Molecular Mechanism of KCNQ Channels For Reward Behavior

Daisuke Tsuboi[1], Takeshi Otsuka[2], Takushi Shimomura[3], Yoshihiro Kubo[3], Yasuo Kawaguchi[2], Kozo Kaibuchi[1]

[1]Dept. of Cell Pharmacology, Grad. Sch. of Midicine, Nagoya University, [2]Division of Cerebral Circuitry, National Institute of Physiological sciences, [3]Division of Biophysics and Neurobilogy, National Institute of Physiological Sciences

Dopamine plays a key role in the modulation of the circuit activity in striatum for reward behavior. We have reported that dopamine type 1 receptor (D1R) signaling in the striatum presumably regulates neuronal excitability and reward-related behaviors through PKA/Rap1/MAPK pathway. However, how D1Rs and its downstream signaling regulate neuronal excitability and behavior remain largely unknown. We focus on the post-modification of ion channels for neuronal excitability and reward behavior because protein phosphorylation of ion channels is vital for neuronal function. In this study, we identified a voltage-gated potassium channel, KCNQ2, as a phospho-candidate that is regulated by D1R signaling. Phosphorylation of KCNQ2 by MAPK cascade altered the open probability of KCNQ2/3 channels in Xenopus oocyte. The expression of phospho-defective mutants of KCNQ2 suppressed the functional modulation of KCNQ channel by MAPK. D1R agonist, SKF38393 caused a decrease in KCNQ-sensitive current in striatal slices, whereas D2R agonist, Quinpirole did not cause the effect. These results suggest that D1Rsignaling controls the channel activity of KCNQ via its phosphorylation for neuronal excitability and reward behavior.