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### Molecular mechanism and intervention studies of regenerative mossy fiber sprouting in hippocampus following developmental seizures

Developmental seizure-induced brain damage can cause serious neurological sequelae. Denervation and regenerative mossy fiber (MF) sprouting in the hippocampal dentate gyrus and CA3 subfields are the main neuroanatomical bases. We used several developmental epilepsy animal models to study the mechanism of seizure-induced mossy fiber sprouting and intervention strategy. We found that recurrent prolonged developmental seizures induced by penicillin or inhalant flurothyl can cause long-term cognitive deficit and hippocampal regenerative sprouting in adulthood, which is in parallel with long-term significantly up- or down-regulated expression of zinc transporters (ZnT1, ZnT3, ZIP6), plasma membrane damage associated-lipid metabolism molecules (PRGs, Cyp46a1, cPLA2, ACAT1, nSMase, Kcnj11, Lepr, Drd2, Mc4r, Apo1, Oprk1, Pdk4, ApoE) and autophagy markers (beclin-1, LC3, p62, cathepsin E) in the hippocampus. Moreover, there were significantly correlation among autophagic, Zn transporter signaling and lipid metabolism molecules. Ketogenic diet, plasma membrane oxidant injury protectant melatonin, lipid metabolism regulating molecule leptin, autophagy inhibitors (3-MA, CBI, E-64d), as well as early physical exercise were able to restore the abnormal expressions to normalize and alleviate the aberrant hippocampal MF sprouting, neurobehavioral and cognitive changes, which may be achieved through cPLA2/drp1/autophagy pathway, and by regulating the expression of Zinc/CaMK II signaling. Our study will be helpful for exploring the target genes of axonal regeneration following developing seizures from a new point of view and will contribute the efforts for making proper early intervention, as well.

#### Biography

Ni Hong works in the Children's Hospital of Soochow University (China) as Pediatric Neurologist with main interest in Pediatric Neurological Rehabilitation, Cerebral Palsy and Epilepsy since 1995. He is a Professor and the Lead of the Department of Brain Science, Institute of Pediatric Clinical Research, Soochow University. He has published more than 60 journal articles mainly within Developmental Neuroscience. He is now a Member of the Chinese Society of Microcirculation Council.

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#### Notes: