Identification, Characteristics, Regulation, and Pharmacology of T-Lymphocyte Plasma Membrane Constitutive-Active Calcium Channel

V. P. Zinchenko and A. I. Sergeev

*Institute of Cell Biophysics, Russian Academy of Science, Pushchino, Moscow oblast, 142290 Russia;
e-mail: vpz@mail.ru*

DOI: 10.1134/S1990747809030519

Compensated influx and efflux of Ca^{2+} ions provide the maintenance of constant Ca^{2+} ion concentration in cytoplasm of quiescent cells in variable external conditions. Pumping of calcium from cells is carried out mainly by plasma membrane Ca^{2+} -ATPase (PMCA). As far as at physiological levels of cytosolic calcium PMCA is constitutively active, there is also constantly active Ca^{2+} channel. It is known that activity of PMCA as an enzyme, unlike other Ca^{2+} -transporting systems, has characteristic strong dependence on temperature [1]. It is known also that concentration of cytosolic Ca^{2+} in resting cells is maintained constant in a wide range of temperatures [2]. To keep the $[\text{Ca}^{2+}]_i$ constant, the activity of compensating, constitutively active Ca^{2+} channel should depend on temperature similarly. There are several types of Ca^{2+} -channels having different properties, regulation mechanisms and pharmacology in plasma membrane. Using fluorescent Ca^{2+} -sensitive probes, it is shown in the present work that Ca^{2+} influx in T-lymphocytes in resting conditions occurs through special constitutively active Ca^{2+} channel, permeable for Ni^{2+} and Mn^{2+} . The channel differs from the receptor-activated SOC-channels, from Ca^{2+} -channels activated by arachidonic acid or calmidazolium. The strong dependence of the constitutive-active channel activity on temperature coincided with the PMCA dependence, indicating that intracellular enzymes regulate the chan-

nel activity. Ca^{2+} influx rate in quiescent cells increases with a rise in temperature ($Q_{10} = 1.9$). To identify the constitutive-active channel we analyzed the effects of L-type Ca^{2+} -channels, SOC-channels, Ca^{2+} -independent phospholipase A2 and calmodulin inhibitors. Of all inhibitors listed only dihydropyridine blocker of L-type potential-dependent Ca^{2+} channels, isradipin, completely suppressed the calcium influx rate at a concentration of 1.5 μM . However, the channel did not exhibit sensitivity to membrane potential changes. As a result of the research, a new nonselective Ca^{2+} channel in T-lymphocyte plasma membrane is identified and characterized pharmacologically. The data obtained are important for understanding the regulation mechanisms of the plasma membrane Ca^{2+} channels in non-excitable cells.

The work was supported by the Russian Foundation for Basic Research (project no. 07-04-00704).

REFERENCES

1. Zinchenko, V.P., Nikiforov, E.L., and Kaimachnikov, N.P., *Receptors and Intracellular Signaling*, ONTIPNC RAN, Pushchino, 2003, pp. 65–68.
2. Efremova, A.S. and Zinchenko, V.P., *Biochemistry (Moscow), Suppl. Series A, Membr. Cell Biol.*, 2008, vol. 2, no. 4, pp. 372–379.