Cox2 Inhibition Ameliorates Seizure Susceptibility in a Mouse Model of Autosomal Dominant Lateral Temporal Epilepsy

Lin Zhou, Liang Zhou, Li-Da Su, Sheng-Long Cao, Ya-Jun Xie, Ying Shen

**Abstract:**

Autosomal dominant lateral temporal epilepsy (ADLTE) is an inherited epilepsy syndrome caused by mutations in Lgi1 gene. It has been shown that glutamatergic transmission is altered in Lgi1-knockout mice and increased seizures can be reduced by restoring Lgi1 function. However, the underlying mechanism for ADLTE epilepsy is unclear. Here, we examined intrinsic excitability of pyramidal neurons in the temporal lobe cortex. We found that Kv1 channels were downregulated while cyclooxygenase 2 (Cox2) was elevated in Lgi1-knockout mice. Cox2 inhibition effectively restored dysregulated voltage-gated potassium channels (Kv1) and reduced intrinsic excitability of pyramidal neurons. Interestingly, in vivo injection with celecoxib, a Food and Drug Administration-approved therapeutic, rescued defective Kv1.2, ameliorated increased neuronal excitability and seizure susceptibility in Lgi1-knockout mice. Together, we propose that Cox2 is a therapeutic target to suppress epileptogenesis in ADLTE patients.

**Key words:** ADLTE; Cox2; epilepsy; potassium channel; celecoxib

**个人简介（请附上照片）：**

沈颖，浙江大学教授，博士生导师。教育部新世纪优秀人才。自然出版集团子刊Scientific Reports、Cerebellum和Neurochemistry International杂志的审稿编辑。在神经信息传递的三个重要层次，即突触传递和可塑性、转运体功能和调节机制、髓鞘发育和轴突传递，开展了系统研究，发现了影响神经信息传递、整合和功能的多个重要分子和机制。作为通讯作者和第一作者在Nature Neuroscience, Neuron, PNAS, J Neurosci, Glia等国际顶尖杂志上发表研究论文。近年来发表通讯作者论文18篇，包括J Neurosci和PNAS。多次获国家自然科学基金，科技部973和重大科学研究计划，教育部新世纪人才，省基金人才和重点项目资助。主要研究方向：1）神经突触传递和可塑性的细胞分子机制及疾病；2）神经髓鞘发育及脱髓鞘疾病的机制。

联系方式：浙江省杭州市浙江大学紫金港校区医学院科研B楼515房间

电话：0571-88208240

近期代表性论文（限2篇）：

1. Zhou L, Yang D, Wang DJ, Xie YJ, Zhou JH, Zhou L, Huang H, Han S, Shao CY, Li HS, Zhu JJ, Qiu MS, De Zeeuw CI\*, **Shen Y**\*. Numb deficiency in cerebellar Purkinje cells impairs synaptic expression of metabotropic glutamate receptor and motor coordination. ***Proc Natl Acad Sci USA 2015***; 112(50):15474-15479.
2. Wang YN, Zhou L, Wang Z, Li YC, Zhang YW, Wang Y, Liu G, Li YH, **Shen Y**\*. Protein interacting with C-kinase 1 deficiency impairs glutathione synthesis and increases oxidative stress via reduction of surface excitatory amino acid carrier 1. ***J Neurosci*** 2015; 35(16):6429-6443.