

神経細胞生物学セミナー

「 Structure and mechanism of TRPC channels 」

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場所 東京大学医学系研究科教育研究棟2階 第2セミナー室

講演要旨

In the mammalian brain the majority of fast excitatory transmissions are mediated by the ionotropic glutamate receptors (iGluRs), which are sub-classified into the AMPA, kainate and NMDA types. The iGluRs are ligand gated ion channels activated by neurotransmitter glutamate. Importantly, glutamate is also a ligand for the metabotropic glutamate receptors (mGluRs), which are G protein coupled receptors in the synapse. Activation of mGluRs recruits G proteins and triggers a cascade of events that results in gating of the canonical transient receptor potential (TRPC) channels, although not exclusively but among various other downstream targets. Regulation of membrane potential by the TRPC channels occurs over tens of seconds. Because of the slower and persistent kinetics, the TRPC channels is suggested to play a significant role in setting the neuronal sensitivity to fire action potentials in response to co-activation of the iGluRs that transmit information in milliseconds time scale. Consistent with this idea, in mice, mutations in the TRPC channels cause neurological symptoms, learning deficits, and anxiety dysfunction. In other parts of the body, the TRPC channels regulate vascular and kidney functions; for example mutations in TRPC6 causes focal segmental glomerular sclerosis in humans. Despite their physiological importance the molecular mechanism of TRPC gating and functional modulation remain elusive due to lack of structural information. Recently we obtained cryoEM structures of the TRPC ion channels in collaboration with Julio Cordero-Morales and the results will be discussed in this talk.

多数の皆様のご来聴をお待ちしております。

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