical role for PLCg1 in neuropsychiatric functions and suggest a new candidate gene related to psychiatric diseases.

BIOGRAPHY
Pann-Ghill Suh, DVM&Ph.D., obtained PhD majoring in biochemistry, after receiving DVM degree in 1980 at Seoul Nati onal University. He started his career as a professor at Pohang University of Science & Technology (POSTECH) in Pohan g, Korea. After moving to Ulsan National University of Science and Technology (UNIST), Ulsan in 2010, he served as a d ean and vice president of research affairs.
Dr. Suh purified and gene-cloned phosphoinositide-specific phospholipase C isozymes(PLCs) for the first time and has s ystemically studied signal transduction to understand the entity and basic principles of PLC-mediated communication. He has established a new paradigm in communication formed by molecular and cellular networks in signal transductio n. It is noted that the balance of cellular signaling pathway is important and defects in balance of signaling cause variou s diseases . From these research achievements, he has published many prestigious papers and won Asan Medical Prize and appointed as the National Scholar in 2007.
In addition, he has been working as a research administrator to establish infrastructure for university research and national R & D policy in Korea, with being in charge of president of Industry-Academy Cooperation Committee and chairman of the National Science and Technology Council.