Poster | Neural Excitability, Synapse and Glia

[2P]Receptors and Transporters

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*Videos are available throughout the meeting period.

[2P-032]Ca^{2+} imaging in epileptic brain

*Leona Shigemitsu[1], Makoto Kashima[1], Akira Muto[2,3], Koichi Kawakami[3], Hiromi Hirata[1] (1.Dept Sci and Eng, Aoyama gakuin Univ, Kanagawa, Japan, 2.Sci of Med, Toho Univ, Tokyo, Japan, 3.National Inst. of Genetics, Mishima, Japan)

Epilepsy, a chronic brain disorder, is pathologically characterized by sudden spasm and/or loss of consciousness and is caused by hyperexcitability of the CNS. The excess neurological excitability can be induced by the efflux of chloride ion from the cell. One of the causes of brain seizure is upregulation of chloride ion reversal potential induced by the loss of KCC2, which is known as a potassium-chloride cotransporter, resulting in excess activation of neural networks. Zebrafish have two paralogs of KCC2 genes (KCC2a and KCC2b) that were generated by an ancestral gene duplication and are expressed by the CNS. Here, we found that KCC2a-KCC2b double mutant zebrafish (DKO) exhibits the seizure-like phenotype when exposed to flash light. However, how this epileptic behavior is triggered by external optical stimuli remains unclear.
We thus aimed to characterize the location of focal area of the epileptic brain in larval zebrafish. First, we established a locomotive assay to induce epilepsy following exposure to red flash light. Second, we generated DKO larvae (5 dpf) that express GCaMP6s in the CNS to visualize neural activity in epileptic brain. Finally, we performed in vivo calcium imaging and demonstrated excess neural excitation in the telencephalon, optic tectum, cerebellum and hindbrain but not in the olfactory bulb and habenular nucleus. Our analysis suggests that inhibitory transduction under high chloride reverse potentials generates excess neural activity, which is different from a simple enhancement of neuronal excitability induced by PTZ. In addition, bath application of bumetanide, which is an inhibitor of chloride-importing transporter NKCC1, ameliorated seizure-like behavior of DKO larvae. Taken together, we established a new pathologically-relevant zebrafish seizure model that would be useful for screening antiepileptic drugs.