Signaling pathway in extracellular calcium sensing of frog parathyroid cells

Yukio Okada[1], Toshihiro Miyazaki[2], Hitoshi Hotokezaka[3], Rie Fujiyama[1] and Kazuo Toda[1]
[1]Integrative Sensory Physiology, [2]Cell Biology and [3]Orthodontics & Biomedical Engineering, Graduate School of Biomedical Sciences, Nagasaki University, Japan.

Elevation of extracellular Ca^{2+} concentration induces intracellular Ca^{2+} signaling in parathyroid cells. The response is due to stimulation of the phospholipase C/Ca^{2+} pathways, but the direct factor for rise of intracellular Ca^{2+} concentration is unknown. Here, we report the electrophysiological property associated with intracellular Ca^{2+} signaling in frog parathyroid cells and show that Ca^{2+}-activated Cl^- channels are activated by intracellular Ca^{2+} increase through IP_3-independent pathway. High extracellular Ca^{2+} induced an outwardly-rectifying conductance in a dose-dependent manner (EC_{50} ~ 6 mM). The conductance was composed of an instantaneous time-independent component and a slowly activating time-dependent component and displayed deactivating inward tail current. Extracellular Ca^{2+}-induced and Ca^{2+} dialysis-induced currents reversed at the equilibrium potential of Cl^- and were inhibited by niflumic acid. All blockers for phospholipase C, diacylglycerol (DAG) lipase, monoacylglycerol (MAG) lipase and lipoxygenase inhibited extracellular Ca^{2+}-induced current. IP_3 dialysis failed to induce conductance increase, but 2-arachidonoylglycerol (2-AG), arachidonic acid and 12(S)-HPETE dialysis increased the conductance identical to extracellular Ca^{2+}-induced conductance. These results indicate high extracellular Ca^{2+} raises intracellular Ca^{2+} concentration through DAG lipase/lipoxygenase pathway.